II. Croonian Lecture.—*The Developmental History of the Primates.*

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Contents.

Introduction.

Although the embryologist has long ago given up the hope of being able to solve the phylogeny of any group of animals by his own labours alone, it is nevertheless just as true to-day as it was in the times he was buoyed up by that hope, that the data of Embryology, properly interpreted can and do furnish striking and demonstrative evidences of genetic relationships. That thesis constitutes the main theme of my discourse, and in the course of it I hope to show you how, starting from the relatively simple and generalised developmental conditions met with in the Lemuroidea, the much more specialized and secondarily modified relations found in the higher Primates may be supposed to have arisen as the result of continued adaptive modification,

involving more especially acceleration and abbreviation in the developmental processes. The germ of the higher mammal, developing as it does in the uterus of the mother, has its old ancestral tendencies modified as the result of adaptation to its maternal environment and before it can proceed in earnest to carry out its primary function of forming an embryo, its most pressing necessity, since it has little or no food-reserves stored up in itself, is to make the earliest possible provision for its own nutrition. Consequently we find in the different Orders of Mammals the most varied structural adaptations designed to this end and affecting particularly the fœtal membranes and their relations to the uterus. But no Order, I venture to think, can compare with the Primates in the wealth of material it provides for the study of such developmental adaptations.

The story I have to tell is an intensely interesting one, both in its special and its general bearings and that I am able to outline it, however imperfectly, is due to the generous co-operation and help I have received from numerous colleagues and fellow-workers both in this country and abroad. My co-workers at University College, Dr. C. J. Hill, Miss F. E. Ince, Dr. G. S. Sansom and Dr. J. Florian have given me throughout, loyal and unstinted help. To Dr. Florian I am under very special obligations, for he placed not only his unique collection of early human embryos but his wide knowledge of early human development freely and unreservedly at my disposal. To other colleagues I am greatly indebted for the opportunity of studying at first hand Primate material in their possession. Professor Dr. H. Bluntschli, of Frankfurt a/M., sent me for investigation the very valuable collection of developmental stages of Platyrrhine Monkeys which he had made in S. America in 1912 (Bluntschli, '13), and I desire to express to him my grateful thanks and my appreciation of the generous and kindly feelings which prompted his action. The following colleagues have also aided me with material and to each of them I offer my thanks: Professor W. E. Le Gros Clark, Dr. W. H. L. Duckworth, Professor R. Anthony, Professor Pol Gerard, R. H. Burne, Esq., Professor J. L. Shellshear, Professor J. T. Wilson and Dr. S. Zuckerman. To Dr. Dan. de Lange, Director of the Hubrecht Laboratory, I am greatly indebted for the loan of sections, much help and many kindnesses during my visits to Utrecht.

I take this opportunity of expressing my grateful thanks to the Government Grant Committee for grants in aid of my work, to Mr. A. K. Maxwell, Artist to the Department, for the patience, care and skill he has displayed in the preparation and labelling of the illustrations and for much help in other ways, to Mr. F. J. Pittock, for his untiring zeal and skill in the preparation of the photomicrographs on which the great majority of the illustrations are based, and to Mr. H. Barker for his admirable work as technician.

Lastly, I wish to acknowledge my indebtedness to the labours of the long line of distinguished investigators who have laid the foundations of our knowledge of Primate development, and in particular to the work of those two great men, Emil Selenka

and A. A. W. HUBRECHT, who were the real founders of our knowledge of the comparative embryology of the Primates. Let me on this occasion pay homage to them by dedicating to their memories this Croonian Lecture.

The Phylogeny of the Primates.

Just over thirty years ago HUBRECHT published a little book entitled "The Descent of the Primates," being the substance of lectures delivered at Princeton University in 1897, in which he expounded the startling and revolutionary views on the phylogeny of the Primates at which he had arrived as the result of his study of the blastocyst of Tarsius (GEGENBAUR'S 'Festschrift,' 1896), and which, with his characteristic tenacity, he continued to uphold for the rest of his life, to wit, that Tarsius is "not a lemur at all," that its position lies somewhere between an unknown type of insectivore and our modern monkeys and man, that it should be included with the latter in a group to which the ordinal name Primates should be restricted and that the lemurs are in no way related to that group, though at the same time he admitted that they "are in no respect a very specialised order of mammals."

In the following year HAECKEL (1898), at the Cambridge meeting of the International Congress of Zoology, delivered a striking address entitled "On our Present Knowledge of the Descent of Man," in which he maintained that the Primates form a natural monophyletic group, all descended from a common ancestral stock, which he designated the Lemuravida. He recognised five successive stages in the evolution of man, within the limits of the Primate group, viz., the basal stage of Lemures or Prosimiæ, which approach most nearly to the hypothetical Lemuravida, the stage of Simiæ, descended directly or indirectly from a branch of the Lemures, and comprising the Catarrhinæ and Platyrrhinæ, the stage of Catarrhinæ Cercopithecidæ, followed by the stage of Catarrhinæ Anthropoidæ or Apes and the stage of Pithecanthropi leading to man. The significant points in HAECKEL'S phylogenetic scheme which are of interest in the present connection are these: (i) His insistence on the basal position of the Lemurs in the Primate series; (ii) his recognition of the occurrence of a Simian stage succeeding the Lemurine stage and its divergence into Catarrhine and Platyrrhine branches, the latter being regarded as a lower side branch off the main line of descent; (iii) his derivation of man by way of a tail-less anthropoid ape, from an ancestral Catarrhine stock.

It is remarkable that Haeckel in his address completely ignores HUBRECHT'S views with which, presumably, he was acquainted, and although these views have never met with general acceptance, and, indeed, have been vigorously contested, their enunciation reawakened the old controversies originally raised by the publication of DARWIN'S "Descent" and HUXLEY'S "Man's Place in Nature," and gave a new impetus to the study of Primate phylogeny, the repercussions of which are still apparent to-day.

If you ask what is the present-day attitude of the systematist to these and like questions, as reflected in his system of classification, I cannot do better than refer you to that authoritative work on the classification of the Mammalia, "Die Säugethiere," by MAX WEBER ('28), wherein, in the latest edition the author has at last adopted that tripartite mode of subdivision of the order into Lemuroidea, Tarsioidea and Anthropoidea which was first suggested by HANS GADOW* ('98) in 1898 as a compromise between the conflicting views of HAECKEL and HUBRECHT, and subsequently advocated by my colleague, ELLIOT SMITH ('07) in 1907 as the outcome of his extensive studies on the Primate brain, and which I also accepted in 1919, on embryological grounds (HILL, '19).

After a wider review of the development of the Primates than was possible at that time the only modification of that scheme which now seems to me necessary is the subdivision of the Anthropoidea into two groups—a lower or Pithecoid group comprising the Old World and New World monkeys, and a higher, to which I propose, for my purpose to restrict the name Anthropoid, comprising the great apes and man.†

Accordingly, in tracing the evolution of the developmental processes in the Primates, I shall recognize four main developmental stages, viz., a basal or Lemuroid stage, a transitional or Tarsioid stage, an annectant or Pithecoid stage which leads directly on to the terminal Anthropoid stage.

CHAPTER I.

LEMUROID STAGE.

Our knowledge of the earlier stages in the development of the Lemuroidea is confined to the Lorisiformes and rests partly on HUBRECHT'S observations ('07) on a series of early embryos of *Nycticebus tardigradus*, partly on those of Miss F. E. INCE, A. SUBBA RAU and myself on the development of *Loris lydekkeriana*, of which a preliminary account appeared in 1928 ('28). More recently we have been able to study some additional material of which two early blastocyst stages are specially important since they represent what may be termed critical stages in the history of the blastocyst which have not hitherto been examined. We are accordingly now in a position to outline the development of the Lemur with a fair degree of completeness.

Such an outline will show us that the Lemurs in the totality of their development exhibit a remarkable combination of what we may, for convenience, speak of as primitive

* GADOW used the names Lemures (HUBRECHT), Tarsii, and Simiæ (v.d. HOEVEN) for his three sub-orders.

† R. I. POCOCK ('18) in his proposed classification of the Primates subdivides the Order into two groups, the Strepsirhini (including the Lemuriformes and the Lorisiformes) and the Haplorhini, with two sub-orders, Tarsioidea and Pithecoidea, the latter including "the Platyrhini (American monkeys) and the Catarhini (Old-World Monkeys, Apes and Man)." Throughout this lecture, I shall use the terms Pithecoid and Anthropoid in the sense indicated above.

Monodelphian features, *i.e.*, features which are characteristic of the development of lower Monodelphia with certain others which we may term progressive or advanced, since they may be interpreted as foreshadowing conditions characteristic of the development of the higher Primates. So far as the earlier stages of development are concerned, we would here emphasize our conviction that in no essential respect are they to be regarded as specialized in comparison with those of lower Monodelphia. On the contrary, the Lemur in its early development, exhibits precisely those features we should expect to find in a basal ancestral group such as we hold the Lemuroidea to be.

What we regard as essentially primitive Monodelphian features are seen in the structure of the ovum, in the development and constitution of the blastocyst, in its central type of development and its rapid growth in size, in the early exposure of the embryonal ectoderm, in the formation and extension of the mesoderm, in the mode of formation of the amnion by the closure of amniotic folds and in the outgrowth of the allantois in the form of a free, stalked vesicle which secondarily unites with a localised area of the chorion.

Amongst the features in which the Lemur anticipates the higher Primates, we should emphasize the following: (1) the relatively early extension of the extra-embryonic cœlom throughout the entire extent of the primitive blastocyst-wall or omphalopleure and the consequent early establishment of a complete chorion and a yolk-sac vesicle with an independent wall of its own; (2) the remarkably early vascularisation of the entire chorion as the result of the direct ingrowth into it of the allantoic vessels, following on the union of the allantois with a small localised area of its inner surface.

Before passing to a brief exposition of our knowledge of the early development of the Lemuroids, I wish to call attention to a very interesting feature in the structure of the ovarian oocyte of Loris, first described by NARAYAN RAO ('27), and that is the presence in it of a rich store of deutoplasm in the form of fat-spherules, of variable but mostly large size, such as VAN DER STRICHT ('23) and others have shown to be of common occurrence in the ova of lower Monodelphia (Dog, Cat, Ferret, Pig, Goat, Guineapig, etc.). In the oocyte figured (Pl. 1, fig. 1), the fat-globules occupy a broad sub-peripheral zone encircling a central mass of fat-free cytoplasm in which the nucleus is situated, and leaving on its outer side a narrow peripheral zone, immediately below the zona, almost free from globules. The existence of these fat-globules in Loris and their known absence in the Human ovum led me to investigate the deutoplasmic content of other available Primate ova, with the result that I have been able to demonstrate the presence of fat-globules in the oocyte of Tarsius in a corresponding position to those of Loris, but (so far as one can judge from an oocyte in process of growth, and after a long sojourn in formalin) in less abundance (Pl. 1, fig. 2), a very interesting point of agreement between the Lemuroid and the Tarsioid. On the other hand, fat-globules comparable with those of Loris are apparently not present in the oocytes of the Platyrrhine, *Hapale jacchus*, which I have been able to examine (fig. 3) and are definitely absent from those of the Catarrhine, *Macacus rhesus* (fig. 4),

just as they are absent in the Human ovum, so that it would seem that a reduction in the deutoplasmic content of the egg has taken place in the passage from the lower to the higher Primates. Having established these facts, the question arose, is this reduction in the amount of deutoplasm accompanied by any appreciable diminution in the size of the oocyte in the higher types? Unfortunately the available data are not sufficient, in view of the well-known variation in the size of the ovum in one and the same species, to provide a conclusive answer to this question, but so far as the measurements set forth in the accompanying table go, they tend rather to emphasize a striking and unexpected general agreement in the size of the ovum in the Primate series, though we still stand in need of accurate records of the size of the full-grown Human oocyte.*

COMPARATIVE Sizes of Primate Ovarian Oocytes.

	Diameter, including Zona.	Diameter, without Zona.	Condition of Follicle.
Loris lydekkerianus.			
Loris 38	0·106 × 0·099 mm.	0·103 × 0·096 mm.	0·9 × 0·5 mm. diam. Follicular cavity discontinuous.
Fig. 1, oocyte	0·112 × 0·09 mm.	0·10 × 0·084 mm.	0·39 × 0·3 mm. diam. Solid.
Average of 12 "fully grown" oocytes, Narayan Rao	0·109 × 0·099 mm.	—	
Tarsius spectrum.			
	0·108 × 0·096 mm.	0·102 × 0·092 mm.	Large, almost ripe.
Fig. 2, oocyte (immature)	0·081 × 0·07 mm.	0·073 × 0·064 mm.	0·25 × 0·23 mm. diam. Follicular cavity in form of discontinuous clefts.
Hapale jacchus.			
Fig. 3, oocyte	0·103 × 0·086 mm.	0·094 × 0·077 mm.	0·76 × 0·51 mm. diam., with follicular cavity.
Macacus rhesus.			
Fig. 4, oocyte	0·10 × 0·09 mm.	0·092 × 0·079 mm.	1·0 × 0·7 mm. diam.
Average of five oocytes	0·107 × 0·093 mm.	0·091 × 0·081 mm.	
Human	0·103 × 0·090 mm.	0·090 × 0·077 mm.	5·2 × 4·47 mm. diam.
	0·111 × 0·098 mm.	0·094 × 0·086 mm.	3 × 2·5 mm. diam.

The details of the processes of cleavage and blastocyst-formation are not known, but we have examined two 4-celled eggs of Loris from the Fallopian tube in which the

* For further details in regard to the size of the ovum in the Primates, the recent paper by C. G. HARTMAN, "How large is the Mammalian Egg? A Review" ('Quart. Rev. Biol.,' Vol. iv, No. 3, Sept., 1929) may be consulted. HARTMAN'S measurements of the ovarian oocytes (exclusive of the zona) of *M. rhesus* are as follows: Maximum, 0·108 × 0·10 mm., minimum, 0·105 × 0·09 mm. Average, 0·11 × 0·093 mm., and of one oocyte of the gorilla (exclusive of zona), 0·09 × 0·087 mm.

blastomeres are arranged in two pairs, forming an irregular cross-shaped group (Pl. 1, fig. 5), an arrangement which is typical of this stage in other Monodelphia and which is also apparent in the 4-celled egg of Macacus nemestrinus, described and figured by SELENKA ('03, fig. 1, p. 331).*

The earliest blastocyst-stage recorded is one of Nycticebus 241, described and figured by HUBRECHT ('07, figs. *a* and *b*, p. 36), but his figures fail to do justice to the specimen and I have had it refigured (Pl. 1, figs. 6 and 7). Apart from its developmental condition, the blastocyst is of interest inasmuch as it occurs in the Fallopian tube, showing that here the germ reaches the uterine horn not in the form of a solid morula but as a vesicular blastocyst. It measures $0{\cdot}13 \times 0{\cdot}11$ mm. in diam. and in its structure agrees closely with the corresponding stage in other Monodelphia. A quite thin zona is still present. The trophoblast forms a complete cellular wall to the vesicle, being thinner over the lower hemisphere and thicker over the upper. The covering trophoblast is clearly distinguishable from the underlying inner cell-mass (embryonal knot), which has the form of a flattened mass of circular outline, $0{\cdot}06$ mm. in diam. The endoderm has already segregated from the embryonal ectoderm and is just beginning to spread beyond the periphery of the latter.

Our earliest blastocyst of Loris (45) is just a little older than that of Nycticebus 241. It occurs in the lumen of the uterine horn partially wedged in a bay of the mucosa (Pl. 1, fig. 8) and in its folded condition has an estimated diameter of about $0{\cdot}16$ mm. It is still invested by the thin zona and inside that is a complete but thin layer of trophoblast. The covering trophoblast overlying the embryonal ectoderm is for the most part distinct and clearly marked off from the latter. It shows no obvious signs of degeneration. The subjacent lenticular mass of embryonal ectoderm contains numerous vacuoles, no doubt occupied during life by fat-globules such as are present in the ovarian oocyte. Similar intracellular vacuoles are also present in the blastomeres of the 4-celled egg and in the embryonal ectoderm of Nycticebus 241. The endoderm is now well marked and is in process of spreading over the inner surface of the trophoblast so as to provide a lining to the blastocyst-cavity, but the lower pole is still unilaminar.

A somewhat later stage is provided by the blastocyst of Nycticebus 264, described by HUBRECHT ('07, fig. *c*) and refigured here on Pl. 1, fig. 9. It has a diameter of about $0{\cdot}3$ mm. The endoderm now forms a complete lining to the vesicle, the zona has disappeared and the embryonal ectoderm has assumed the form of a plano-convex ovalish mass, $0{\cdot}08 \times 0{\cdot}05$ mm. in diam., in which the cells seem to be in process of becoming arranged to form a columnar layer. It is probable that the covering trophoblast has not yet completely disappeared, but it is difficult to be certain owing to the obliquity of the sectional plane. HUBRECHT, on the evidence of this stage, asserts that the disappearance of the covering trophoblast is effected not as the result of gradual attenuation as in Lepus and Sorex, but in the same way as in Tupaia, Tarsius

* See also STREETER ('31, fig. 1) for 2- and 4-celled eggs of *Macacus rhesus*.

and Sus, where the embryonal ectoderm in the course of differentiating becomes bent V-like and so brings about the rupture of the covering layer. The point is perhaps of no great importance, but the appearances in this stage and the next rather suggest that it simply becomes stretched and ruptured by the gradual expansion of the embryonal ectoderm.

The next stage of Nycticebus available is the blastocyst of Nycticebus 190, shown in section on Pl. 1, fig. 10, lying free in the uterine lumen. The blastocyst has now increased greatly in size and measures as figured $2 \cdot 16 \times 0 \cdot 68$ mm. in diam., the uterine lumen measuring $2 \cdot 6 \times 1 \cdot 8$ mm. in diam. Its wall is now bilaminar throughout and the shield-ectoderm is established as a circular plate ($0 \cdot 2$ mm. in diam.) composed of columnar cells and definitely intercalated in the trophoblast, the covering layer having completely disappeared (Pl. 1, fig. 11). The endoderm underlying the shield-ectoderm is thickened and slightly folded, especially towards one margin of the latter (fig. 11, *p.pl.*) and between the thickened endoderm and the ectoderm a few cells appear to be present. Possibly we have to do here with the prochordal plate thickening of the endoderm, which has already commenced to proliferate mesoderm.

Following on the preceding stage, we have examined two blastocysts of Loris (5), measuring about 3 mm. in diam. in which important advances have taken place. The blastocyst has now increased so much in size that it practically fills the lumen of the uterine horn (Pl. 1, fig. 12). Its thin bilaminar wall closely follows the folds and irregularities of the surface of the mucosa and though it appears in the sections separated over most of its extent from the uterine epithelium, it can still be found in places in the closest possible attachment to the same and there can be no doubt that during life this relationship existed over the greater part of the wall.

The marked growth in size of the blastocyst seen in this and the preceding stage is to be regarded as a lowly feature and is characteristic of all those Monodelphia which have retained the primitive, so-called central type of development in the uterine lumen. It serves the double purpose of keeping the blastocyst in place and of providing a large yolk-sac cavity for the storage of the nutritive fluid secreted by the uterine glands.

The shield-ectoderm is thicker and more extensive than that of Nycticebus 190 and is irregularly folded (Pl. 2, fig. 13). Beyond its limits, the bilaminar wall of the vesicle consists of an outer layer of cubical trophoblast cells and an inner thin layer of endoderm, and as Pl. 2, fig. 14, shows, it is still in places most intimately attached to the columnar uterine epithelium, whilst in those regions where the two are separated, and excepting the areas differentiated for absorption, the structure of the trophoblast shows that there also attachment occurred during life. This attachment is effected in a remarkable, indeed we think unique, manner. The outer ends of the trophoblast cells are delimited by terminal bars and are provided with a delicate cuticular border (Pl. 2, fig. 15), and not only are they moulded to fit over the surface of the uterine epithelial cells, but the cuticular border is produced into thin flanges, appearing in section as tapering spike-like processes which penetrate for some distance between

the uterine epithelial cells (Pl. 2, fig. 14). Such a peculiar mode of trophoblastic attachment, so far as we are aware, has never been met with in any other mammalian order. Whether or not the presence of this cuticular border is causally related to the non-penetrative character of the trophoblast in the existing Lemuroids we are not prepared to say, but there can be little doubt that this intimate attachment of the trophoblast to the uterine epithelium has rendered necessary the development of special structural arrangements to facilitate the absorption of the secretion of the uterine glands. These comprise (*a*) the differentiation of localised patches of the trophoblast specially concerned with absorption and forming the so-called chorionic vesicles and "absorptive areas" and (*b*) the establishment of common openings to groups of the uterine glands, so that their secretion is poured out in the immediate proximity of the absorptive structures. As testimony to the pressing need for means of rapidly absorbing the uterine gland secretion, it is noteworthy that already in this 3 mm. blastocyst, the chorionic vesicles are well advanced in development, appearing as easily recognisable thickened areas of the trophoblast, saucer- or bowl-shaped in form and situated opposite the common openings of groups of uterine glands (Pl. 2, fig. 16). The trophoblast of these areas is greatly thickened and markedly vacuolated and is evidently already actively functioning in taking up the secretion of the highly active uterine glands. In addition to these developing chorionic vesicles, a large "absorption area," over which the trophoblast is correspondingly modified, is already established over the lower pole of the blastocyst in relation to the mucosa covering the cornual septum (Pl. 1, fig. 12, *a.a.*).

It is an interesting fact that the chorionic vesicles of the Lemurs find their closest parallel in the so-called areolæ of the allanto-chorion of the Pig, where also the uterine glands are actively secretory and the trophoblast of the allanto-chorion lies in intimate apposition with the uterine epithelium. There can be little doubt, I think, that we are dealing here with homoplastic formations.

These absorptive organs of the Lemurs are practically the only specialisations which are observable in their early ontogeny. In all other respects, and in particular in the disappearance of the covering trophoblast and the consequent exposure of the embryonal ectoderm at the surface of the blastocyst, the Lemurs conform to what I regard as the primitive Monodelphian type of development and here it would not be out of place to lay emphasis on another very primitive feature which they exhibit in common with the Monotremes, Marsupials, Ungulates and others, and that is the persistence of the uterine glands in an actively functional condition during the entire period of gestation.

Following on the 3 mm. blastocyst of Loris, the HUBRECHT collection contains two blastocysts of Nycticebus numbered 55 and 209, which are of interest since they are the earliest known in which the primitive streak is definitely established.

Blastocyst 55 is stated in Dr. DE LANGE'S invaluable Catalogue ('21) to have a diameter of $\pm$ 5 mm. The series is a poor one, but suffices to show that a very short

primitive streak (about 0·2 mm. in length) is present in the caudal portion of the embryonal area which has a length of about 0·5 mm. A short head-process seems also to be present, as well as a prochordal plate with scattered mesodermal cells in relation to it. The primitive streak mesoderm does not extend laterally beyond the limits of the embryonal area.

Blastocyst 209 (possibly earlier than 55 according to HUBRECHT) is also damaged, but fortunately the embryonal area is fairly intact and in good condition histologically. The sections are slightly oblique to its long axis (see HUBRECHT's fig. *d*, '07, p. 37). Judging from the size of the uterine lumen which the blastocyst no doubt filled, we may estimate the diameter of the latter as about 4·5 mm. The embryonal area (about 0·7 mm. in length) possesses a distinct Hensen's knot with a slight blastoporic depression on its surface, a very short head-process and a primitive streak which extends back from the knot to the posterior margin of the shield-ectoderm, its length being about 0·23 mm., measured from the blastoporic depression. At the hinder end of the streak, the mesoderm extends back below the trophoblast for only a very short distance, but laterally to the streak it fails to reach the margins of the shield-ectoderm, indeed proliferation of mesoderm does not yet seem to be very active. A short distance in front of the head-process, the endoderm is thickened to form what HUBRECHT recognises as the " protochordale Platte (in erster Anlage)."

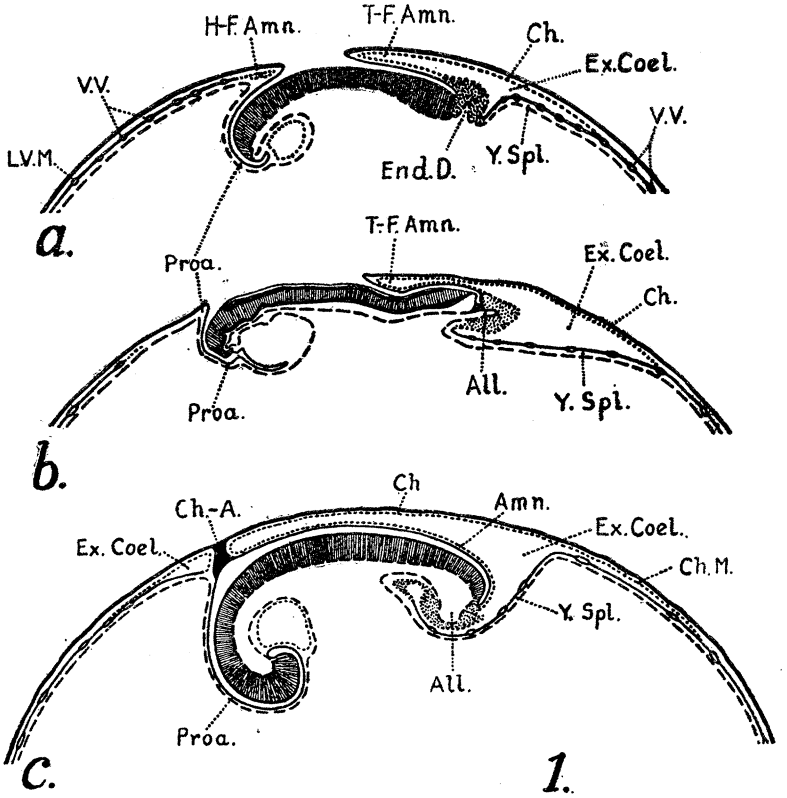
HUBRECHT ('07, p. 38) states that in blastocysts 55 and 192, and to a less marked extent in blastocyst 209, there is evidence of the formation of extra-embryonal mesoderm directly from the endoderm and concludes on the basis of his observations that there is present in Nycticebus as in Sorex and Tarsius a peripheral zone where blood-vessels and blood originate from cells proliferated from the endoderm. I have examined all the blastocysts mentioned in regard to this point and must confess I have failed to find any evidence of vasifactive activity on the part of the endoderm. As a matter of fact, in a presomite embryo of Loris 49 in which the embryonal area measures 1·92 × 1·25 mm. and the primitive streak about 0·76 mm. and in which the head-process has already given origin in its caudal half, to a chorda plate, blood-islands are only just appearing in the trilaminar extra-embryonal region of the blastocyst-wall, adjoining the embryonal area.

Passing to the later stages of development, the mode of formation of the fœtal membranes calls for brief consideration and here I shall draw on our own published and unpublished observations (HILL, INCE and SUBBA RAU, '28). The three graphic reconstructions by Miss INCE, shown in text-fig. 1, *a*, *b*, *c*) and depicting the arrangement of the membranes in Loris embryos of G.L. 2·49 mm., 2·86 mm. and 2·9 mm., respectively, demonstrate that up to the 2·9 mm. stage, the development of the membranes proceeds along very much the same lines as in Monodelphia such as Lepus or Felis.

The amnion is formed by the closure of head- and tail-folds and by the splitting of the proamnion. This we regard as the old ancestral method, though HUBRECHT and

other authorities have maintained that the "closed" method, as seen for example in Cavia, Tatusia, Pteropus and the higher Primates, is for Mammals the primitive method. That view we are quite unable to accept for reasons we have set forth in detail elsewhere (HILL and TRIBE, '24) and which need not be repeated here.

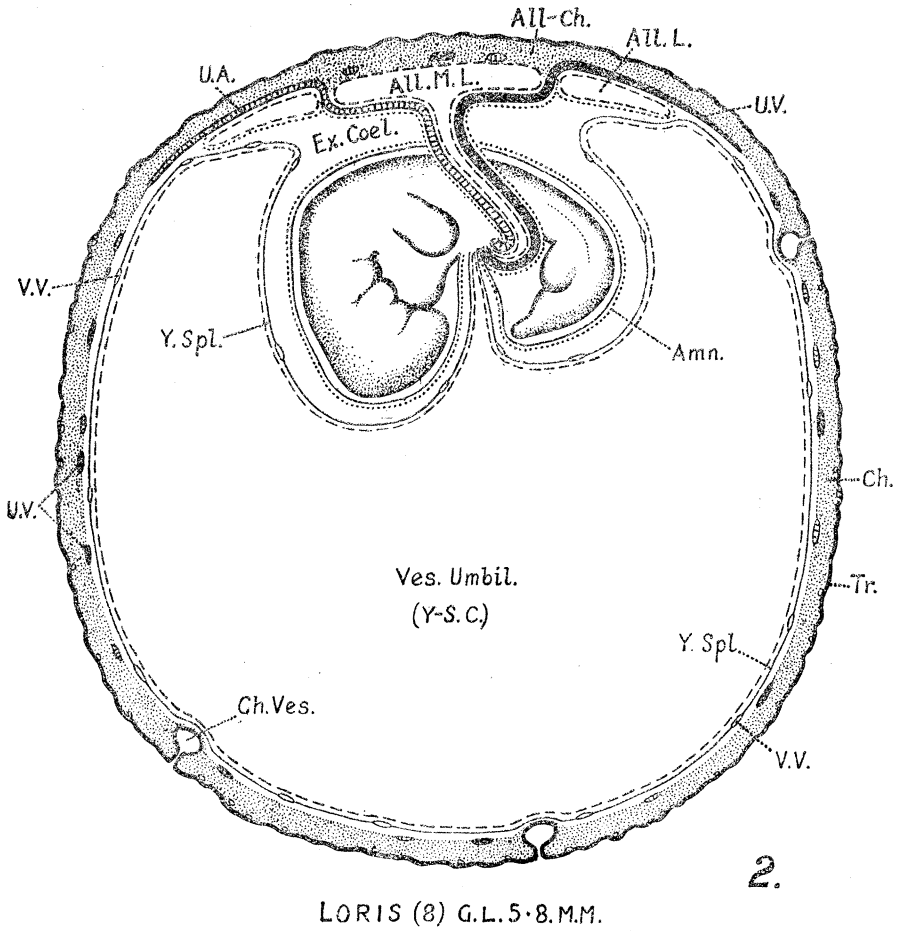
The trunk portion of the amnion is formed by the gradual closing in and final union of the amniotic head- and tail-folds. In correspondence with the fact that the extra-embryonal cœlom appears first round the hinder end of the embryo and gradually



TEXT-FIG. 1.—Graphic reconstructions of three embryos and their fœtal membranes, of Loris lydekkerianus (*a.* and *c.* after HILL, INCE and SUBBA RAU, *b.* from a reconstruction by Miss F. E. INCE). *a.* Loris (9B), G.L. 2·49 mm. *b.* Loris (33), G.L. 2·86 mm. *c.* Loris (9A), G.L. 2·9 mm. *all.* Allantoic diverticulum. *amn.* Amnion. *ch.* Chorion. *ch-A.* Chorio-amniotic connection. *Ch.M.* Chorionic mesoderm. *End.D.* Endodermal diverticulum. *Ex.Coel.* Exocœlom. *H.F.Amn.* Head-fold of amnion. *L.V.M.* Limit of vascular mesoderm of the trilaminar omphalopleure. *Proa.* Proamnion. *T-F.Amn.* Tail-fold of amnion. *V.V.* Vitelline vessels. *Y.Spl.* Yolk-sac splanchnopleure.

extends cranialwards, the tail-fold appears first and has grown forwards for some distance over the back of the embryo, before the head-fold is differentiated. The latter grows but little caudalwards, closure taking place on a level with the 6th pair of somites so that the tail-fold forms the greater part of the trunk-amnion. The cephalic part of the amnion develops later and in continuity with the latter by the gradual splitting of the extensive proamnion.

The yolk-sac also arises in normal fashion by the gradual extension of the mesoderm throughout the entire extent of the vesicle-wall or omphalopleure and its subsequent splitting into somatic and splanchnic layers as the result of the extension of the extra-embryonal cœlom. The omphalopleure thus undergoes separation into an inner layer or yolk-sac wall carrying the vitelline vessels and an outer layer, the chorion, in continuity with the amniogenetic chorion over the embryo (Pl. 2, fig. 17). It is, we



TEXT-FIG. 2.—Diagram to show the structure and relations of the fœtal membranes in Loris (8), G.L. 5·8 mm. (after HILL, INCE and SUBBA RAU). *All-Ch.* Allanto-chorion. *All.L.* Accessory lobe of allantois. *All.M.L.* Main lobe (primary sac) of allantois. *Amn.* Amnion. *Ch.* Chorion. *Ch.ves.* Chorionic vesicle. *Ex. Coel.* Exocœlom. *Tr.* Trophoblast. *U.A.* Umbilical artery. *U.V.* Umbilical vein. *Ves.Umbil.* (*Y-S.C.*) Yolk-sac. *V.V.* Vitelline vessel. *Y.Spl.* Yolk-sac splanchnopleure.

think, a most significant fact that by the time the embryo has reached a length of 5·8 mm., this separation has been completely effected with the result that we now have established a relatively large yolk-sac with a complete wall of its own and a continuous outer chorionic membrane bounding the embryonal formation and what is even more remarkable than its early separation is the fact that this membrane is already vascularised throughout its entire extent by allantoic vessels (Pl. 2, fig. 17, *u.vl.* cf. also text-fig. 2,

u.v.). Prior to the extension of the cœlom, the vitelline vessels ramify in the unsplit mesoderm of the omphalopleure and, as the latter is in intimate attachment with the uterine epithelium, there exists temporarily in the earlier embryonic stages, a simple yolk-sac or omphalopleural placenta such as we find in varying degrees of complexity in many of the lower mammals prior to the establishment of the definitive allantoic placenta.

The relatively early differentiation of a complete chorion in the Lemur, we regard as a feature of the greatest significance, for it is just the precocious formation of this membrane which is one of the distinctive characters of the blastocyst of Tarsius and the higher Primates.

Equal in importance to the chorion as an index of genetic affinity is the allantois, the history of which in the Lemur is of quite exceptional interest.

In our Loris embryo (33) with 18 pairs of somites, the primordium of the allantois (text-fig. 1*b*, *all.*) appears as a small somewhat conical mass projecting freely backwards into the extra-embryonal cœlom, from the hinder end of the embryo. It consists of a mass of already vascularised mesoderm continuous with the caudal knot of the primitive streak, and internally of a very short endodermal diverticulum, forming the direct backward prolongation of the hind-gut, the limit between the two being marked on the dorsal side by the cloacal membrane.*

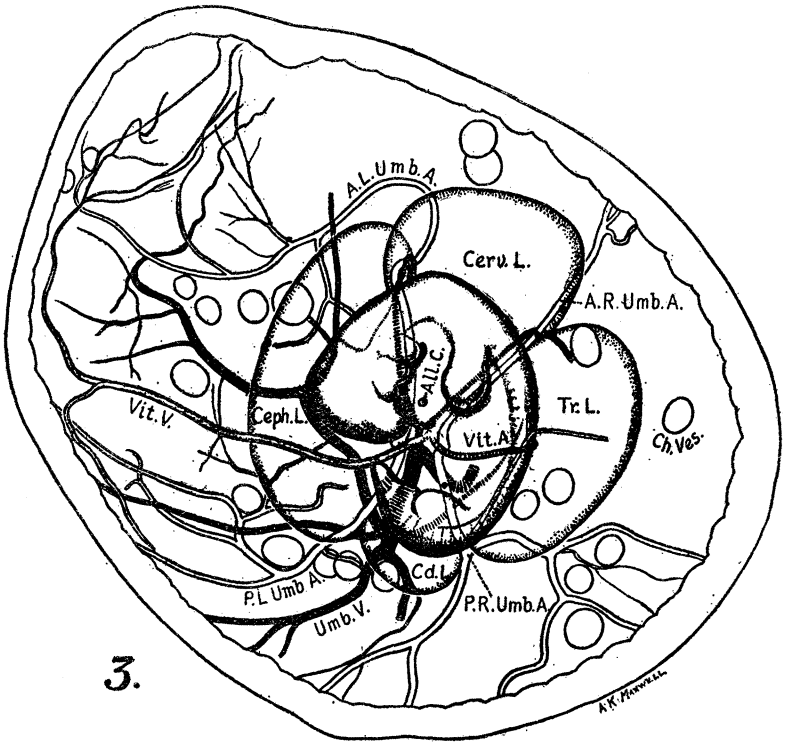
In the immediately succeeding embryo (9A with 22 pairs of somites (text-fig. 1*c*, and Pl. 2, fig. 18), the allantois has made noteworthy progress and now appears as a small stalked vesicle depending into the cœlom from the ventral wall of the hind-gut. Its mesodermal wall is very thick and richly vascularized, the umbilical circulation being already established. In its relations, it differs in no essential respect from the allantois of an embryo of Felis of the corresponding stage of development.

If we pass now to our next embryonic stage (Loris 8) with about 39 pairs of mesodermal somites and thus much in advance of the preceding embryo, we find that the allantois, as we have described elsewhere ('28), exhibit certain very remarkable features, which we regard as of the greatest significance. It has not only increased greatly in size and at the same time become quite thin walled, but it has grown out through the extra-embryonal cœlom and its outer wall has fused with the chorion over the back of the embryo to form a discoidal area of allanto-chorion. Moreover, it has now assumed the lobulate form which is so distinctive of the Lemuroid allantois. It consists of a main lobe or primary sac, evidently representing the much enlarged allantoic vesicle of the preceding stage, into which the allantoic canal of the stalk opens and of four

* In our 15 somite embryo (Loris, 9B) we ('28) originally interpreted the transversely expanded mass of mesoderm forming the hind end of the embryo and the endodermal diverticulum which extends vertically into it as together representing the allantoic primordium (text-fig. 1*a*, *End. D.*). Our subsequent examination of Loris (33) has, however, thrown doubt on that interpretation and it now seems more probable that the endodermal diverticulum represents the hind-gut, but this question can only be decided when further material becomes available for study.

sub-equal accessory lobes, representing secondary outgrowths from the primary sac (Pl. 2, fig. 19, and text-figs. 2 and 3).

When we proceeded to work out the distribution of the allantoic (umbilical) vessels, certain remarkable facts came to light. We found that the four branches of the umbilical arteries (three of them accompanied by corresponding veins) which radiate outwards from the attachment of the allantoic stalk, on the inner (cœlomic) wall of the primary sac, did not extend on to the accessory lobes at all, but on reaching the



TEXT-FIG. 3.—Embryo of Loris (8). G.L. 5·8 mm. *in situ*, viewed from the left side to show the distribution of the extra-embryonal vitelline and umbilical vessels and the relations of the latter to the accessory lobes of the allantois. The embryo is seen through the yolk-sac splanchnopleure and the amnion (after HILL, INCE and SUBBA RAU). *All.C.* Position of opening of allantoic canal into the primary allantoic sac. *Ch.Ves.* Chorionic vesicle. *Ceph.L.*, *Cerv.L.*, *Tr.L.*, *Cd.L.* "Cephalic," "cervical," "trunk" and "caudal" lobes of allantois. *A.R.Umb.A.*, *P.R.Umb.A.* Anterior and posterior branches of right umbilical artery. *A.L.Umb.A.*, *P.L.Umb.A.* Anterior and posterior branches of left umbilical artery. *Umb.V.* Umbilical vein. *Vit.A.*, *Vit.V.* Vitelline artery and vein.

periphery of the primary sac, passed directly into the chorionic mesenchyme at the angles formed by the junctions of the accessory lobes with it (text-fig. 3). Having gained direct access to the chorion in this way, the vessels proceeded to branch and to vascularize not simply the small area of allanto-chorion but the whole extent of the chorionic membrane.

These relations led us to conclude (1) that the main branches of the umbilical vessels must pass directly into the chorionic mesenchyme very soon after the primary sac has

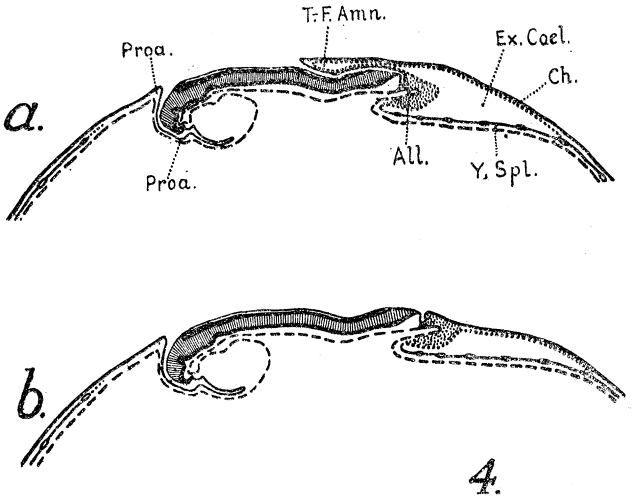
fused with the chorion; (2) that in so doing they produce at the margin of the primary sac a number of fixed points between which the accessory lobes grow out as non-vascular and purely secondary structures, whose sole use apparently is to increase the cubic capacity of the allantoic sac (HILL and BURNE, '22); (3) that in the Lemur, as exemplified by Loris, the vascularization of the chorion does not depend on the slow spreading of the allantois over its inner surface as is the case for example in the Carnivores and Ungulates amongst the lower Monodelphia, but is effected precociously by the direct ingrowth of the umbilical vessels as soon as the necessary pathway has been provided by the union with it of the primary allantoic sac.

Having established these facts for Loris, we took the earliest opportunity of examining the Lemuroid material in the HUBRECHT collection and there we found the serial sections of the very fine embryo of Nycticebus 302, study of which has served to show that in this genus also, the chorion is directly vascularized by the primary allantoic sac. This embryo 302 (No. 6 of HUBRECHT'S Normentafeln ('07), fig. 5, Pl. IV) is distinctly earlier than our embryo of Loris 8 and has been sectioned along with the related fœtal membranes. It measures in G.L. 4·8 mm. and is stated to possess 39 pairs of somites (*v.*, p. 40). The amnion is closed and the proamnion is still extensive. According to HUBRECHT'S description, the allantois has lost its earlier thick-walled character and has become transformed into a membranous sac (with a maximum diameter of 7 mm.) whose outer wall spreads out against [is actually fused with] the diplotrophoblast [chorion].

The general relations of the fœtal membranes are shown in Pl. 3, figs. 20 and 21, fig. 20 depicting a section at the level of the yolk-stalk and the opening of the gut into the yolk-sac cavity, and fig. 21, a section at the level of the opening of the allantoic canal into the primary sac. The lower hemisphere of the embryonal formation is lacking in the serial sections, but all round the allanto-chorionic area the chorion is already established, being separated from the yolk-sac wall by the extra-embryonal cœlom which here appears more extensive than in our Loris (8) and moreover it is already well vascularized. Study of the sections further shows that the allantois is not really the simple sac suggested by HUBRECHT'S description, but possesses the same lobulated character as that of Loris (8). As in the latter, it consists of a primary sac, with a diameter of about 5 mm., into which the allantoic canal opens (Pl. 3, fig. 21, *o.all.c.*) and of four sub-equal accessory lobes (two smaller more caudally situated lobes, evidently comparable with the trunk and caudal lobes of Loris (8) and two situated more cranially, one of which is long and narrow, comparable with the cephalic and cervical lobes of the same embryo. As in Loris (8), the umbilical arteries and veins run in the mesenchyme of the inner wall of the primary allantoic sac and at its margins, in the bays between the accessory lobes, they enter and leave the mesenchyme of the chorion (Pl. 3, fig. 21, *l.umb.a.* and *umb.v.*, on left), which is in this way directly vascularized.

The demonstration of the occurrence of this direct and precocious mode of vascular-

ization of the chorion in the Lemur constitutes, we venture to think, the most important result of our incursion into the field of Lemurine embryology and as regards its phylogenetic significance, we have pointed out that in our view, " it represents the first and most significant step towards the evolution of that characteristic structure, so long regarded as distinctive of the higher Primates, the connecting or body stalk (pédicule ventral, Haftstiel, Bauchstiel) which in Tarsius and the Anthropoidea directly connects the embryo with the chorion and serves as the pathway for the umbilical vessels to and from that membrane " (HILL, INCE and SUBBA RAU, '28, p. 714). The definitive connecting stalk is now generally recognized as the reduced and precociously developed representative of the allantois of other mammals but, as we have already had occasion to observe (*loc. cit.*), " up till now we have had no precise knowledge of the first stages in its evolutionary history." To convert the Lemurine condition into that characteristic of Tarsius involves no profound alteration in the developmental processes. All



TEXT-FIG. 4.—*a*. Graphic reconstruction of the embryo and fœtal membranes of Loris (33), *b*. in text-fig. 1. *b*. Diagram to show what would happen if the allantoic primordium (*All.* in *a*.) came to be established prior to the formation of the amniotic tail-fold (*T-F.Amn.* in *a*.).

that is necessary is a speeding up or acceleration during the earlier stages of development whereby the allantoic primordium such as is seen in our Loris embryo (33) is laid down at an earlier period prior to the establishment of the amniotic tail-fold round the hinder end of the embryo (text-fig. 4, *a* and *b*). The result of this would be that its mesoderm (of direct primitive streak origin) would lie from the first in contact with the trophoblast of the future chorion, immediately behind the embryo and so would provide a connecting stalk serving as the most direct route for the passage of the umbilical vessels from the embryo to the chorionic membrane and available as soon as vasculogenesis in the embryo is sufficiently advanced, and indeed for vasculogenesis in the connecting stalk and chorion independent of that of the embryo as is known to be the case in Tarsius and the higher Primates, so that the chorion or at least its placental area (as in Tarsius) can be vascularized at the earliest possible moment.

We claim then that the Lemur, in respect of the relatively early differentiation of a complete chorion and in the mode of vascularization of that membrane, foreshadows in the most remarkable way, features which are distinctive of the development of Tarsius and the higher Primates.

Placentation.

The placentation of the Lemurs is now comparatively well known (see HILL and BURNE, '22). It has been described in more or less detail in representatives of all the existing families and sub-families of the two sub-divisions of the group, the Madagascar Lemuriformes and the Asiatic and African Lorisiformes and, though it shows differences in detail in the two groups and from genus to genus, it exhibits in all a most striking uniformity in the essentials of its structure, being diffuse, non-deciduate and epitheliochorial in type. In these respects it presents a most marked contrast to the placenta of all other Primates which is a localized massive placenta, discoidal or bidiscoidal, deciduate and hæmochorial, whilst it shows an extraordinarily close general resemblance to the placenta of such an Ungulate as the Pig. The Lemuroid placenta is constituted simply by the interlocking of vascular chorionic processes or villi, with corresponding depressions or crypts of the vascular uterine lining or maternal decidua (Pl. 3, fig. 22). The villi, which may be simple (Pl. 3, fig. 23) or branched, are clothed by a single layer of cellular trophoblast which comes into close apposition with the uterine epithelium and is locked with the same by the cuticular processes previously referred to, but there is never any organic continuity between the two, and at parturition the villi are simply withdrawn from their crypts, there being no loss of maternal tissue, *i.e.* the placenta is non-deciduate. The uterine lining, apart from an increase in its vascularity, is hardly altered during pregnancy. The uterine epithelium and the uterine glands persist throughout gestation in an active condition, the glands producing a rich secretion which is apparently of prime importance for the nutrition of the fœtus since special structures, the chorionic vesicles (fig. 23, *ch. ves.*) and chorionic " absorptive areas " have been differentiated to facilitate its absorption. Here, then, we see in the Lemuroids, a placenta not far removed from its lowest term and the question arises are we dealing with an essentially primitive type of placenta, a direct inheritance from the non-deciduate ancestors of the Primate stock, as TURNER ('77) seemed inclined to believe and as JENKINSON ('16), HILL ('19), and HILL AND BURNE ('22) have advocated, or are we to regard it as having been derived in the course of evolution from a complex form of deciduate placenta as the result of a sudden mutation or developmental arrest or other happening ? In other words, are we to regard it, along with others of the same non-deciduate type, as a secondarily simplified placenta as maintained by HUBRECHT ('10), ASSHETON ('10), FLYNN ('23) and more recently by WISLOCKI ('29) ? These authorities have nothing in the way of direct evidence to put forward and they make no attempt to explain why the Lemurs, once having attained to the possession of a deciduate placenta, should have been at pains to get rid of it. There is no conclusive evidence so far as I am aware

that the Lemurs have suffered a reduction of corresponding magnitude in any other part of their organisation, and since no correlative support is furnished from that side, the advocates of the simplification view base their belief on theoretical considerations concerning the phylogeny of the placenta in Mammals generally. It would be out of place to attempt a detailed discussion of that very disputed problem here, but something must be said if only in a quite summary fashion.

It did not fit in with HUBRECHT'S theoretical views on the evolution of the trophoblast that the Lemurs should possess an amnion formed by folds, a vesicular allantois and a diffuse, non-deciduate placenta and he regarded all three as secondary. He frankly admitted that he was unable to indicate how " this simplification of a placenta of the Insectivorous or Primate type down to that of the present Lemurs was brought about " ('10, p. 115). ASSHETON ('10), however, did make an attempt to show how the Lemur placenta might have been derived from such a deciduate placenta as is found in the Carnivora, but most unsuccessfully as we think (HILL and BURNE, '22).

In his paper on the placentation of the Primates, WISLOCKI ('29) discusses the question of the phylogeny of the placenta in Mammals generally and that of the Primates in particular at considerable length, but without, we think, adding materially to its solution. Whilst he admits that the hypothesis of the secondary derivation of the Lemuroid placenta " is in no way established " (p. 74), he considers that " the observed facts accord more with such a view than with the opposite one," the acceptance of which lands us, he says, in " almost unsurmountable difficulties " (p. 74). One of these difficulties, for the author, is that the Lemurs appear to be completely isolated " among groups in which the penetration of the trophoblast to form a labyrinthine placenta is the cardinal feature " (p. 79), and a second is that " we have to accept the rodents, insectivores, Galeopithecus, Tupaja, Tarsius and the Simiæ as separate and individual products from a stem which possessed a diffuse type of placentation " (p. 74). His general conclusions are that the placenta hæmochorialis represents the most primitive type (p. 77) and that " the recent diffuse placentals, as well as their fossil prototypes . . . appear to be, if the present hypothesis be true, quite independently derived from mammals which possessed penetrating trophoblast " (p. 79).

WISLOCKI derives a considerable part of his support for these conclusions from the consideration of the genetic relationships of the Mammals as set forth in a phylogenetic scheme, devised by W. K. GREGORY ('10) nearly twenty years ago. In this scheme, the insectivores, the bats in common with Galeopithecus and the Tupaioids, are represented as the successive lateral branches of a common stem which terminates by giving off first the Lemurs, then Tarsius, and finally the three divisions of the Simiæ. In effect, this part of WISLOCKI'S argument may be summarized as follows: because Tarsius and the Tupaioids possess a deciduate type of placenta and the Lemurs branched off from the common stem between them, therefore the Lemurs must also at one time have possessed the same kind of placenta and consequently their present simple type can only have arisen from the more complex form as the result of secondary reduction.

But, unfortunately, even admitting that the forms mentioned above are all derived from a common stock, the palæontologists are not able to tell us precisely how and when they separated from that stock. We do not know whether they branched off in succession at longer or shorter intervals from the common stem or whether they represent, as we prefer to think, so many more or less independent lines of radiation from an ancestral stock.

The former alternative which WISLOCKI accepts, necessitates the belief in the secondary nature of the Lemuroid placenta and the recognition of transitions between the varieties of hæmochorial placenta met with in the various orders, regarded as related to the common stem. Thus he writes (p. 72), " moreover, a series can be selected with the rodents and insectivores on one end, the bats, *Galeopithecus*, *Tupaja*, Tarsius, the platyrrhine monkeys and the lower catarrhine monkeys in the middle, in the order named, and the anthropoids and man at the extreme opposite end which will show a gradual but complete transition in morphology of the placenta fœtalis." In our opinion, such a series, interesting as it may be from the structural and functional aspects, is of no phyletic significance whatever, since it groups together placental formations which, while conforming to the hæmochorial type, differ to an extraordinary degree in the details of their development. For that reason, we prefer to regard them as homoplastic rather than homogeneous structures.

In further support of his thesis, WISLOCKI goes on to make the following statement : " If we examine his chart (text-fig. 1) [phyletic scheme of GREGORY] we find that the Mammals which possess a diffuse and hence, generally considered, primitive type of placentation are with the exception of Manis not archaic, and not close to the main stems, but are by far the most divergent and specialised forms in the group. This applies to the Lemuridæ, Cetacea, Artiodactyla, Perissodactyla, Proboscidea and Sirenia " (p. 76). Surely so far as the Lemuridæ are concerned, a remarkable statement, since it is hardly necessary to point out that the assertions that they are not close to the main Primate stem and are " by far the most divergent and specialized forms in the group " are in direct contradiction not only to prevalent opinion but also to the well-known views of GREGORY himself on the phylogeny of the Primates (GREGORY, '20*a*, '27*b*) ; whilst as to their not being archaic, that depends of course on what we connote by " archaic," but " true Lemuroids are certainly represented by Pelycodus " in the lower Eocene (MATTHEW, '27), and some lower jaw fragments, possibly referable to the Notharctinæ, have been described from the Basal Eocene (Paleocene) of Rheims (*cf.* ABEL, '28, p. 742), so that the possibility that Lemurine remains may eventually be found in the Cretaceous is by no means excluded.*

But, even admitting that the existing Lemuroidea are specialized in certain respects as compared with the ancestral Lemurine stock, we cannot agree to the implication that adaptive specializations in bodily organization, *e.g.*, in the teeth and limbs are necessarily accompanied by correlative alterations in the developmental processes.

Nor, we may remark here, are we prepared to accept the conclusions on placental

* *Cf.* also J. W. GIDLEY : " Paleocene Primates of the Fort Union," ' Proc. U.S. Nat. Mus.,' Vol. 63, 1923.

phylogeny which FLYNN ('23) has advanced on the basis of his study of the development of the allantoic placenta of Perameles and which WISLOCKI is inclined to regard as supporting the hypothesis " that the heaping up of the trophoblast to invade the uterine wall is a primitive condition which existed before the present-day diffuse placentæ arose " (p. 78). In spite of the views I expressed in my paper of 1897 (HILL, '97) and of the positively expressed opinion of FLYNN ('23) that " the *absolute agreement* even to minute details, of allantoplacental preparation and formation in Perameles with the phenomena occurring in Monodelphia show *with the utmost certainty* that the placenta in Perameles is no independently acquired organ " (italics mine), I am no longer prepared to regard the allantoic placenta of Perameles in that light. I now accept the conclusion of HUBRECHT ('08, pp. 116–8), which has been fully substantiated by FLYNN ('23) and by our own unpublished observations, that the syncytial layer of the allantoic placenta of Perameles is not purely maternal as I erroneously concluded in my original paper ('97), but is of composite origin and really formed by the fusion of the allanto-chorionic trophoblast with the maternal syncytial layer which results from the proliferation of the uterine epithelium and the concomitant ingrowth of maternal capillaries. In respect of its possession of a composite syncytial layer of this peculiar character, the allantoic placenta of Perameles is in my opinion unique, and for this and other reasons I have come to the conclusion that the view I originally adopted can no longer be maintained and that the allantoic placenta of Perameles is to be regarded as a structure, *sui generis*, which like the Marsupium has been evolved within the limits of the Order Marsupialia and perhaps even of the Family Peramelidæ. I am now of opinion that it has been independently derived from a primitive ancestral form of allantochorionic-omphalopleural placenta of the diffuse or apposed type, which also give origin to the relatively simple allantochorionic-omphalopleural, and the purely omphalopleural placentas of other Marsupials as well as to the various types of placenta characteristic of the Monodelphia. I would still maintain that the Didelphia are derived from a " protoplacental stock " (WILSON and HILL, '97), but only in the foregoing sense and accordingly I am unable to accept the hypothesis that the trophoblast exhibited invasive properties " before the present-day diffuse placentæ arose " (WISLOCKI, *loc. cit.*, p. 78).

In examining the trophoblast of our early Loris embryos we have met with a condition which might be seized upon by advocates of the simplification-hypothesis as supporting their view, but of which a quite other explanation is possible, and that is the occurrence here and there at the free surface of the trophoblast of light staining cells, ovalish to irregular in form. They occur singly or two or three may lie in proximity. The ovalish cells are often seen to be superimposed each on a basally situated cell of roughly corresponding size (Pl. 2, fig. 24), and their nuclei frequently exhibit an early phase of mitosis (fig. 25). Careful study of these cells shows that the division is rarely if ever completed and that they eventually assume an irregular form and undergo degeneration, all stages of which are to be met with in our preparations (figs. 26 and 27).

It might be held that these cells are the last remnants of former proliferative activity on the part of the trophoblast, but the fact that they appear to be produced by the division of a parent trophoblast cell tangentially to the surface, instead of radially thereto, as is normal, suggests that they are to be regarded simply as the products of accidental deviations from the normal mitotic plane.

Apart from these cells, we have not observed in the development of the placenta of Loris any structural feature which in the slightest degree suggests its derivation from a more complicated type.

Turning to the opposite view that the Lemuroid placenta is essentially primitive, what evidence, apart from theoretical considerations, can we adduce in its support ?

Earlier in this lecture (*ante*, p. 60) we have expressed our conviction that certain events in the development of the Lemur, viz., the relatively early establishment of the chorion and its precocious and direct vascularization by way of the allantois as soon as that had fused with a localised area of its inner surface, were of the greatest phyletic significance, since they paved the way for the still more precocious differentiation of the chorion and the connecting stalk which is such a characteristic feature in the development of Tarsius and the higher Primates. If, as we maintain, the chorion and the allantois of the Lemur are the direct progenitors of the chorion and the connecting stalk in the other Primates, then it is difficult to avoid the conclusion that the Lemuroid placenta (the essential fœtal constituent of which is the chorion) is likewise the progenitor of that of the higher forms. We see no escape from that conclusion, and if, in addition, we can outline with some approach to probability, how the more complex deciduate placenta came to replace the simpler non-deciduate type, then the case for the primitive character of the latter would be difficult to assail.

It does unquestionably seem an enormous step from the simple placenta of the Lemur (Pl. 3, fig. 22) to the massive deciduate organ of Tarsius (Pl. 3, fig. 28) and the other Primates in which the maternal blood actually circulates through lacunar spaces hollowed out in the fœtal trophoblast, but, large as that step appears, it is to my mind an incomparably easier process to visualize from the developmental point of view than it is to imagine the Lemuroid placenta arising secondarily from the more highly differentiated, presumably Primate, type by some process of reduction or developmental arrest. In either case, during the transition period, the embryo must have been in possession of a functionally active placenta, and that necessity must be borne in mind in any hypothetical explanation of how the substitution of the one type of placenta for the other was effected. Moreover, we must assume, I think, that the process of substitution did not take place suddenly, but was accomplished only quite gradually in the course of many generations.

Now, the first step towards the evolution of the deciduate type of placenta was taken when, in the primitive Lemuroid or Tarsioid, the blastocyst effected a direct attachment to the uterine mucosa, through the proliferative activity of its trophoblast. What induced that activity on the part of the trophoblast, or what factor or combination of

factors rendered attachment necessary, it is impossible to say. It may have been due to a retardation in the growth-rate of the blastocyst, resulting in a temporary diminution of its size, to the earlier disappearance of the enclosing zona, or to some alteration in the secretory activity, or in the amount of folding of the uterine lining, to mention only a few of the possibilities. However induced, it may have served in the first instance simply to keep the blastocyst in place in the uterine lumen, and only later came to be utilized for placental purposes. And that the mammalian blastocyst can effect a temporary fixation in order to maintain itself in position is borne out by the case of the blastocyst of the Rodent, *Spermophilus citillus*, described by REJSEK ('04) and also by VÖLKER ('08), in which the trophoblast at the lower pole of the quite young blastocyst gives off a syncytial projection which penetrates through the uterine epithelium and spreading out below it, serves as an efficient temporary hold-fast until the definitive placental attachment is effected, when it disappears.

On the other hand, it is possible to conceive of the attachment having been first effected by the trophoblast over the primary allanto-chorionic area at a much later stage of development, in an attempt to increase placental efficiency, and that in the course of phylogeny the proliferative activity of the allanto-chorionic trophoblast was, so to speak, telescoped forwards into earlier and earlier stages until it finally manifested itself in the blastocyst. (See addendum, p. 178.)

However that may be, judging from the development of Tarsius, it is legitimate to suppose that fixation was effected through the activity of the trophoblast of a localized area of the blastocyst-wall and was not merely appositional as in existing Lemurs, but involved actual penetration, and eventual destruction of the uterine epithelium. Once that condition was established, it is easy to picture how the trophoblast might be stimulated by direct contact with the vascular sub-epithelial tissue and so came to penetrate more and more deeply into the latter. From this condition and postulating a configuration of the fœtal membranes essentially similar to that of the existing Lemurs, I find no great difficulty in visualizing the gradual evolution of the hæmochorial type of placenta. The opening up of the maternal capillaries and the establishment of a lacunar circulation in the in-growing trophoblast would be the first step and the penetration of prolongations of the chorionic mesenchyme, carrying the fœtal umbilical vessels, into the vascularized mass of trophoblast so formed, would constitute the second. And all this could happen without serious interference with the functional activity of the old diffuse placenta, but as the new organ gradually became perfected in course of time, more and more of the umbilical blood-stream would be directed into it and so it finally came to supersede the old.

That, then, is our idea of how the substitution of the more complex type of placenta for the simpler ancestral type may have been accomplished. We must leave it to the advocates of the simplification-hypothesis to find another explanation of the facts established by us, and to indicate more precisely from what variety of hæmochorial placenta they consider the process of simplification to have started. By most authorities

the Lemurs are regarded as members of the Order Primates, and one would naturally suppose that their simplified placenta was derived from such a deciduate type as is found in the more primitive members of the Order, but in that event we should have to imagine the connecting stalk retracing its steps and re-acquiring its ancestral free vesicular condition, in defiance of any such Law as that of the Irreversibility of Evolution (DOLLO).

Finally, let us see how the view we are advocating fits into the general scheme of placental phylogenesis as we envisage it.

So long ago as 1876, TURNER ('77), it is interesting to note, when discussing the affinities of the Lemuroidea, in view of their possession of a diffuse non-deciduate placenta, wrote as follows : " It seems to me, therefore, to be more in accordance with a theory of descent that the complex form of placenta should be regarded as having been evolved out of the simple, than that each should have arisen independently, as is assumed by HAECKEL, out of a non-placental sub-class of mammalia " (p. 584). GROSSER ('09) also, when he put forward in 1909 his well-known and widely-used scheme of placental classification into four types, distinguished as epithelio-chorial, syndesmo-chorial, endothelio-chorial and hæmo-chorial, regarded them as forming in a broad way an evolutionary series, the epithelio-chorial representing the simple, ancestral, non-deciduate type, and the hæmo-chorial, the most advanced final phase in placental evolution. A like view of the primitive character of the epithelio-chorial placenta, as exemplified by that of the Lemurs, was advocated by JENKINSON ('16), by HILL ('19), and by HILL and BURNE in their paper on the placentation of Chiromys ('22, pp. 1162–1165). In that paper the authors set forth in summary fashion their conception of placental evolution, which differs somewhat widely from the views held by certain other writers on this subject.

They point out that in their opinion any attempt to trace the phylogeny of the various types of placentation met with in the Mammalia must be based on a consideration of the probable arrangement of the fœtal membranes which obtained at the time when, in the primitive mammals, the viviparous habit replaced the oviparous. The arrangement of the membranes in the existing Monotremes and Marsupials being known, they postulate that the common ancestral stock from which the Didelphia and Monodelphia are assumed to have diverged must have possessed much the same type of arrangement as is common to these mammals, *i.e.*, the outer wall of the embryonal formation consisted, over the lower hemisphere or thereabouts, of omphalopleure, vascularized in part or throughout by the vitelline or yolk-sac vessels, and over the remainder, of allanto-chorion, vascularized by the umbilical vessels of the allantois. The vestigial shell membrane and the zona having already disappeared during the earlier stages of development, the primitive placenta was simply constituted by the close apposition of these two regions with the vascular lining of the uterus, and so was partly allanto-chorionic, partly omphalopleural in nature. Here, then, we have the simplest possible type of appositional placenta, the trophoblast being as yet a single

layer, functional in absorption and gas-exchange, but exhibiting no proliferative or invasive properties.

From this ancestral form of placenta there were derived, it is suggested, on the one hand the placental arrangements characteristic of the Didelphian radiation, and on the other the various types of placenta met with in the Monodelphian orders. Of these latter the non-deciduate, epithelio-chorial placenta, in its simplest condition, exhibits only a slight advance on the primitive type ; the omphalopleural portion of the latter has been replaced by the extension of the allanto-chorionic, the allanto-chorion has increased in surface-extent by folding or by the outgrowth of simple or branched villous processes, and in some cases special areas of the trophoblast have been differentiated for purposes of absorption ; but in its most advanced condition, as seen, *e.g.*, in the horse, it attains a relatively high degree of differentiation, as is the case also in the syndesmo-chorial placenta of the sheep, which is suggestive of a further elaboration of the epithelio-chorial type.

We suggest that the occurrence of this non-deciduate type of placenta in such diversely-related groups as the Lemuroidea, Manidæ, Perissodactyla, Artiodactyla, Cetacea, Proboscidea, and possibly the Sirenia, is not to be explained by any hypothetical process of secondary simplification, but by the persistence of the ancestral type without any very essential modification in these branches of the Monodelphian radiation.

The varieties of endothelio-chorial and hæmo-chorial placentas (contradeciduate and deciduate), which are the outcome of the assumption by the trophoblast of proliferative and invasive properties, are to be regarded as having evolved in the remaining ordinal radiations of the Monodelphia, along so many independent lines of placental differentiation, their precise form and structure resulting from a complex of conditions, partly intrinsic or germinal, partly environmental or uterine.

It would be out of place in this lecture to develop the arguments which could be advanced in support of this view of placental evolution, and we would merely remark that it is in consonance with the occurrence of noteworthy differences in the details of the development of the varieties of placenta classed together as hæmo-chorial, with the presence in the Rodent, Anomalurus, of a hæmo-chorial villous placenta (Branca and Cretin, '25), presenting such an extraordinarily close resemblance to that of the Catarrhina that it might readily be mistaken for such, and with the occurrence of the endothelio-chorial type of placenta in the Carnivora, and elsewhere, so far as known, only in the Bradypodidæ (Wislocki, '27, *cf.* also de Lange, '26, and Becher, '21.).*

* Since writing the above, I find to my great satisfaction that Hubrecht ('97*b*) so long ago as 1897, in protesting against the imputation that he removed Tarsius from the Lemurs solely because of its possession of a discoid type of placenta, expressed himself as follows : " Thus, for instance, I have shown that the placenta of the hedgehog, the shrew and the mole is in each case a structure *sui generis*, all these different insectivores having placentas of the discoid shape, but which reveal themselves, on close and careful examination, both in their structure and in their genesis, as more different *inter se* than is the diffuse placentation of the horse from that of the Lemurs or from the cotyledonary placentation of the ruminants."

As concerns the Didelphia, it will be evident from what has already been said (*ante*, p. 64) that we regard the placental arrangements in the Marsupialia as likewise susceptible of interpretation along the same lines as those of the Monodelphia.

In our opinion, homoplasy (LANKESTER) or parallelism in placental differentiation is a phenomenon which has been insufficiently recognised, largely, we think, because some of the embryologists who have concerned themselves with this problem have failed to keep in view that fundamental evolutionary principle of the truth of which the palæontologists have furnished abundant proofs and which has been enunciated by H. F. OSBORN in the dictum: "the *same* results appear independently in descendants of the *same* ancestors ('08, p. 105).*

In a paper which appeared very shortly after the delivery of this lecture, Professor O. GROSSER ('29), returns to the question of the phylogeny of the placenta and in particular that of the Lemuroidea, in view of the resuscitation by WISLOCKI of HUBRECHT'S opinion that the hæmo-chorial type of placenta represents the ancestral form from which the other types have been secondarily derived.

Whilst still maintaining his view of the primitive character of the epithelio-chorial type so far as the Ungulates (more especially the Pig) are concerned and for essentially the same reasons as those advanced by HILL and BURNE ('22) in favour of the primitive character of the Lemuroid placenta, GROSSER thinks a case may be made out for secondary simplification in the Lemuroidea, "die mit ihren epitheliochorialen Placenten phylogenetisch zwischen Formen mit hämochorialen Placenten (Insectivoren und Primaten) stehen" (p. 298), and he proceeds to offer an explanation of how such a surprising replacement as that of a highly organised hæmo-chorial placenta by a much simpler (epithelio- or syndesmo-chorial) one may have taken place.

His explanation is based on physiological grounds and is unfortunately very brief. He suggests that the assumption of the nocturnal habit and the sluggish mode of life

* In two communications which have appeared since the delivery of this lecture, Dr. DAN. DE LANGE ('30*a*, '30*b*), as the outcome of his studies on the placenta, more especially in representatives of the "Edentata," has been led to enunciate views on placental phylogeny which, I am glad to find, are in essential agreement with those herein advocated. He formulates his main thesis as follows ('03*a*): "Tous les critériums qui sont employés pour classifier les différentes formes du placenta ont en premier lieu une valeur descriptive et, strictement considéré, elles n'ont que peu de valeur morphologique. Des stades terminaux qui se ressemblent assez entre eux peuvent être le résultat d'un développement tout à fait différent. Dans ce cas ils ne sont pas homologues." He goes on to remark, "Je veux dire que toutes le formes diverses du type épithéliochorial comme ceux du type syndesmochorial, endothéliochorial ou hémochorial ne se dérivent pas d'un type central épithéliochorial, syndesmochorial, etc., mais, qu'en maints cas, elles ont pris naissance independamment. La circonstance que deux placenta appartiennent au même type de Grosser n'est pas une preuve qu'ils sont réelement homologues." In his second paper ('03*b*), he points out that "there are at least four types of hæmochorial placenta which have probably arisen quite independently from a more primitive attached, histiotrophic stage," and he considers that the examples he has given "are sufficient to make it probable that each of Grosser's placental types has a polyphyl[e]tic origin."

(such as are characteristic of existing Lemurs) may have resulted in a diminished need for oxygen (on the part presumably of the adult animal). He suggests that, as a consequence, the complex hæmo-chorial labyrinth-type of placenta, whose primary function is to permit of the freest gaseous exchange, was no longer necessary and so became replaced by the simpler placental type, possessing an equal capacity to that of the higher, for the absorption of the essential proteins (" Eiweissbausteine ").

He goes on to point out that this secondary derivation of the epithelio-chorial placenta may not after all prove to be a genuine exception to DOLLO's Law of the Irreversibility of Evolution since we have to do with the latency or the omission (" ein Stehenbleiben ") of a developmental stage otherwise rapidly effected, viz., the stage of attachment (" Anlagerung ") of the blastocyst to the uterine epithelium. Without attempting to discuss the question whether this particular replacement of a complex organ by a simpler, more primitive one does or does not form an exception to DOLLO's Law, I would only point out that the stage of attachment in Loris is not passed over though it is effected quite differently to that in other mammals, indeed, in a manner which is unique. Viewing it from the standpoint of Professor GROSSER, the most remarkable feature of the Lemuroid trophoblast is, it seems to me, the complete loss it has suffered of the active invasive qualities it must have originally possessed. I suggest it is much more likely that it had never acquired them.

If, however, this remarkable substitution of the one type of placenta for the other actually did take place, then I am inclined to agree with Professor GROSSER that the only way in which it could have been effected was by the sudden loss by the trophoblast of its invasive properties. But it is when he proceeds to find an explanation of why this substitution was permissible or necessary, that I am unable to follow him.

He holds that a diminished oxygen-consumption on the part of the mother so definitely reacted upon the oxygen-supply to the developing embryo as to lead to the replacement of the original hæmo-chorial labyrinthine placenta by the simpler epithelio-chorial type. He does not tell us in so many words whether it increases or decreases the supply to the embryo. If it increases the supply, his argument might be put as follows: because the mother, owing to the adoption of an inactive, nocturnal life, has less need for oxygen, there would be more available for the embryo and so in order to secure an economy of growth, the more complicated labyrinthine placenta was replaced by the simpler type. But is there any evidence or probability that under the given conditions, the embryo would tend to receive a richer oxygen-supply? One would expect *a priori* that in two animals with comparable developmental rates and embryos of comparable size, the oxygen-requirements of the embryo would remain fairly constant whether the parent was sluggish or active. Surely under normal circumstances, the combined oxygen-needs of the parent + the embryo would be so regulated through the maternal respiratory mechanism that there would always be an available and sufficient surplus, above the maternal requirements, for the use of the embryo and which would be independent of the habits (whether active or sluggish) of the parent.

If, on the other hand, decreased oxygen-consumption by the parent resulted in a dimnution of the supply available for the embryo, then it would obviously be necessary to show that the epithelio-chorial placenta is more efficient in gaseous exchange than the hæmo-chorial, though this is not only contrary to the view generally held, but is clearly also inconsistent with GROSSER'S attempted explanation.

In either case, we find it difficult to believe that a slight alteration, one way or other, in the oxygen-supply reaching the embryo through the placenta, could of itself induce so profound a morphological change as that suggested. But assuming that it did occur in the evolution of the Lemuroidea, we may still be permitted to ask why the same change did not take place in the Tarsioidea as represented by Tarsius, whose habits of life are to all intents and purposes similar to those of the Lemurs.*

The foregoing review of the early developmental history and the placentation of the Lemuroidea has been directed to sustaining the conclusion that so far as their development is concerned the existing Lemuroids are to be regarded as the remnants of that basal stock from which the higher Primates took their origin. We have attempted to demonstrate that " they have retained in their development many primitive mammalian features, including a primitive form of diffuse non-deciduate placenta," and we hold that " they present us with a developmental ground-plan of such a generalised type as to be easily susceptible of such adaptive modifications as have occurred in the higher types in the course of evolution " (HILL, '19, p. 489). If these conclusions are accepted, it follows that the primitive Lemuroids must have branched off from their hypothetical Insectivore (Menotyphlous) ancestors before the latter had acquired a hæmo-chorial type of placenta and that accordingly, the placentation of the existing Menotyphla must have developed quite independently of that of the higher Primates.

CHAPTER II.

TARSIOID STAGE.

Turning now to that remarkable creature, *Tarsius spectrum*, the sole surviving representative of a race widely distributed over the Northern Hemisphere in Eocene times, but now confined to the East Indian Islands and the Philippines, let us see how the known facts of its development help us in the elucidation of the problem we are considering.

As is well known, our knowledge of the embryology of Tarsius rests on the monumental labours of A. A. W. HUBRECHT. In a series of papers dating from 1896 he

* My friend, Professor GROSSER, has been good enough to read the above criticism and authorizes me to say that he concurs in its validity and that consequently he would no longer maintain the particular explanation he put forward in his paper of how the simple Lemuroid placenta came to replace one of the hæmo-chorial type.

has provided us with richly illustrated accounts of its early development (including cleavage, blastocyst-formation and the early history of the embryo) and of the development of its fœtal membranes and placenta. Most fortunately for the science of Embryology, his priceless collections, through the generosity of the HUBRECHT family and with the active support of the Dutch Government, have found a permanent home in his old residence at Utrecht, now the Hubrecht Laboratory, and are freely available for reference and study. Without the facilities thereby afforded, the present review of the development of Tarsius would have been impossible.

In its development, Tarsius presents an extraordinary combination of lowly or primitive features with others which are clearly advanced or progressive together with yet others which are just as certainly specialized and peculiar to itself.

If we look into the details of the developmental occurrences as a whole, we observe :—

(1) The retention of certain lowly features which we may regard as direct inheritances from the ancestral Lemuroid, viz., the central type of development, the early disappearance of the covering trophoblast and the exposure of the embryonal ectoderm in the form of an embryonal disc and as the outcome of that, the formation of the amnion by the closure of head- and tail-amniotic folds.

(2) The realization of certain developmental tendencies already forshadowed in the Lemuroids, *e.g.*, the still more precocious differentiation of the extra-embryonal mesoderm, cœlom, chorion and yolk-sac and the replacement of the vesicular allantois by the precociously formed connecting stalk, all of them features in which Tarsius anticipates the Pithecoids.

(3) Certain definite advances on the Lemuroid condition, in particular the acquisition by the early blastocyst of a direct attachment to the uterine lining and the resulting formation of a massive discoidal placenta of the deciduate hæmo-chorial type, features in which Tarsius again appears to anticipate the Pithecoid.

It accordingly appears at first sight as if HUBRECHT had considerable justification for his contention that Tarsius is developmentally an Anthropoid, but if we proceed to evaluate these resemblances and differences, I think we shall find that he over-emphasized the former and took no notice at all of the latter and that the proper position for Tarsius in our embryological classificatory system is somewhere between the Lemuroid and the Pithecoid developmental phases. The value of Tarsius to the embryologist lies in this, that a knowledge of its development enables him to visualize and to characterize what was perhaps the most interesting phase of all in the developmental history of the Primates, viz., the transition from the relatively simple and primitive Lemuroid to the developmentally specialized Pithecoid.

We can most easily summarize the chief events in the early development of Tarsius by reference to the accompanying series of text-figures (7–13).

Certain details in the formation of the blastocyst are unfortunately not well known. HUBRECHT ('02) describes the endoderm as arising by " delamination " from the inner

cell-mass just as in other mammals, but the details of the formation of the endodermal yolk-sac vesicle are not accurately known. He ('09, p. 8) insists that in Tarsius as in the monkeys and man, "the entoderm cells never clothe the whole of the inner surface of the trophoblast, the entodermic vesicle remaining of smaller size than the trophoblastic sphere." He goes on to say "to a certain extent this is explained by the fact that another vesicle . . . develops, at an uncommonly early period, fills up part of the vesicle formed by the trophoblast and prevents the entoderm cells from reaching the entire outer surface." The other vesicle to which he refers is that formed by the extra-embryonal mesoderm enclosing the extra-embryonal cœlom (text-fig. 7, *ex.cœ.*). I find HUBRECHT'S explanation difficult to follow. His figures of early blastocysts show that the delaminated endoderm forms at first not a solid mass, but a layer underlying the embryonal ectoderm and the only way such a layer can give origin to a vesicle is by spreading in contact with a surface. Such a surface is provided by the trophoblast, and I suggest that the endoderm spreads round in contact with it to form a lining to the blastocyst-cavity, just as it does in the Lemur and the lower mammals, and that it soon becomes separated therefrom, over the hinder portion of the blastocyst, by the precocious formation of the extra-embryonal mesoderm and cœlom.

At the time of separation of the endoderm, the embryonal ectoderm appears as a rounded mass, underlying the covering trophoblast. As the blastocyst slowly increases in size, it flattens out and expands to form the shield- or embryonal ectoderm composed of columnar cells. The covering trophoblast as the result is ruptured and disappears and so the shield-ectoderm becomes exposed at the surface just as in the Lemur (text-fig. 7, *embr.ecto.*). But very early two important advances on the latter type manifest themselves. In the first place, the minute blastocyst, measuring only about 0·3 mm. in diameter and at the stage when the embryonal ectoderm is still an ovalish mass and the endoderm is delaminated and in process of spreading (Tarsius 110, Pl. 4, fig. 30), becomes definitely attached to the uterine lining in a way presently to be described, and, secondly, when the blastocyst is still well under 0·5 mm. in diameter, the extra-embryonal mesoderm and cœlom are already established. Whereas in the Lemur, the mesoderm arises relatively late (in Loris, in the blastocyst exceeding 3 mm. in diam., in Nycticebus, in the blastocyst ± 4·5 mm. in diam.) and in the same fashion as in lower mammals, from a primitive streak thickening of the ectoderm, the extra-embryonal mesoderm being simply an outward extension of the mesoderm produced by the latter, in Tarsius, the extra-embryonal mesoderm, as HUBRECHT has shown, is produced most precociously in the blastocyst well under 0·5 mm. in diam. and before there is any definite trace of a primitive streak (Tarsius 617, Pl. 4, fig. 31). Here then we have a remarkable anticipation of a feature which is characteristic of all the higher Primates and a noteworthy example of developmental acceleration.

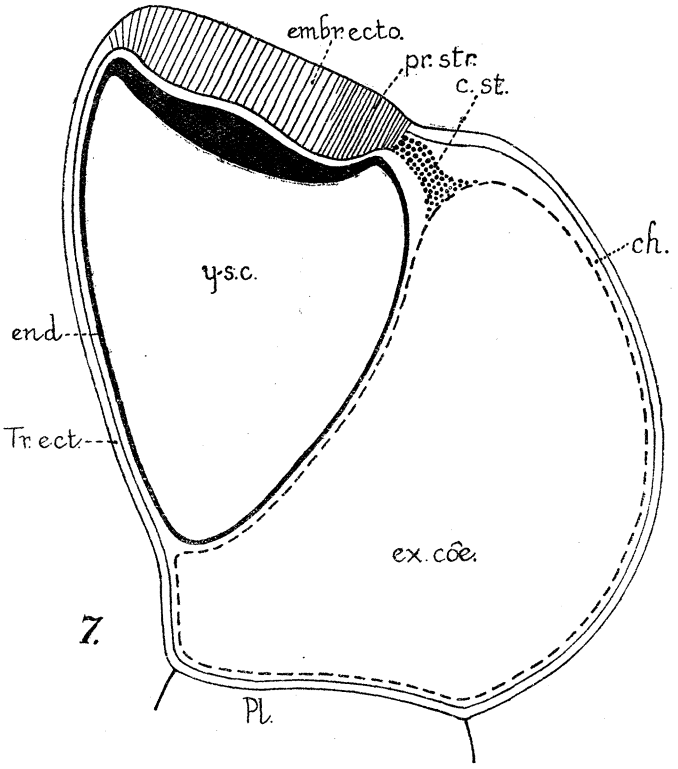
Unfortunately we have no positive knowledge of just when and how the extra-embryonal mesoderm develops in Tarsius. HUBRECHT describes it as arising as a

proliferation from the posterior margin of the shield-ectoderm, "there where the trophoblast is often quite sharply differentiated (*cf.* figs. 48 and 49) from the embryonic ectoderm." He continues, "We encounter this proliferation as soon as the endoderm after its delamination from the embryonic knob is busy forming a vesicle under the embryonic ectoderm (figs. 44 and 62)" ('09, p. 38). The latter figures, however, are diagrams in which the exocœlom is depicted as already established and the like holds true for his sectional figs. 47–49. These figures are from blastocysts much too old to provide critical evidence of the first origin of the extra-embryonal mesoderm, whilst HUBRECHT'S identification of mesoderm in earlier blastocysts (Tarsius 618, fig. 40, *c–e*, Taf. III, and Tarsius 110, fig. 41*b*, Taf. IV, '02), the serial sections of both of which I have examined, is open to doubt.

That the mesoderm and cœlom appear extraordinarily early is abundantly clear; for example, they are well established in blastocyst 617 (Pl. 4, fig. 31) measuring 0·48 by 0·176 mm. in diam., shield-ectoderm 0·152 mm. in diam., but unfortunately this blastocyst provides no certain evidence of the origin of the exocœlomic mesoderm, though in one section there is an indication of its extension upwards towards what seems to be the posterior margin of the shield-ectoderm. What this blastocyst does clearly demonstrate, however, is that the exocœlomic mesoderm is formed before there is any definite indication of a primitive streak thickening in the shield-ectoderm. It will probably be agreed that the most likely source of origin of that mesoderm is from the said ectoderm, but whether it arises as a localised proliferation from its postero-median margin as HUBRECHT inferred or as a more diffuse proliferation, must for the time being remain undecided, though from what I have seen of the early development of the mesoderm in the Pithecoids, I am inclined to believe that the former alternative will turn out to be the correct one.

If we pass now to the slightly later blastocysts represented by Tarsius 86 and 235, certain noteworthy facts are brought to light. Both blastocysts are of about the same size (± 0·5 mm. in diam., shield-ectoderm in 86, 0·2 mm. in diam.; in 235, 0·235 mm. in diam.), blastocyst 86 being slightly the earlier of the two. An obliquely longitudinal section of the embryonal area and the yolk-sac of blastocyst 86 is figured by HUBRECHT (fig. 47, Taf. VII of his '02 paper and fig. 49, Pl. I of his '09 paper) and is reproduced here as fig. 5*a*, Pl. 21. It is specially referred to as showing how the exocœlomic mesoderm arises by proliferation from the extreme hinder margin of the shield-ectoderm, just at its junction with the trophoblast. If fig. 5*a* be examined (*cf.* our text-fig. 7 which is based on it), it will be seen that the exocœlomic mesoderm is connected with the posterior margin of the shield-ectoderm by what appears as a short stalk-like cord or band of mesoderm (text-fig. 7, *c.st.*) and that the portion of the shield-ectoderm situated immediately in front of its junction with the mesoderm is thickened and contains numerous nuclei irregularly arranged and thus contrasts with the more extensive anterior portion of the ectoderm which is not quite so thick and in which the nuclei exhibit a more regular arrangement. In HUBRECHT'S fig. 49 ('09), this thickened area

is labelled *pw.* signifying " protochordal wedge," the term HUBRECHT applies to HENSEN'S knot, but its position at the extreme hinder end of the embryonal area is entirely against its being regarded as such. In text-fig. 7, it is indicated by close-set cross lines and is

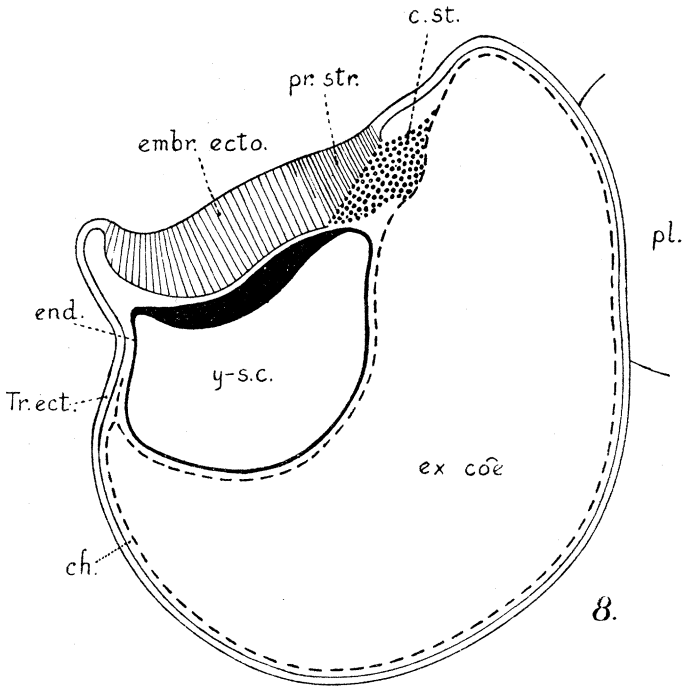


TEXT-FIG. 7.—Semidiagrammatic view of blastocyst of Tarsius 86, *cf.* fig. 5*a*, Pl. 21. Blastocyst, ± 0·5 mm. in diameter. Embryonal area, 0·2 mm. in diameter. *ch.* chorion. *c.st.* connecting stalk promordium. *embr.ecto.* embryonal ectoderm. *ex.cœ.* exocœlom. *end.* endoderm. *Pl.* ectoplacental area of attachment. *pr.str.* primitive streak primordium. *Tr.ect.* trophoblast. *y-s.c.* yolk-sac cavity.

labelled *pr.str.* If we pass now to Tarsius 235 (fig. 6*a*, Pl. 21, and text-fig. 8) we observe again the same short solid tract of mesoderm extending between the shield-ectoderm and the exocœlomic mesoderm, but it is now thicker and, moreover, instead of being connected merely with the posterior margin of the ectoderm as appears to be the case in Tarsius 86, it is now seen to be in direct proliferative continuity with its under surface, over an area roughly corresponding in extent with the marginal thickening in blastocyst 86. Clearly we have to do here with a very short primitive streak (actually about 0·1 mm. in length) which by its proliferative activity has given origin to the mesoderm which extends back to join the exocœlomic mesoderm.

Further, I think we may conclude with reasonable certainty that HUBRECHT'S " protochordal wedge " in Tarsius 86 is not HENSEN'S knot but none other than a primitive streak thickening, probably less developed than in Tarsius 235 but still sufficiently active to have given origin to a relatively slender mesodermal connecting strand. The serial sections through Tarsius 86 are definitely oblique to the antero-posterior axis of the embryonal area, a fact which possibly accounts for the apparent exclusively marginal

origin of the mesoderm in the section figured by HUBRECHT; very probably, if a median reconstruction of the area were made, it would be found to resemble that of Tarsius 235.



TEXT-FIG. 8.—Semidiagrammatic view of blastocyst of Tarsius 235. Blastocyst, 0·53 mm. transverse diameter. Embryonal ectoderm, 0·235 mm. in diameter. Lettering as in text-fig. 7.

It is evident, then, that in Tarsius, not only are the extra-embryonal mesoderm and cœlom precociously formed but the like holds true for the primitive streak. In respect of both these occurrences, Tarsius exhibits, on the one hand, a noteworthy advance on the conditions prevailing in the Lemuroids, as already indicated, and on the other, a really remarkable anticipation of developmental features met with elsewhere only in the Pithecoids and Anthropoids. In both these latter groups we know that the extra-embryonal mesoderm and cœlom appear extremely early in the quite small blastocyst, long before there is any trace of the primitive streak, whilst as regards the latter, though we have no definite knowledge of its first appearance in the Pithecoids, we do know that in man it is very early laid down, though in a manner which differs in an interesting respect from that of Tarsius. To take but two examples, for the details of which I am indebted to Dr. FLORIAN; in the embryo Fetzer, the chorionic vesicle of which has an internal diameter of 1·566 × 1·048 mm., the primitive streak appears as a small circular thickening situated just behind the centre of the embryonal area (text-fig. 17, p. 111).* In the later stage, represented by the Beneke embryo (embryonal shield, 0·375 mm. in length × 0·23 mm. in breadth), the streak has extended in the caudal direction and so has acquired its definitive linear form. It attains a length of

* *v.* FETZER and FLORIAN ('30).

0·08 mm. but does not yet reach the cloacal membrane situated at the hinder margin of embryonal ectoderm.*

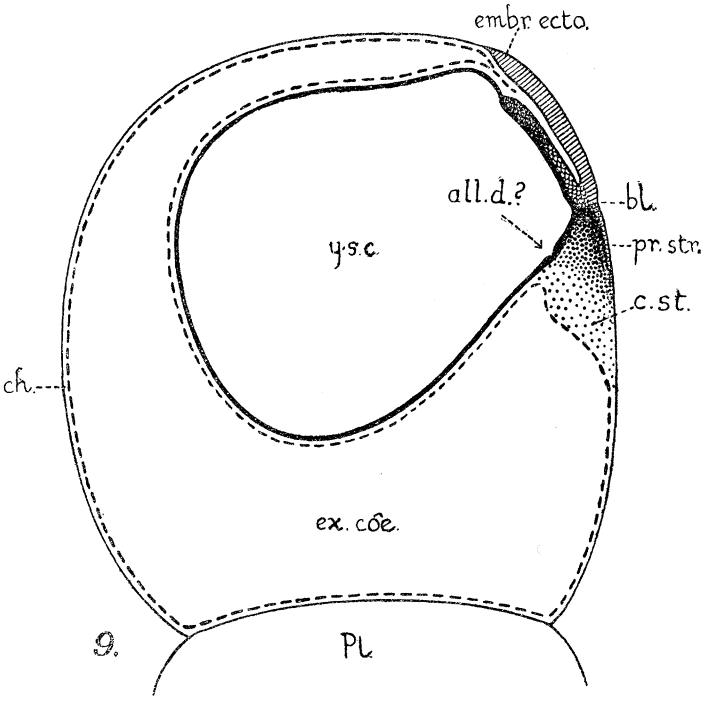
It would therefore appear that whilst in Tarsius the primitive streak thickening at its first origin extends right back to the caudal margin of the shield-ectoderm, in man the same thickening makes its first appearance close to the centre of the embryonal area and subsequently differentiates in the caudal direction. Has this difference in the mode of appearance of the primitive streak primordium in Tarsius and the higher Primates as exemplified by man any significance ? I think it has, and venture to suggest that it is correlated with the very striking difference in the mode of origin of the primordium of the connecting stalk in the two. In Tarsius, the most obvious result of the activity of the caudally situated primitive streak is the formation of the tract or band of mesoderm which extends posteriorly to connect with the exocœlomic mesoderm. HUBRECHT identified this tract as the primordium of the mesoderm of the connecting stalk, and with this identification I am in full agreement. From the stage represented by text-fig. 7 its progressive increase at the expense of mesoderm contributed by the primitive streak can be followed through the succeeding text-figures until it culminates in the mesoderm of the definitive connecting stalk shown in text-figs. 12 and 13. In the early human embryo as also in that of the Pithecoids, on the other hand, the connecting stalk primordium is formed not by mesoderm of direct primitive streak origin but by extra-embryonal or so-called " primary " mesoderm, the mode of origin of which is discussed in a later section of this lecture (p. 110). Here it need only be stated that there is evidence pointing to the existence in early embryos of the Pithecoid and man of a mesodermal proliferating area involving the postero-median margin of the shield-ectoderm and the immediately adjoining portion of the amniotic ectoderm which contributes to, if it does not entirely form, the connecting stalk primordium. This proliferating area, it may be suggested, functionally replaces, if it does not actually represent, the hinder end of the primitive streak of the Tarsioid and the Lemuroid, and here it may not be out of place to recall that in the latter the allantoic mesoderm, the homologue of the connecting stalk mesoderm, is derived from just this same posterior end of the primitive streak.

Finally, by way of summarizing our present knowledge of the early history of the mesoderm in Tarsius, I suggest the following sequence of events. In the early blastocyst, very soon after the endodermal yolk-sac vesicle has been established, the extra-embryonal mesoderm is laid down in the form of a solid sheet, extending over the hinder half of the blastocyst, between the trophoblast and the endoderm. In all probability, it is formed by proliferation from the caudo-median margin of the shield-ectoderm, as HUBRECHT concluded. Then through the appearance of the exocœlom, this sheet becomes split into an inner or splanchnic layer applied to the endoderm forming the hinder wall of the yolk-sac vesicle and an outer or parietal layer applied to the trophoblast of the hinder half of the blastocyst and forming with that an area of chorion (text-fig. 7). Later, the

* *v.* FLORIAN and BENEKE ('30/'31).

definitive primitive streak thickening appears as the direct forward continuation of the presumed marginal proliferative area, and the mesoderm produced from it, extending directly backwards in continuity with the exocœlomic mesoderm, constitutes the strand which, following HUBRECHT, we have identified as the primordium of the connecting stalk.

If a marginal proliferation of mesoderm such as HUBRECHT postulated actually does occur prior to the appearance of the primitive streak thickening, I suggest that it is to be regarded not as something new but simply as the product of the precociously differentiated hinder end of the primitive streak, in other words, I suggest that in Tarsius the extra-embryonal mesoderm is none other than precociously developed primitive streak mesoderm (a suggestion previously put forward by BRYCE ('08)), the immediate results of its formation being the early establishment of the exocœlom and the hinder portion of the chorion.

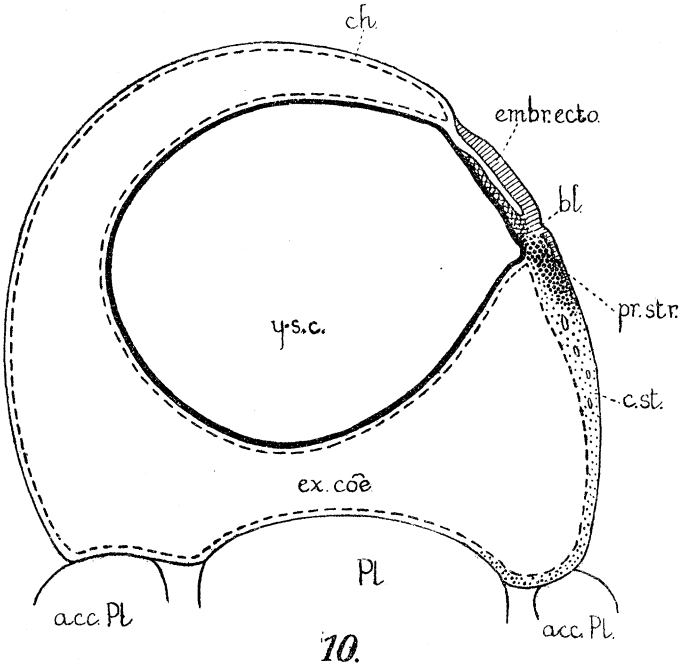


TEXT-FIG. 9.—Semidiagrammatic view of blastocyst of Tarsius 175. Blastocyst, ± 2 × 1·7 mm. diameter. Embryonal area, 0·62 mm. diameter, Primitive streak 0·18 mm. in length. *all.d.* (?) endodermal allantoic primordium (?). *bl.* blastoporic depression on surface of primitive knot. *Pl.* placental primordium. Other letters as in text-fig. 7.

If we follow now the later history of these structures, we find in the blastocyst just under 2 mm. diam. (text-fig. 9) that the sheets of extra-embryonal mesoderm and the cœlom have not only extended forwards round the sides of the yolk-sac endoderm, but have met and fused in front of the same, with the result that the yolk-sac now possesses a complete splanchnopleural wall of its own and depends freely into the extra-embryonal cœlom, whilst the chorion is established all round the blastocyst.

The embryonal area has increased in size, whilst the primitive streak has lengthened

and has given origin to a thick mass of connecting stalk mesoderm, more compact close to its origin, looser below, which has incorporated the stalk-like primordium of the earlier stages (text-figs. 7 and 8) and is now in process of growing back between the parietal cœlomic mesothelium and the trophoblast (text-fig. 9). In our next stage (Tarsius 273, text-fig. 10), the connecting stalk primordium has made great progress and has now extended down between the trophoblast and the parietal mesothelium of the chorion to reach the site of the developing placenta. In this way the mesodermal part of the connecting stalk is established in the form of a flattened narrow band (with, in Tarsius 273, a length of about 1·6 mm. and a breadth of about 0·22 mm.) situated in the chorion and directly connecting the hinder end of the embryo with the margin



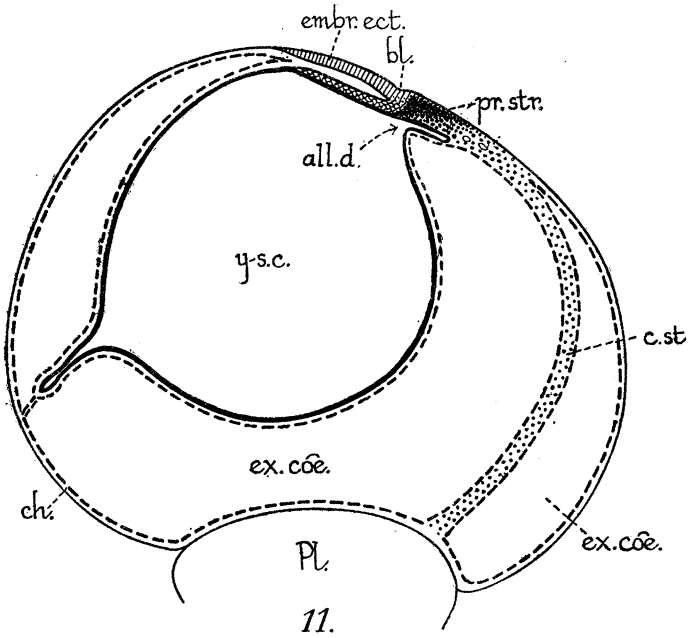
TEXT-FIG. 10.—Semidiagrammatic view of blastocyst of Tarsius 273. Blastocyst about 2·25 × 1·5 mm. in diameter. Embryonal area, 0·8 mm. in length. *acc.Pl.* accessory area of attachment. *c.st.* connecting stalk (1·6 mm. in length × 0·22 mm. in breadth) now reaches margin of placental primordium (*Pl.*).

of the placental primordium. Moreover, endothelially lined spaces, apparently derived, as HUBRECHT has described, from involutions of the cœlomic epithelium have now appeared in it. They represent the primordia of the future umbilical vessels of the stalk, and it is noteworthy that they are formed when there is as yet no trace of vascular primordia in the embryo itself or even in the yolk-sac wall. Here, then, we see yet another example of developmental acceleration and another feature in which Tarsius anticipates the higher Primates.

In the next stage illustrated (Tarsius 22, text-fig. 11), a blastocyst measuring ± 4·5 mm. in diameter, the connecting stalk has become separated from the chorion as the result of the extension of the mesoderm and cœlom around it, and now appears as a

flattened band-like structure running through the extra-embryonal cœlom from the hinder end of the embryo to the placental primordium. Moreover, although there is as yet nothing that can be definitely identified as hind-gut, a tubular diverticulum of the endoderm of the yolk-sac, arising directly below the primitive streak, extends for a short distance (about 0·24 mm.) into its proximal end. This diverticulum (possibly already indicated in the stage of text-fig. 9) is the endodermal constituent of the allantois, or connecting stalk. It strikingly recalls the allantoic duct or canal of the early human embryo.

In text-fig. 11, the yolk-sac is seen to be prolonged antero-ventrally into a beak-like projection, which is connected with the chorion by a thin mesodermal strand. This

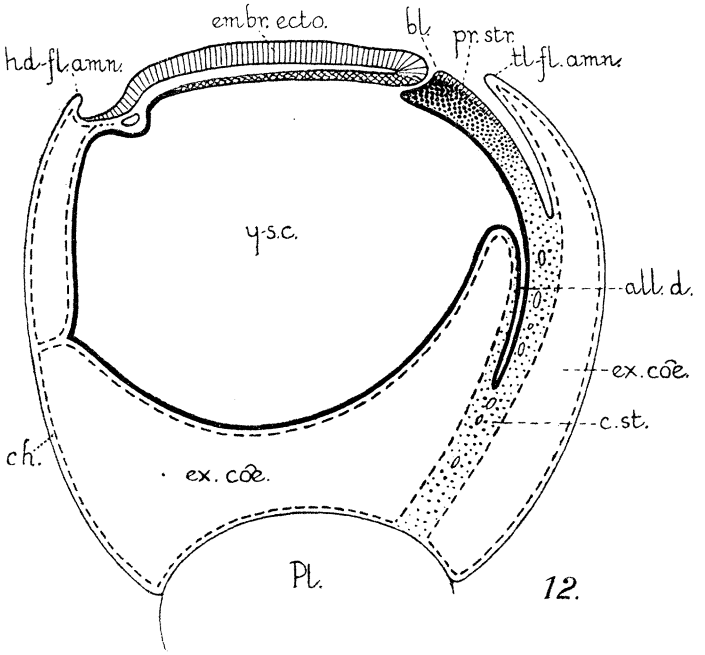


TEXT-FIG. 11.—Semidiagrammatic view of blastocyst of Tarsius 22. Blastocyst ± 3·4 × 5·9 mm. in diameter. Embryonal area 1·5 mm. in length. Connecting stalk (*c.st.*), 4·4 mm. in length, is now freed from the chorion. *all.d.* endodermal allantoic diverticulum.

curious condition was originally figured by HUBRECHT ('07, fig. 103) and is also met with in later stages (*cf.* text-fig. 12), and probably also occurs in stages immediately preceding that of text-fig. 11. It would seem to owe its origin to the persistence of a small piece of unsplit mesoderm at the antero-ventral extremity of the yolk-sac, at the time the endoderm of the latter became separated from the trophoblast by the forward extension of the mesoderm and cœlom. This connection offers an interesting parallel (for it is probably nothing more) to the so-called yolk-sac process, the elongated thin strand into which the yolk-sac in the early human blastocyst is prolonged and which is likewise attached to the chorion. A corresponding but quite short prolongation of the yolk-sac endoderm is also found in the early blastocyst of Hapale. How this yolk-sac process originates in the early human embryo is quite unknown. It seems unlikely

that the endoderm of the human yolk-sac ever lies in contact with the trophoblast as does that of Tarsius, so that we must suppose the yolk-sac process arises in a quite different fashion to the connection in the latter.

Text-figs. 12 and 13 illustrate the mode of formation of the amnion and the attainment by the fœtal membranes of their definitive condition. The amnion is formed in essentially the same way as in Loris by the gradual closing in of amniotic head- and tail-folds, but in Tarsius, owing to the very early extension of the extra-embryonal cœlom below and in front of the head-region of the embryo, there is no proamnion. In text-fig. 12, we see the tail-fold of the amnion definitely established and in process of extending



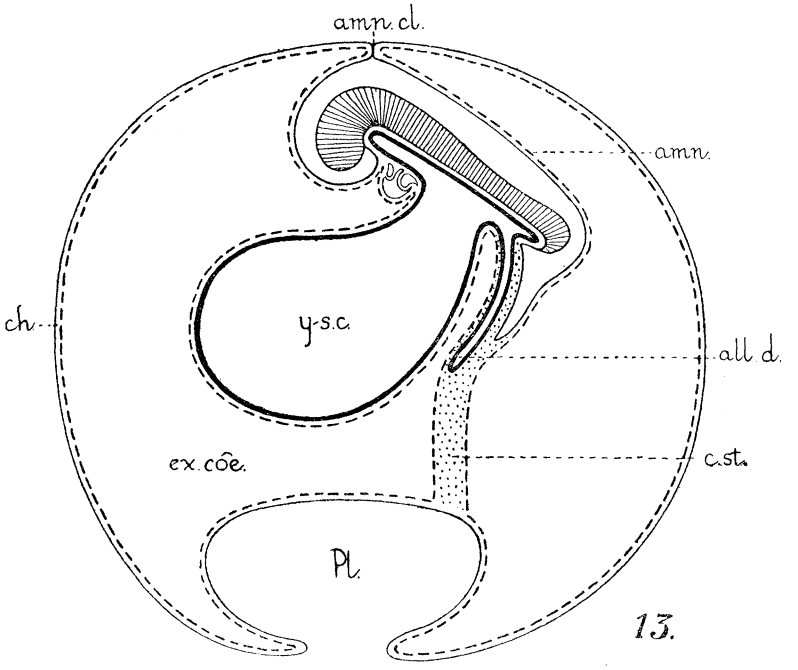
TEXT-FIG. 12.—Semidiagrammatic view of blastocyst of Tarsius 710 (partly after HUBRECHT, '07, fig. w⁴. p. 57, *cf.* also '02, fig. 73, Taf. IX, and fig. 84, Taf. X), to show the arrangement of the fœtal membranes prior to the closure of the amnion. Blastocyst, ± 7 mm. in diameter. Embryonal area, about 2·15 mm. in length. Embryo with flat medullary plate and 2–3 pairs of somites. Primitive streak, about 0·45 mm. in length. *bl.* dorsal opening of neurenteric canal. *hd-fl.amn.* Head-fold of amnion, *tl-fl.amn.* tail-fold of amnion.

forwards, whilst the head-fold has just appeared. In text-fig. 13, amniotic closure is completed, the point of closure lying above the hinder part of the head of the embryo, so that, as in Loris, the main part of the amnion is derived from the tail-fold.

There is one further point in connection with the amnion that calls for brief comment, and that is the apparent prolongation of the amniotic cavity along the posterior (morphologically dorsal) aspect of the connecting stalk (text-figs. 12 and 13). This condition appears to be brought about by the non-separation and subsequent elongation of the proximal segment of the connecting stalk, situated immediately behind the primitive streak, between that and the upper limit of the extra-embryonal cœlom, so that the tail-fold of the amnion, arising at that limit, overlaps it in its forward growth.

The interest of this condition lies in the fact that it is met with in all the higher Primates from the Platyrrhine monkeys to man. In the human embryo, Dr. FLORIAN* considers that it subserves two purposes: (1) it provides room for the free backward growth of the tail-end of the embryo, and (2) it facilitates the rotation of the connecting stalk from its original postero-dorsal position to its definitive attachment to the ventral body-wall. In Tarsius, it clearly subserves the first purpose (text-fig. 13) but it should be noted that, in this form, the connecting stalk never occupies a postero-dorsal position but is, from its first origin, posterior to the embryonic body.

The foregoing brief summary of the salient features in the early development of Tarsius affords ample justification for the contention that in the mode of development



TEXT-FIG. 13.—Diagram (based on HUBRECHT, '96, fig. i, p. 170) to show the arrangement of the fœtal membranes in Tarsius, after closure of the amnion. *amn.cl.* last point of amniotic closure.

of its extra-embryonal mesoderm and cœlom, in the precocious formation of its yolk-sac and chorion, and in the replacement of the allantois by the precociously established connecting stalk, Tarsius, so far as its ontogeny is concerned, has advanced far beyond the Lemuroid and is well on the way towards the Pithecoid type, whilst at the same time it has retained evident traces of the ancestral mode of origin of these structures as well as certain primitive features which it has inherited, with but little modification, directly from the ancestral Lemuroid stock, so that it presents us with a remarkable combination of primitive and progressive characters.

Now the two features in the development of Tarsius to which HUBRECHT attached

* See his interesting paper on the formation of the connecting stalk in young human embryo. 'Journ. Anat.,' vol. 64, 1930.

almost exclusive importance in estimating its affinities are the occurrence of a connecting stalk and the presence of a discoidal deciduate placenta of the hæmochorial type. Leaving the placenta for later consideration, let us here try to evaluate the significance of the acquisition by Tarsius of a connecting stalk.

As I have elsewhere pointed out (HILL, '19, p. 483), "when HUBRECHT first put forward his views, the existence of a connecting stalk outside Tarsius and the Anthropoids was unknown, and so he naturally attached great importance to it as a token of affinity, but we now know, through the researches of NEWMAN and PATTERSON, that a genuine connecting stalk, presenting a remarkable similarity to that of Tarsius, is also present in the Armadillo (*Tatusia novemcincta*), in which obviously it must have been evolved quite independently of that of the Primates. Nevertheless, the common occurrence of this structure in these two groups of the Primates is a feature of very great interest, . . ." Now the facts of development demonstrate conclusively that the connecting stalk of Tarsius is none other than the reduced and precociously developed homologue of the vesicular allantois of the Lemur. Like the latter, it consists of mesoderm of direct primitive streak origin and into it there extends a diverticulum of the yolk-sac endoderm and also, like the latter, its function is to provide, at the earliest possible moment, a pathway along which the umbilical (allantoic) vessels can pass to and from the chorion. Moreover, I have shown (*ante*, p. 60) that all that is necessary to convert the Lemuroid allantoic primordium into the Tarsioid connecting stalk is a slight acceleration of the developmental processes whereby the allantoic primordium is laid down at an earlier period, prior to the appearance of the tail-fold round the hinder-end of the embryo. If that were to happen, the allantoic mesoderm would then lie between the chorionic trophoblast and the cœlomic mesothelium, precisely in the position it occupies in the Tarsius blastocyst depicted in text-fig. 9. Now it is just in this phenomenon of developmental acceleration or heterochrony (RAY LANKESTER) that the explanation of the transformation of the allantois into a connecting stalk is, I venture to suggest, to be found. In Tarsius, as in the higher Primates, the extra-embryonal mesoderm and cœlom are precociously formed and the endodermal yolk-sac vesicle and the chorion are correspondingly early established. The consequence of these events is that a yolk-sac placenta vascularised by the vitelline vessels, cannot be formed at all and so, as a compensation, what seems to have happened is that the development of the allantois was accelerated and at the same time abbreviated, so as to enable it to vascularise the placental area of the chorion directly and at the earliest possible moment (*cf.* HILL, '19, p. 484). And I may here remark, when we understand how developmental acceleration is brought about, we shall have advanced a long way towards the solution of the problem of developmental adaptation.

Lastly, in the present connection, it should be emphasised that, in face of all the facts furnished by comparative embryology, the view of HUBRECHT to the effect that the connecting stalk of Tarsius and the higher Primates represents a more primitive condition than that of the free vesicular allantois of any of the other Amniotes, cannot for a

moment be entertained. In my opinion, the allantois of the Lemur, the connecting stalk of Tarsius and that of the higher Primates represent three stages in an evolutionary series which is to be interpreted from the Lemur upwards and not in the contrary direction as maintained by HUBRECHT, and the interest of the connecting stalk of Tarsius lies in this, that it presents us in its development with just that intermediate or transitional stage between the generalised Lemuroid and the specialised Pithecoid conditions which the conception of Primate phylogeny advocated in this lecture demands.

Placentation.

We have already emphasised the contrast between the placenta of Tarsius and that of the Lemuroidea, and here we need only again note that, like the Pithecoid and Anthropoid placenta, it is of the localised, massive, deciduate type, discoidal or knob-like in form, and hæmochorial in structure, *i.e.*, the maternal blood circulates through lacunar spaces in the fœtal trophoblast, whilst vascular outgrowths of the chorionic mesenchyme, penetrating into the trophoblastic spongework, carry the fœtal umbilical capillaries into close proximity to the circulating maternal blood (Pl. 3, figs. 28 and 29, and Pl. 8, figs. 52–54).

Our knowledge of its development and structure we owe almost entirely to HUBRECHT ('99), *cf.* also HILL ('19). Thanks to the kindness of Dr. D. DE LANGE, I have had the opportunity of studying certain of the early stages described by HUBRECHT, and I have also examined some late placentas kindly placed at my disposal by my friend, Professor W. E. LE GROS CLARK; but there are still many points in its development that stand in need of further elucidation. My interpretations differ from those of HUBRECHT in certain important respects.

The Tarsius blastocyst effects its attachment to the uterine lining when it is still quite minute. The earliest attached stage (Tarsius, 110) figured by HUBRECHT ('99, Pl. 7, fig. 55), and which I have also examined (Pl. 4, fig. 30), has an estimated diameter in its somewhat folded condition of $\pm 0{\cdot}2 \times 0{\cdot}3$ mm. Unfortunately the serial sections are very lightly stained, and by no means easy to interpret. The blastocyst is at the stage when the embryonal ectoderm is in the form of a rounded mass, and the endoderm has been delaminated and is in process of spreading. HUBRECHT thinks that mesoderm is already present, but this, in my opinion, is very problematical. In fig. 30, the minute blastocyst is seen to be attached to the bottom of a slight groove or depression on the surface of the mucosa, on the mesometrial side of the relatively large uterine lumen. In the mucosa, outside the area of attachment, the uterine glands are conspicuous. They are arranged in club-shaped groups, each group formed of a small number (three or four) of branched convoluted glands, the narrow neck portions of which pass up to open separately into the uterine lumen (*cf.* Pl. 5, fig. 34). In the region of attachment certain definite changes have already taken place in the mucosa. The uterine epithelium is definitely hypertrophied, being here twice as thick as elsewhere, and is composed of

narrow columnar cells, with crowded nuclei and a wavy irregular surface, a condition which recalls that seen in the early pregnant uterus of the Platyrrhine monkey, Hapale. The lumina of the gland-necks have also become enlarged, and in the case of those more centrally situated, have become occluded by the proliferated gland-epithelium, whilst in between them the compressed interglandular connective tissue appears as more deeply stained strands. Enlarged capillaries are present below and around the region of attachment, but are not yet very numerous.

The attachment itself is very simple and primitive-looking in character—just such a type of fixation as one might expect *a priori* if the view I advocate is correct, viz., that Tarsius shows us one of the first attempts at the formation of a hæmochorial placenta. It is effected by a small number of independent sprout-like outgrowths of the trophoblastic wall of the vesicle to one side of the embryonal ectodermal mass, which in this blastocyst lies adjacent to the uterine epithelium. These sprouts consist, so far as one can make out, of narrow, elongated, lightly-stained cells, closely massed together, and they penetrate separately and directly through gaps in the uterine epithelium, to terminate shortly below the same in contact with the glandular tissue. It is remarkable that such a relatively slight penetration on the part of the trophoblast should produce such definite changes in the uterine epithelium and in the neck-portions of the uterine glands.

Between this early stage (Tarsius, 110) and the next older available for examination (Tarsius, 617), there is a considerable gap, in which great progress has been made. The blastocyst is again attached to the bottom of a fairly deep groove, but here it is the anti-embryonal, or lower pole, which is attached (Pl. 4, fig. 31). The blastocyst is now much larger, measuring about $0{\cdot}48 \times 0{\cdot}176$ mm. in diameter, and much more advanced developmentally. It is roughly cylindrical in form, and is attached over its flattened lower pole, whilst situated obliquely at its opposite or upper end is the disc of shield-ectoderm, fully differentiated and freely exposed. The yolk-sac and extra-embryonal mesoderm and cœlom are established.

Below the region of attachment there is now visible a new formation, not present in the earlier stage, in the form of a rounded mass of parenchymatous-like tissue, $0{\cdot}4 \times 0{\cdot}5$ mm. in diameter, surrounded at the sides and below by the altered necks of the uterine glands (Pl. 4, fig. 31, *tr.m.*). The mass in question occupies the site of the altered gland-necks in the preceding stage, so that these must have been displaced during its formation. There can be no question of their transformation into it. Examination of the region of attachment under high powers demonstrates that the parenchymatous-like mass (*tr.m.*) is directly connected with the somewhat irregular layer of trophoblast of the lower pole of the blastocyst by a number of narrow strands separated from each other by isolated fragments of uterine epithelium in active degeneration (Pl. 4, fig. 32, *tr.sp.* and *ep'*.).

If we pass to the still older stage represented by Tarsius 235, with a blastocyst about $0{\cdot}5$ mm. in diameter, we find that in the area of attachment the remnants of the uterine

epithelium have completely disappeared, whilst the trophoblast of the vesicle-wall is no longer apparent as a separate layer, but has become indistinguishably merged with the parenchymatous-like tissue (Pl. 4, fig. 33). Moreover, it is clearly seen that the trophoblast of the vesicle-wall is, marginally, in direct continuity with the latter, and that shortly below the point of continuity a small blood-extravasation is present.

The only conclusion to be drawn from these observations is that the parenchymatous cell-mass is of trophoblastic origin. HUBRECHT, however, considered that it is maternal in origin, and formed by the thickening of the sub-epithelial inter-glandular connective tissue. He accordingly spoke of it as a "trophospongia." He believed that it soon becomes invaded by the trophoblast cells overlying it, and that these alone furnish the fœtal constituent of the placenta, whilst the trophospongial mass undergoes retrogression, appearing as a deeply staining zone underlying the trophoblastic placental primordium. If HUBRECHT's interpretation is correct, then Tarsius in the development of its placenta would be even more unique than it appears to be, since in no other Primate has such a definitely localised thickening of the maternal decidua ever been observed. But after very careful study of the preparations, I am satisfied that HUBRECHT was mistaken in his interpretation, and that the mass is formed of trophoblast alone, but of trophoblast of such a peculiar and unique type that he may well be excused for failing to recognise it as such. He appears, indeed, to have been greatly impressed as well by its appearance as by its histological structure, and spoke of both as "ganz eigenthümlich" ('99, p. 350). He states that cell-limits are not everywhere visible in it, and that it is specially characterised by the presence of an adenoid framework which separates the different nuclear regions like a honeycomb. His description of it is deserving of quotation in his own words. He writes ('99, p. 350): "Die Trophospongia hat in frühen Stadien ein ganz eigenthümliches Aussehen. . . . Anfänglich stehen deutliche und zahlreiche Kerne dichtgedränkt in einer körnigen, plasmareichen Grundmasse, in welcher Zellgrenzen nicht allerwege erhalten sind (fig. 70). Ganz kennzeichnend für diese Region ist das Auftreten eines eigenthümlichen, adenoiden Gerüstwerkes, welches sich in dieser Grundmasse absetzt als Product des Zellplasmas und das verschiedene Kerngebiete wabenartig trennt. Es lässt sich mit einigen Tinctionsmitteln färben (fig. 100, Pl. 15), bleibt aber den verschiedenen Carminfarben gegenüber blass oder schwach gelblich."

From this description it is not very clear whether HUBRECHT regarded the mass as cellular or syncytial in nature, or partly the one, partly the other. It will be noted that he describes the nuclei as lying in a granular, plasma-rich matrix in which cell-limits are not everywhere preserved, whilst he regards the framework which separates the nuclear regions as arising in this matrix as the product of the cell-plasma. But it is not easy to conceive of such a framework arising in a continuous cytoplasmic matrix, though its origin by the transformation of the superficial cytoplasm of adjoining cells or as an intercellular substance is more readily understandable.

As already mentioned, the trophoblastic mass, when examined under medium magnification, presents the appearance of a fairly uniform parenchyma, apparently composed of small cells separated from each other by thin cell-walls (Pl. 4, figs, 31, 32, *tr.m.*). More careful examination under higher powers, in combination with the binocular stereoscopic attachment of Zeiss, shows that the light staining, refringent framework described by HUBRECHT, really forms the walls of compartments or " cells " of somewhat variable size and shape in which are situated small masses of cytoplasm, each containing a relatively large oval nucleus (Pl. 5, fig. 36). What is the nature of these " nucleated units "? If we knew the full history of the attaching trophoblastic sprouts and in particular the details of the origin from them of the trophoblastic mass, we should doubtless be able to answer this question with certainty. Meantime, in the absence of that knowledge and until I have had the opportunity of making a more detailed study of the available material, I am not prepared to express a definite opinion as to whether the units in question really represent cells, or constituents of a syncytium, though I incline to the belief that the trophoblastic mass in the earliest stages available is cellular and not syncytial in character, and that the framework has been laid down between its constituent elements. Whether or not this framework is in any way related to the cuticular border with which the trophoblast of Loris is provided, I will not attempt here to decide.

As may be seen from fig. 36, the " units " do not completely fill the compartments in which they lie; they may project more or less freely from one of the enclosing walls or they may extend across the middle part of a compartment. Spaces are thus left around them, and it is these which give to the tissue its characteristic vacuolated appearance.

Nowhere else in the Primates has an ectoplacental trophoblast of this peculiar type been found to occur, and equally remarkable is the fact that the part of the trophoblast of the blastocyst concerned in its formation and corresponding to the cytotrophoblast of the ectoplacental area in the higher Primates is completely used up in its formation by the time the blastocyst has reached a diameter of $\pm$ 0·5 mm., so that the trophoblastic mass must depend for its further growth on its own inherent capacity. Moreover, once it is established, it never exhibits the invasive properties we associate with this layer in the higher Primates. Apart from sending out basally a stalk-like process, and apart from a noteworthy increase in size, its growth-activity is of the non-invasive order. The ectoplacental trophoblastic mass of the early Tarsius blastocyst is thus sharply distinguishable from that of all the other Primates by the following features: its massive form, its strictly localised character, and its deep subepithelial position in the endometrium; its peculiar histological structure, the early and complete incorporation in it of the parent cytotrophoblastic layer, and its lack, once it is established, of actively invasive properties.

To these may be added the extremely simple and localized character of the original trophoblastic proliferations which effect the primary attachment, though their restricted origin is no doubt to be correlated with the minute size of the blastocyst at the time

attachment takes place, and in this connection it should also be mentioned that the marginal trophoblast in the somewhat older blastocyst, when it happens to come into contact with the uterine epithelium, is capable of giving origin to small accessory masses on either side of the primary one (*cf.* text-fig. 10 and HUBRECHT, '99, Pl. 9, fig. 63).

And not only is the ectoplacental trophoblast of Tarsius unique in its structure and character, it is equally without parallel amongst the other Primates in its behaviour during the formation of the definitive placenta as we shall presently see. The facts, set forth above, however, are sufficient in themselves to justify the conclusion that, so far as its placental development is concerned, Tarsius took a line of its own, right off the main track leading up to the Pithecoids. And the remarkable thing is that, in spite of these initial peculiarities, Tarsius manages to develop a hæmochorial placenta of the trabecular type which is not so very dissimilar in its general plan of structure to that of the Platyrrhine Pithecoids (*cf.* Pl. 8, fig. 54, with Pl. 16, fig. 96).

If now we pass on to a brief survey of the later stages in the development of the placenta, we find that the tropho-placental primordium (as we may term the ecto-placental trophoblastic mass) once established begins to increase in size, but, as already indicated, it retains its individuality throughout the growth period and apart from sometimes producing a stalk-like prolongation from its under surface (Pl. 5, fig. 37, and Pl. 6, fig. 40, *sta.*) shows no tendency to proliferate and to invade the surrounding decidual tissue as does the syncytiotrophoblast of the higher Primates.

Entirely subepithelial in Tarsius 617 (blastocyst, $0{\cdot}48 \times 0{\cdot}17$ mm. in diameter) and measuring $0{\cdot}4$ mm. in transverse diameter and $0{\cdot}5$ mm. in thickness, the tropho-placental primordium has attained in Tarsius 261 (blastocyst, $\pm$ $4{\cdot}5$ mm. diameter) a diameter of $2{\cdot}1$ mm. and a thickness of $1{\cdot}3$ mm. and is beginning to project as a convex elevation on the surface (Pl. 6, fig. 40), whilst in Tarsius 22 (blastocyst, $\pm$ $3{\cdot}4 \times 5{\cdot}9$ mm.), it has increased in diameter to $2{\cdot}4$ mm. and in thickness to $1{\cdot}9$ mm. and its upper half or thereabouts projects beyond the level of the uterine epithelium.

This growth of the tropho-placental mass, prior to its invasion by the chorionic mesenchyme, is the result of a remarkable activity on the part of its nucleated units, well deserving of detailed description, but of which we can give here only the barest outline.

HUBRECHT devotes the major part of his paper on the placenta of Tarsius ('99) to an attempt to demonstrate that one of the results of this activity is the formation of maternal red-blood corpuscles from the fragmented nuclei of the trophoblastic as well as the maternal trophospongial cells of the tropho-placental mass, " surely an unexpected histological phenomenon " as he himself remarks ('08, p. 106), and in the course of that attempt he describes the appearance in it of large giant-cells with very peculiar nuclei and provides a series of very fine figures (in colour) illustrating their form and structure ('99, Pl. 14, figs. 91-97 ; Pl. 15, figs. 99-104). It is by the amitotic budding and fragmentation of these nuclei that he believes maternal red-blood corpuscles are formed.

The formation of large multi-nucleate bodies, so-called "giant cells," is certainly a very remarkable feature in the growth of the trophoblastic mass of Tarsius, but we cannot

accept HUBRECHT'S view that their chief rôle is that of providing nuclei destined to give origin to maternal red-blood corpuscles. Their significance becomes clear when we examine the successive growth-stages of the placental mass illustrated in figs. 37-47, Pls. 5–7. From these figures it will be seen that they increase in number *pari passu* with the increase in size of the mass and gradually fuse together so that by the time the mesodermal villous outgrowths of the chorion are established, the larger part of the trophoblast of the placental mass consists of a fairly uniform syncytial network, enclosing lacunar spaces, occupied by maternal blood (figs. 44-47). Accordingly, we conclude that the appearance of these multi-nucleate masses simply heralds the commencing transformation of the trophoblast of the early stages into the definitive syncytiotrophoblast of the later stages and that they represent a growth-stage in the formation of the latter.

If we look into the details, we find that the growth of the placental mass is initiated by a general increase in the size of its nucleated units. This is very soon followed by the appearance in it of darkly staining uni- and multi-nucleate bodies of quite variable size and shape, but mostly quite large (Pl. 5, figs. 37, 38, and Pl. 6, fig. 39). They are formed by the hypertrophy, often accompanied by fusion of the units. Their nuclei at the same time increase greatly in size and become extremely rich in chromatin and they increase in number by active amitotic division which may be effected by simple constriction into two or more fragments or by budding or branching, so that the nuclei can present the most complicated and bizarre forms (Pl. 6, figs. 41 and 42, *cf.* also in a later stage, Pl. 7, figs. 48-50). Sparse at first, these structures rapidly increase both in number and in size, the latter increase being due partly to their own growth, partly to the fusion with them of other elements, and at the same time they acquire an appearance as of quasi-independence and come to resemble independent giant-cells so closely that HUBRECHT actually identified them as such and spoke of them as " megalokaryocytes."

Moreover, lacunar spaces soon become evident between the larger syncytial masses and, sooner or later, maternal blood, at first in small quantity, begins to penetrate into these spaces, whilst areas of degenerating syncytium become distinguishable especially in the peripheral region of the basal half of the mass. The contrast, accordingly, between the uniformity of the newly-formed primordium and the heterogeneity of such a stage as that seen in Tarsius 261 (*cf.* Pl. 5, fig. 35, with Pl. 6, fig. 40) is most striking.

In no other Primate have phenomena in any way comparable with those indicated above for Tarsius, ever been described, so that we are justified in concluding that Tarsius is unique amongst the Primates and indeed amongst the mammals, not only in respect of the histological characters of its trophoblast but also in the details of its subsequent differentiation.

In Tarsius 261 (blastocyst $\pm 4{\cdot}5$ mm. diameter, tropho-placental mass $2{\cdot}14 \times 1{\cdot}3$ mm. diameter), maternal blood is already present in the syncytial lacunæ, though in no great quantity and the chorionic mesenchyme is definitely thickened (Pl. 6, figs. 40

and 41). In the somewhat later stage represented by Tarsius 22, maternal blood is more abundant in the lacunæ, whilst the chorionic mesenchyme is now much thicker and has given origin to a series of localised down-bulgings from its under surface (Pl. 6, fig. 42, *mes. v.*). These are the beginnings of the " villous " outgrowths of the chorionic mesenchyme which, in Tarsius 164 (Pl. 6, figs. 43 and 44), are seen to be in process of penetrating into the tropho-placental mass. As they grow in, so the syncytium re-organises itself, assuming a more regular reticular character and provides round each villous process a covering of syncytio-trophoblast, wonderfully regular, considering its source, in which the small nuclei are spaced out irregularly in a single row (Pl. 6, fig. 44).

A slightly later stage is shown in Tarsius 595 (Pl. 7, figs. 45 and 46), in which the outgrowths (mesodermal " villi ") have increased in length and are beginning to branch. Moreover the umbilical vessels, conveyed to the chorion by the connecting stalk, have now grown into them and as maternal blood has already penetrated into the lacunæ in the syncytio-trophoblastic network and is present in the lacunar spaces around the " villous " outgrowths, we may say, with HUBRECHT, that the formation of the definitive placenta is now initiated. At this stage, the blastocyst measures + 8 mm. in diameter, and the placenta, 4·6 mm. in diameter × 2·6 mm. in thickness. The placenta now projects freely into the uterine lumen as a knob-like mass, with a somewhat constricted base of attachment to the greatly reduced decidual layer of the uterine wall (Pl. 7, fig. 45). It is invested all over by a layer of chorionic mesenchyme, the " villous" outgrowths arising from that part of it clothing the upper or flattened surface of the mass being longer and more branched than those round the periphery. These outgrowths form roughly about one-third of the thickness of the placenta, the remaining two-thirds consisting of a network of syncytio-trophoblast resting below on a thin zone of degenerate syncytium.

A somewhat more advanced stage in placental development is furnished by Tarsius Cl. 1, for which I am indebted to Professor W. E. LE GROS CLARK. The embryo, so far as I am able to determine, appears to be somewhat earlier than Tarsius 444A, No. 7 of KEIBEL'S Normentafeln ('07) and possesses well-marked primary optic vesicles and about 15 pairs of somites. The placenta has a diameter of 6 mm. As will be seen from Pl. 7, fig. 47, the mesodermal chorionic outgrowths have penetrated more deeply into the syncytio-trophoblastic network, they are more branched and are more richly vascularised by umbilical capillaries than those of 595. The syncytial network, in addition to providing the syncytial investment for the outgrowths, persists between them and encloses wide lacunar spaces occupied by maternal blood, whilst below their deep extremities, it forms a well-marked basal zone also enclosing conspicuous blood-filled lacunae. Figs. 48, 49 and 50 show the details of the syncytium under higher magnification. Its nuclei are specially noteworthy. They vary extraordinarily both in size and in shape but are mostly large, quite irregular in form and very deeply staining. Many of them are in active amitotic division as is evidenced by their lobed and irregularly branched character, the branches frequently appearing as bud-like

prolongations composed of a filamentous stem and an expanded extremity. In no other placenta have I ever observed such remarkable and bizarre nuclear forms as are depicted in figs. 49 and 50. It is also worthy of note that the syncytial surfaces bounding the lacunae are provided with what appear to be " brush borders," recalling those of the syncytio-trophoblast of the human chorionic villi.

In the course of further development, the mesodermal " villous " outgrowths, continuing to grow in length and branching repeatedly, ramify throughout the greater part of the syncytio-trophoblastic network. This latter, as in Cl. 1, appears as a more or less uniform but coarse reticulum and as the mesodermal processes penetrate into it, so it becomes spun out round them in the form of a thin enveloping layer, whilst still retaining its continuous net-like character.

The result is that the placenta comes to consist of coarse " villous " branches or trabeculæ, each formed of a mesodermal axis, enveloped by a thin layer of nucleated syncytio-trophoblast and all joined together into a more or less continuous net-like system by intervening portions of the original syncytial reticulum (Pl. 8, figs. 51 and 52). In between the trabeculæ are the irregular cleft-like lacunæ in which the maternal blood circulates, whilst in their mesodermal axes, immediately below the enveloping trophoblast, are situated the small umbilical capillaries. That is the condition we find for example in Tarsius 76, in which the fœtus measures in G.L. 2·9 cm. and the conical placenta 10 × 11 mm. in diameter (Pl. 8, figs. 51 and 52).

During the later stages of development, the placenta continues to increase in size and at term (Tarsius Cl. 2), it appears as a relatively large massive organ (17 × 14 mm. in diameter and 8 mm. in thickness), ovoidal in form and attached to the thin decidual layer of the uterine wall over only a very small area of it under surface, through which the maternal vessels enter and leave the placenta (*cf.* Pl. 3, fig. 29). The afferent (central) artery runs up through a mass of deeply staining tissue, composed apparently of degenerate syncytium and extravasated maternal blood, to open into a central sinus from which the placental lacunae are supplied, and from these the blood drains into the larger superficial lacunae which are situated directly below the investing chorionic mesenchyme (*cf.* Pl. 8, fig. 51) and which collectively represent a kind of peripheral sinus and so flows round into the efferent veins.

The marked increase in size which the placenta undergoes during the later fœtal stages of development is the result, according to HUBRECHT, of the centripetal lengthening of the mesodermal villous outgrowths. That is no doubt true, but it involves also their continued branching and subdivision. Whereas in the placenta of medium size such as that of Tarsius 812, which measures 13·5 × 9 mm. in diam. by 4 mm. in thickness (Pl. 8, fig. 53), the trabeculæ are relatively thick strands, the relations and structure of which are readily determinable in section, in the full- and nearly full-term placenta (Pl. 8, fig. 54) they have become so much reduced in thickness and form such a close and fine-meshed network, that their relations as seen in sections 8–10 μ. in thickness, are much less obvious at first sight.

The alterations in the endometrium which accompany the development of the placenta are of a remarkable character; indeed they appear to me to be unique, certainly for the Primates, but it is only possible to refer to them quite briefly here. As a matter of fact no detailed account of the changes in question has ever been given, though HUBRECHT ('99) has described the alterations in the uterine glands and the connective tissue stroma situated immediately below and around the tropho-placental mass. According to his account, which I am able to confirm, the neck-portions of the uterine glands commence to enlarge and their epithelium begins to thicken immediately the attachment of the blastocyst is effected (Pl. 4, fig. 30). The epithelium continues to increase until it completely obliterates the gland-lumen, the cell-outlines disappear and by the time the tropho-placental mass is established the gland-necks adjoining its upper half are represented by lightly staining solid syncytial masses, finely granular in character and containing numbers of mostly small pale staining nuclei (Pl. 4, fig. 31). These changes, first observable in the gland-necks, soon affect the deeper portions of the glands as well as those more remote from the placental mass and these also suffer hypertrophic degeneration with the result that the tropho-placental primordium becomes surrounded below as well as round its periphery by syncytial gland-masses (Pl. 5, figs. 34 and 35). The glands are at first separated by thin strands of delicate connective tissue but very soon, already in Tarsius 622 (Pl. 5, fig. 35), the connective tissue cells begin to enlarge. They proliferate actively and give origin to an irregular network of coarse strands, composed of small compactly arranged cells, in the meshes of which are enclosed the degenerate gland-remains. By the stage of Tarsius 175 (Pl. 5, fig. 37) these latter have largely disappeared, practically all that is left of them being a diffuse material, like a coagulum, in some of the spaces they formerly occupied. HUBRECHT refers to these strands as " " Gefässbahnen " since he thought their principal purpose was to serve as pathways for the placental vessels. In somewhat later stages, their cells undergo further enlargement and so form large glandular-looking elements of the nature of decidual cells which occur grouped around the vessels as well as in the form of irregular masses. As a result, the gland-spaces above mentioned become more or less completely obliterated. In the much later stage represented by Tarsius 72, fœtus G.L. 20 mm. (Pl. 3, fig. 29), the decidual cells themselves are seen to have become greatly reduced in number. Adjacent to the muscularis, masses of them, not greatly altered, are present, but over extensive areas below the placental mass they have undergone granular degeneration, whilst in the same position irregular spaces containing traces of granular debris mark their former sites.

HUBRECHT regarded the degenerate gland-masses as forming a kind of rampart around the early placental primordium, the purpose of which, he suggested, was to limit blood-extravasations during the time the placental circulation is becoming established. Whatever value there may be in this suggestion, I think there can be little doubt but that the degenerate glands and the decidual cells collectively constitute a not unimportant source of embryotrophic material which is available for the

nutrition of the embryo at a time prior to the complete establishment of the placental circulation.

In this connection reference may be made here to the unique condition of the yolk-sac in Tarsius. As may be seen from Pl. 3, fig. 29, it is relatively large and much folded and it is extremely well vascularized, but its most remarkable feature is the transformation of its mesothelial covering into a thick layer (twice or thrice as thick as the somewhat flattened endoderm), composed of large plump cells, columnar or more often pear-shaped in form, with rounded, often freely projecting, outer ends and possessing small, mostly basally situated nuclei. Most significant of all, their cytoplasm is crowded with fine granules. When I first observed the yolk-sac of Tarsius 72 in section, I felt bound to satisfy myself that it had not been accidentally turned inside out! I find that BRANCA ('13) in 1913 had also observed this thickened mesothelial layer in Tarsius 728 of the HUBRECHT collection, but for some unaccountable reason he regarded it as an artifact. In my opinion, it is no artifact, but a perfectly normal condition, an adaptive specialisation, distinctive of the Tarsius yolk-sac, the object of which is to facilitate the absorption of the abundant embryotrophic material present in the exocœlom and represented in preserved material by a dense coagulum such as is seen in Pl. 3, fig. 29. Accordingly, I regard the yolk-sac of Tarsius as playing a highly important rôle in the nutrition of the embryo during at least the earlier part of the gestation period.

The only other Primate in which I have observed the mesothelium of the yolk-sac definitely thickened is *Cebus macrocephalus* 548 of the BLUNTSCHLI collection, with an embryo of G.L. 3 mm.* The mesothelium here is composed of large cubical cells, with rounded outer ends and often separated from each other by clefts extending in for three-quarters of their height. Their nuclei in contrast with those of the mesothelial cells in Tarsius are large, oval or rounded and centrally situated. I have seen no signs of absorptive activity on the part of this layer. In *Cebus gracilis* 475 (embryo, G.L. 3·2 mm.), on the other hand, the yolk-sac mesothelium is in no way remarkable, and appears as a well-defined layer of flattened to low cubical cells, very little thicker than the endoderm. It should be mentioned that Cebus 548 is exceptional in two other respects and does not fit into what I regard as the normal series of stages, inasmuch as the cytotrophoblast has already undergone complete transformation into syncytiotrophoblast and the lacunæ in the latter are abnormally congested with maternal blood. Quite possibly the embryo of 548 would have failed to develop normally.

Returning to the endometrium of Tarsius, outside the region (decidua basalis) in which the glands and the decidual cells undergo the above described alterations, is a periplacental zone of no great thickness in which the glands do not undergo degeneration, but persist, at all events, up to the stage represented by Tarsius 72, though in a somewhat modified form. In that stage the zone extends out from the constricted base of attachment of the placenta for a distance of about 4·5 mm. Its glands are greatly

* I have more recently observed a corresponding condition of the yolk-sac mesothelium in *Papio porcarius* (27), embryo G.L. 2·65 mm.

enlarged, appearing as wide, somewhat flattened tubes, sometimes partially filled by a deeply staining material and bounded by a flattened nucleated layer of no great thickness, in which cell outlines are not apparent. So far, I have failed to observe any of these glands opening on the surface. That is no doubt to be accounted for by the fact that the zone is clothed all over by a very peculiar thick cellular layer, composed of large vacuolated cells, of quite variable form and superimposed on each other, several deep. This irregular layer appears to be of epithelial origin, since it passes into continuity marginally with the low uterine epithelium which clothes the remainder of the endometrium. There are indications that during life the trophoblast of the adjacent chorion was in intimate contact with its surface. Further study of this periplacental zone is necessary in order to determine its precise significance. Meantime we can only surmise that it plays a part in the provision of nutritive materials for the use of the developing embryo. Lastly, it remains to be mentioned that the remainder of the endometrium (corresponding to the decidua parietalis) is reduced (in Tarsius 72) to an extremely attenuated layer composed of the single-layered uterine epithelium and an underlying very thin layer of connective tissue, containing here and there a uterine gland. The extreme thinness of this region of the endometrium is no doubt the result of the stretching to which this portion of the uterine wall is subjected, but it is worthy of note that the chorion in relation to it is also very thin and quite devoid of blood-vessels.

It would thus appear that Tarsius differs from the other Primates in respect of the peculiar changes undergone by the endometrium during the development of the placenta, in the possession of a yolk-sac of high functional importance as an absorptive organ and possibly also in the extent to which the embryo is dependent for its nutrition on histiotrophic materials derived from the maternal uterine tissues.

We have seen that Tarsius develops a deciduate hæmochorial placenta of the net-like or trabecular type, and the question may be asked what is the relation of the Tarsius placenta to that of the Pithecoids and more especially to that of the Platyrrhines which also during its development exhibits a comparable hæmochorial trabecular character ?

I have shown that the trophoblast of Tarsius is unique both in its histological characters and in its behaviour during placental formation, and on these and other grounds set forth above, I conclude that the Tarsius placenta is too specialised to have been the actual forerunner of that of the Pithecoids, and I suggest that it represents one of the several attempts that were made, following on the primary attachment of the blastocyst, to utilize that attachment for placental purposes. In other words, I suggest that the placenta of Tarsius has evolved along lines of its own and that such general resemblance as it presents to the Platyrrhine organ is the result of developmental parallelism.

But I hasten to add the holding of that view in no way lessens the significance or value of the Tarsioid phase as the most important transitional stage in the evolution of the developmental processes in the Primates. We have only to suppose that the Pithecoids took origin from some other branch of the Tarsioid stock in which the attempt

at the formation of a hæmochorial placenta proceeded along lines more comparable with those we find in the existing Pithecoids, than does that of Tarsius.

The significance of the Tarsioid phase lies in this, that it shows us the first definite advances on the ancestral Lemuroid phase and the actual realisation of developmental tendencies foreshadowed in that. We see effected the first attachment of the blastocyst to the uterine lining and, as the outcome of that, an early essay in the development of a localised hæmochorial placenta ; we see commencing those processes of acceleration and abbreviation of the early developmental processes which reach their acme in the higher Primates, and which result in the precocious appearance of the extra-embryonal mesoderm and cœlom and the correlated early differentiation of the endodermal yolk-sac and the chorion and which result also in the replacement of the vesicular allantois by the almost solid connecting stalk, an outstanding example of developmental acceleration. And, lastly, we see in the Tarsioid phase, the retention of certain primitive developmental features, *e.g.*, the exposure of the embryonal ectoderm and the formation of the amnion by the closure of amniotic folds, which may be regarded as a direct inheritance from the ancestral Lemuroid.

CHAPTER III.

Pithecoid Stage.

We pass on now to what I propose to term the Pithecoid stage in the developmental history of the Primates. Under the designation, Pithecoid, I include the Platyrrhine monkeys of the New World (grouped in the two families of the Hapalidæ and the Cebidæ) and the Catarrhine monkeys of the Old World (comprised in the single family of the Cercopithecidæ), and, for my present purpose, I shall use the word Catarrhine in this restricted sense as designatory of the Cercopithecidæ and in contradiction to Platyrrhine. This usage is perhaps unwarranted since the group name Catarrhina has long been employed for the entire assemblage of Old World monkeys, anthropoid Apes and Man, but it is justifiable on embryological grounds, and indeed, for other reasons, has long been desirable. The anthropoid Apes (Hylobates, Orang, Chimpanzee, Gorilla) I shall group with Man as representative of the final or anthropoid stage in Primate development.

The Platyrrhines are commonly regarded on morphological grounds as representing a lower and more primitive grade in Primate evolution than the Catarrhines and that view is in consonance with the embryological data, but the striking resemblances in the early development of these two groups of monkeys point to their origin from a common Pithecoid stock which itself was presumably derived from a branch of the Tarsioidea, distinct from that which gave origin to Tarsius.

The resemblances in question are the justification for the recognition of a Pithecoid stage, but when we come to consider the details of placental development in the two

groups, we shall find certain well-marked differences in the behaviour of the trophoblast and in the structure of the placenta in the two which suggest that they early branched off from the parent stock and evolved along independent but to some extent parallel lines. The Platyrrhines proved to be the more conservative branch and may be supposed to have largely retained the developmental characteristics of the parent stock. They became isolated in the tropical forests of the South American continent and, failing to make any marked progress in the upward direction, they remain with us to-day as an end or terminal product of the Primate radiation. The Catarrhines, with the Northern Hemisphere for their habitat, proved much more progressive and by acceleration and abbreviation of their developmental processes, were able so to perfect them that one of their early branches proved capable of giving origin to the parent anthropoid stock.

The embryological evidence as I interpret it, lends no support to the idea of an independent or diphyletic origin of the two groups of monkeys.

The Pithecoid phase exhibits definite developmental advances on the conditions prevailing in the Tarsioid in respect of the following features, all of them of the nature of secondary adaptive specialisations as SELENKA ('00) clearly recognised :—

(1) The amnion is no longer formed from folds of the somatopleure in the old ancestral way, since its cavity (known in early stages as the primitive amniotic cavity) develops directly as a closed space inside the embryonal ectodermal mass of the very early blastocyst. This, the so-called " closed " method of amnion-formation, was probably induced by the precocious attachment of the covering trophoblast to the uterine lining. Under such conditions, the embryonal ectodermal mass was prevented from opening out on the surface to form the shield-ectoderm and so, we may suppose, it proceeded to differentiate *in situ* as best it could, and to permit of its doing so, the central cells in the upper half of the mass underwent degeneration, with resulting formation of a fluid-filled, eccentrically situated space and this space persisting, was later utilized as the amniotic cavity. Its roof, thinner from the start than the floor, formed the amniotic ectoderm, whilst its thicker floor differentiated to form a disc composed of columnar cells, the embryonal or shield-ectoderm. That is one of a number of possible explanations of the evolution of the amnio-embryonal vesicle as it is termed and, to my mind, the most probable one. On the other hand, the predeterminist might suggest that the amnio-embryonal vesicle developed directly in order to leave the covering trophoblast intact so that it could effect the primary attachment and thus afford the precociously developed connecting stalk the shortest route to the placental area of the chorion. This latter is one important result of the direct formation of the amnio-embryonal vesicle, whatever factor or combination of factors conditioned its origin in the first instance.

Very shortly after the amnio-embryonal vesicle is differentiated, a second closed sac is formed immediately below it. This is the endodermal yolk-sac vesicle. How it originates has been hitherto a matter of speculation, but we are now able to produce evidence based on its condition in SELENKA'S Keim S of *Nasalis larvatus*, which strongly

suggests that it arises directly by the hollowing out of an originally solid mass of endoderm (*v.*, pp. 108, 109 and Pl. 9, fig. 61) and not by the gradual spreading of the endoderm round the inner surface of the trophoblastic shell as is the case in the Lemurs and the lower Monodelphia.

Once the endodermal vesicle is established, we can affirm that the early Pithecoid blastocyst (Pl. 9, fig. 56) is in fundamental agreement with that of the Anthropoid as represented by Man (Pl. 20, fig. 113) in possessing an embryonal primordium composed of two precociously differentiated closed vesicles, super-imposed the one on the other, viz., an upper, larger and earlier formed amnio-embryonal vesicle, situated subjacent to the trophoblast at the upper pole and an underlying smaller and later formed endodermal vesicle, widely separated from the trophoblast by the extensive and precociously formed extra-embryonal cœlom, a structural condition marking a very striking advance on that obtaining in the early Tarsioid blastocyst and affording us at the same time a noteworthy duplex instance of developmental abbreviation.

It may be pointed out here that the occurrence of an amnio-embryonal vesicle and the associated closed method of amnion-formation is not distinctive of the higher Primates but is met with in representatives of several Monodelphian orders, by no means all closely related to each other (Cavia, certain Bats, *e.g.*, Pteropus, Tatusia, Galeopithecus). Whilst it would be hazardous, in the present state of our knowledge, to affirm that in the three forms last mentioned, the condition in question has been independently evolved, it is quite possible, and in the case of Cavia, we need have no hesitation whatever, since it is perfectly clear that this Rodent has evolved its characteristic mode of development involving interstitial implantation and the formation of an amnio-embryonal vesicle, within the limits of the order Rodentia. We regard the acquisition of an amnio-embryonal vesicle and the correlated closed method of amnion-formation as a purely secondary adaptive phenomenon, by no means primitive, as HUBRECHT maintained, but highly specialised. As HILL and TRIBE ('24, p. 588) have pointed out, " in all such cases the blastocyst either becomes directly attached to the uterine lining as the result of the proliferative activity of the trophoblast over at least the embryonal pole (*i.e.*, over an area including the covering trophoblast), or is actually imbedded or in process of becoming imbedded in that lining. We know of no recorded instance of closed amnion formation in a blastocyst which reaches the embryonal shield stage whilst still free in the uterine lumen."

In view of the fact that an amnio-embryonal vesicle can arise quite independently as a developmental adaptation, in Mammals by no means closely related genetically, it might be urged by upholders of the diphyletic origin of the two groups of monkeys that the same developmental parallelism sufficiently accounts for its presence in them. Such a contention I cannot for a moment entertain, since it is not merely the presence in the two groups of an amnio-embryonal vesicle that we have to account for but also the remarkable similarity, amounting to practical identity, in the details of the development and structure of the blastocyst in the two. That all this similarity can be

accounted for by parallelism in development I do not believe. I prefer to regard it as the outcome of heredity and as evidence of the close genetic relationship of the Platyrrhine and Catarrhine Pithecoids, as evidence in fact of their monophyletic origin.

(2) The extra-embryonal mesoderm and cœlom and the chorion are formed even more precociously than in Tarsius. The extra-embryonal mesoderm (the so-called primary mesoderm of the early human blastocyst), the homologue of that of the Tarsioid, is laid down long before the primitive streak is differentiated and is already fully established (along with the exocœlom and the chorion) in the earliest known Pithecoid blastocyst (SELENKA's Keim S. of *Nasalis larvatus*). We have thus no knowledge of its first origin, but in early blastocysts of Hapale and Cebus there is evidence of the existence of a median area involving the hinder margin of the shield-ectoderm and the immediately adjoining amniotic ectoderm which is in proliferative continuity with the extra-embryonal mesoderm, and in Keim S. there are less definite indications of proliferative activity in a precisely corresponding position. It is suggested that we have here the site of origin of the extra-embryonal mesoderm. If future observation should substantiate this mode of origin, then we should be justified in regarding this proliferative area in the Pithecoid, in so far as it involves the shield-ectoderm, as the precociously differentiated representative of the hinder extremity of the primitive streak of Tarsius.

(3) As in the latter, the vesicular allantois is replaced by the connecting stalk, the mesodermal primordium of which, furnished by the proliferative area above referred to, is very early laid down as a strand of cells extending between the latter area and the chorionic mesoderm.

(4) The primary attachment of the blastocyst to the uterine lining is, as SELENKA ('00) insisted, always effected by the trophoblast over the embryonal pole and thus involves the covering trophoblast. This attachment marks the site of formation of the primary placenta. But, owing to the small size and flattened form of the uterine lumen, the anti-embryonal pole of the blastocyst usually also comes into contact with the uterine lining and so establishes a second attachment, leading to the formation of an additional or accessory placenta, in which case the fœtus is provided with two discoidal placentas interconnected by umbilical vessels—the bidiscoidal condition—characteristic of the majority of the Pithecoids.

(5) The trophoblast, in particular its attaching or ectoplacental portion, invariably gives origin at a relatively early period in the history of the blastocyst to a syncytial layer on its outer surface and so becomes distinguishable into a basal parent layer of cytotrophoblast and a superficial derivative layer of syncytiotrophoblast. The cytotrophoblast retains its individuality for a longer or shorter period, and during that time continues to produce syncytiotrophoblast. The latter always assumes a more or less definitely reticular character and encloses lacunar spaces into which the maternal blood penetrates. It participates along with the cytotrophoblast in forming the

investment of the chorionic villous outgrowths and later when the cellular layer has been completely used up in its production, it alone forms the villous covering just as it does from the first in Tarsius. In addition to its investing and absorptive functions, the syncytiotrophoblast in the Pithecoids, as in the Anthropoids, exhibits active erosive and destructive properties and has the capacity of proliferating and of penetrating more or less deeply into the maternal decidual tissue in the form of sprout-like processes which may anastomose to form an irregular network.

The secondary (adaptive) nature of these early developmental occurrences in the blastocyst of the higher Primates was clearly recognised by SELENKA in his "Studien" (Heft 8, pp. 206–8) and in his shorter papers ('00*b*, '01). He instances in particular the formation of an amnio-embryonal vesicle and the correlated closed method of amnion-formation, the precocious appearance of the extra-embryonal mesoderm and cœlom, the early vascularisation of the yolk-sac and the replacement of the vesicular allantois by a connecting stalk. He regarded these happenings as the outcome of the very early attachment effected by the blastocyst to the uterine lining and concluded that "infolge caenogenetischer Anpassungen, sowohl seitens des Embryos wie seitens der Mutter, ist der Ernährungsmechanismus der Primatenkeime leistungsfähiger geworden" (Heft 8, p. 208), a conclusion which I venture to think is amply substantiated by the facts and considerations set forth in this lecture.

The material available for the study of the early development of the Pithecoids is unfortunately by no means extensive. Apart from the four-celled egg of *Macacus nemestrinus* described by SELENKA ('03, fig. 1, p. 331), we know nothing of the processes of cleavage and blastocyst formation in either of the two groups of monkeys. SELENKA, however, has described and figured in his "Studien" ('00, '03) three early blastocysts of Catarrhine monkeys. Of these, the blastocyst of *Nasalis larvatus* (Keim S.) is by far the most important, since it provides us with the earliest Catarrhine embryo so far known, judging from the condition of its yolk-sac; that of *Semnopithecus pruinosus* Lk. is probably just a little older, whilst the third (Keim Ca.) from *Macacus cynomolgus* is still more advanced, but like Lk. is of value mainly from the point of view of early placental development.

As concerns the Platyrrhines, the literature is a complete blank, but fortunately the BLUNTSCHLI collection contains an early blastocyst of *Cebus macrocephalus* (509) as well as a late blastocyst of *Chrysothrix sciureus* (467), with a presomite embryo, which is of importance for the development of the connecting stalk, whilst my own collection comprises an early stage of fused twin-blastocysts of *Hapale jacchus*, at a stage of development just a little later than Keim S. of *Nasalis*.

These twin-blastocysts of Hapale 2 and that of Cebus 509 constitute the earliest Platyrrhine developmental stages so far known.

Apart from some brief notes on the fused blastocysts with special reference to the problem of twinning (HILL, '26, HILL and HILL, '27), no description of this extremely interesting stage of Hapale has yet been published. The following *résumé* of the main

structural features of the embryo are based on the observations of C. J. HILL and myself.

Hapale, as is well known, is exceptional amongst the higher Primates in normally producing twins or even triplets. The twins are enclosed *in utero* in a common chorion, and each twin possesses its own discoidal placenta, though the placental circulations in the two are definitely interconnected. The present specimen demonstrates that we have to do in Hapale with biovular twins. What appears to have happened in this particular case was that the two minute blastocysts settled down side by side in the small uterine lumen, in contact with each other and with their poles reversed, and became attached to the dorsal and ventral walls respectively by their opposite embryonal polar areas. Their apposed walls then fused and subsequently broke down and disappeared, leaving only a slight annular ridge round the periphery to mark their site. As the result, the two embryonal primordia, attached to the chorion and situated diagonally opposite each other, project into a common cavity formed by the united extra-embryonal cœlomic cavities of the two blastocysts (text-fig. 14).

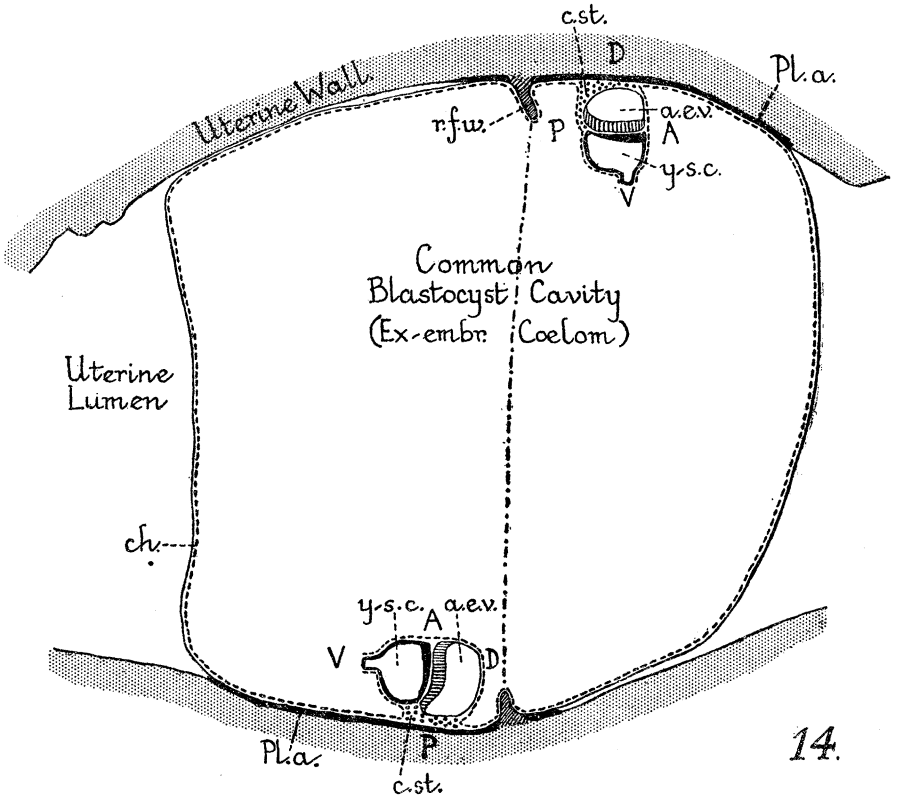
Neglecting this fusion, which is purely secondary and of no significance from our present point of view, we have here a quite small, early blastocyst (the two together having a diameter of just over 1·5 mm.), which has already acquired a relatively broad attachment to the uterine lining over its upper polar area, directly overlying the embryo. This primary attachment, from which the discoidal placenta of later stages originates, is much more extensive than that of the early blastocyst of Tarsius and is effected on quite different lines, the whole of the trophoblast on this surface being involved. Moreover, the flattened lower pole also lies in contact with the uterine lining, a relationship which testifies to the reduced character of the uterine lumen as compared with that of Tarsius, and which leads in most of the Pithecoids, though not in Hapale, to a definite attachment and the formation of an accessory or secondary placenta at the anti-embryonal pole.

The blastocyst is already well advanced developmentally and is comparable with the Tarsius blastocyst of ± 0·5 mm. in diameter, inasmuch as the extra-embryonal mesoderm and cœlom are established and its thin wall is formed of chorion. On the other hand, its ectoplacental trophoblast is nothing like so far advanced as that of the Tarsius blastocyst. But it is in the embryonal primordium itself that we see the most striking advance on the latter, since the embryonal ectoderm is no longer exposed on the surface, but forms the floor of the closed amnio-embryonal vesicle (text-fig. 14 and Pl. 9, figs. 55 and 56).

The embryonal primordium (measuring in the case of A about 0·27 mm. in vertical height × 0·23 mm. in antero-posterior length × 0·3 mm. in transverse diam.) is broadly attached by a thin layer of chorionic mesoderm to the undersurface of the placental area of the trophoblast and consists of two superimposed vesicles, the upper being the amnio-embryonal vesicle, enclosing the primitive amniotic cavity, and the lower the endodermal yolk-sac vesicle (Pl. 9, figs. 55 and 56). Both vesicles are

enclosed in a common investing layer of mesoderm (mesothelium), which passes into continuity with the very thin layer of chorionic mesoderm which lines the trophoblast and forms with that the chorion, and which also limits the extensive exocœlom.

The floor of the amnio-embryonal vesicle is constituted by the embryonal ectoderm, thickened to form the embryonal shield, of circular outline and about 0·15 mm. in



TEXT-FIG. 14.—Hapale 2. Semidiagrammatic figure (by Dr. C. J. HILL) to show the relations of the twin fused blastocysts. All that remains of the common wall (its position indicated by the dot and dash line) formed by the apposition and fusion of the contiguous walls of the two blastocysts is a slight annular ridge (*r.f.w.*, here seen in section on opposite sides) so that the exocœlomic cavities of the blastocysts now form a common cavity in which the two embryonal primordia are situated. That of the right twin is seen attached to the chorion on the upper side, to the right of the ridge (*r.f.w*), that of the left, to the chorion on the lower side, to the left of the ridge, the two primordia lying diagonally opposite each other. *A.* anterior end of the shield-ectoderm. *P.* posterior end. *D.* dorsal surface of embryo. *V.* ventral surface. *aev.* amnio-embryonal vesicle. *ch.* chorion. *c.st.* connecting stalk primordium. *Pl.a.* ectoplacental attachment. *y-s.c.* yolk-sac cavity.

diameter, whilst its roof, its lateral and front walls consist of a thin layer of amniotic ectoderm, continuous with the shield-ectoderm round its periphery. Between the roof of the vesicle and the overlying placental trophoblast is the thin layer of chorionic mesoderm above-mentioned, varying from one to three cells in thickness. The yolk-sac vesicle is noteworthy in several respects. Its endoderm is remarkable on account of its

irregular reticular character, and its penetration by short, branching, deeply staining strands prolonged from its investing mesothelial layer and possibly of angioblastic significance. Attention may also be called to the prolongation of the floor of the yolk-sac into a short, stalk-like hollow process (Pl. 9, fig. 55), suggestive of the yolk-sac process we have already encountered in Tarsius and which has also been described in early human blastocysts, but it is not possible to determine from this one stage whether or not it was ever connected with the chorion.

We come now to what we regard as the most interesting and important feature in this Hapale embryo. One of the two embryos has fortunately been cut longitudinally and in the median sections (Pl. 9, fig. 56) there is clearly visible at the posterior end of the amnio-embryonal vesicle a short but thick tract of compactly arranged cells. This tract is bounded in front, by the hinder margin of the shield-ectoderm and the amniotic ectoderm forming the posterior wall of the primitive amniotic cavity, and behind, by the upward continuation of the yolk-sac mesothelium. At its upper end it is seen to join the chorionic mesoderm, whilst below it can be traced into definite proliferative continuity with the posterior margin of the shield-ectoderm as well as with the adjoining amniotic ectoderm which is here distinctly thickened. Below the proliferating area the tract is prolonged for a short distance between the yolk-sac endoderm and its investing mesothelium as an irregular discontinuous layer of flattened cells from which short strands, similar to those arising from the mesothelium, penetrate into the reticular endoderm.

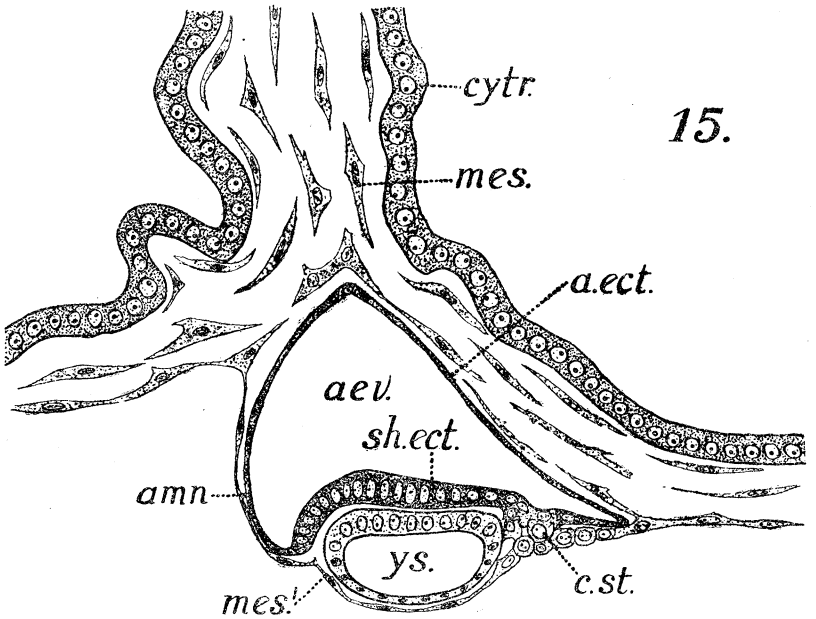
Here, then, we have a very remarkable condition in which a localised area of ectoderm, comprising the junctional region at the posterior margin of the embryonal ectoderm and the adjoining amniotic ectoderm, is in active proliferative continuity with the mesoderm at a stage so early that there can be no question of the presence of a primitive streak. Indeed we may state categorically that a primitive streak thickening does not exist.

The existence of such a proliferating area of ectoderm in this embryo and in this particular position raises a number of very interesting questions: (1) What is the significance of the cellular tract with which the area is directly continuous? We may answer this question at once by the statement that we regard it as the mesodermal primordium of the primitive connecting stalk. That that identification is correct is borne out by what we know of the development of the connecting stalk in early human embryos; for example, in the Fetzer embryo as Dr. FLORIAN'S reconstruction (text-fig. 17) shows, the connecting stalk primordium occupies a position identical with that of the cellular tract in question in the Hapale embryo, and moreover, as we shall see presently (*v.* p. 110), FLORIAN has observed in the Fetzer embryo an ectodermal area in precisely the same position as that of Hapale, which is likewise in proliferative continuity with the mesoderm of the connecting stalk primordium. (2) Apart from the Fetzer embryo, what further evidence is there of the existence of such an ectodermal proliferating area in other early Primate embryos? (3) Does it produce all the mesoderm present in the blastocyst at this stage or only that part which we have identified

as the connecting stalk primordium ? (4) What is its relation to the proliferation from the corresponding region of the shield-ectoderm in Tarsius ? (5) Has a similar and correspondingly early proliferation of mesoderm been met with in any of the lower mammals ?

Before attempting to deal with these questions, we may first give a brief account of the structure of the embryo of Cebus macrocephalus 509 and of SELENKA'S Keim S, both of which are of the greatest interest and importance.

The size of the blastocyst of Cebus 509 is not known, but the embryo is larger than that of the Hapale 2 blastocyst, whilst the trophoblastic differentiation in the region of attachment on the ventral wall of the uterus is enormously in advance of that of the latter (*v. post*, p. 123).



TEXT-FIG. 15.—*Cebus macrocephalus* 509. Median reconstruction of the embryo (by Dr. J. FLORIAN) × 150. *aev.* amnio-embryonal vesicle. *amn.* amnion. *a.ect.* amniotic ectoderm. *cytr.* cytotrophoblast. *c.st.* primordium of connecting stalk. *mes.* mesenchyme. *mes.*¹ mesothelium. *sh.ect.* shield-ectoderm. *ys.* yolk-sac vesicle.

The embryo is unfortunately defective in that the central part of the ventral wall of the yolk-sac is missing, though the portions of that wall which remain are sufficient to enable one to estimate the approximate size of the latter; whilst its preservation is not quite perfect, nevertheless the general structural details can readily be made out from the serial sections, the plane of which is oblique to the median plane. Curiously enough, this Cebus embryo shows certain interesting differences from the Hapale 2 embryo, indicating that the early development of the Hapalidæ and the Cebidæ does not proceed on strictly identical lines.

A semidiagrammatic median reconstruction of the embryo, for which I am greatly indebted to Dr. FLORIAN, is shown in text-fig. 15. The embryo measures approximately

0·35 mm. in length × 0·3 mm. in height × 0·3 mm. in breadth and, as can be seen from the text-figure, is broadly attached to the chorionic mesenchyme over the extent of the roof of the primitive amniotic cavity, only the anterior wall of the latter being established as an independent amniotic membrane.

The amnio-embryonal vesicle (about 0·32 × 0·14 mm. in internal diameter) appears triangular in section and exhibits the narrow caudal prolongation of its cavity over the region of what we regard as the connecting stalk primordium, which we have already observed in Tarsius and which is characteristic of all known embryos of the higher Primates of about this stage of development. The shield-ectoderm (about 0·22 mm. in length) forms the greater part of the floor of the primitive amniotic cavity and is well established as a thick layer of narrow columnar cells. Just behind the caudal margin of the yolk-sac, the shield-ectoderm loses its columnar character and passes over into a small median area, occupying the junctional region between it and the thin amniotic ectoderm and composed of polyhedral cells which pass over below into a thickened band of mesoderm, underlying the caudal prolongation of the amniotic cavity and likewise composed of large rounded polyhedral cells, arranged about two deep. This band thins out cranially and passes over into direct continuity with a layer of mesothelium which evidently continued forwards to clothe the endodermal floor of the yolk-sac vesicle, and it is worthy of note that this caudal part of the mesothelium is distinctly thicker than that clothing the cranial remnant of the yolk-sac floor. Caudally, the thickened mesoderm similarly thins out to become continuous with the mesothelium of the chorion, on a level with the caudal extremity of the amniotic cavity.

Here, then, we have a structural condition at the hinder end of this Cebus embryo which, clearly, is fundamentally identical with that seen in the Hapale embryo. In both there is present a caudo-median proliferative area involving the junction between the hinder end of the shield-ectoderm and the amniotic ectoderm, and in both the area is in proliferative continuity with a more or less thickened tract or band of mesoderm which extends back, in contact with the amniotic ectoderm, to become continuous with the chorionic mesoderm, and which we identified in the Hapale embryo as the primordium of the mesodermal part of the connecting stalk. But there is one significant difference in the mesodermal tracts in the two, since in Hapale the tract is clothed on its hinder surface by a layer of mesothelium, whereas in Cebus such a layer has not yet been differentiated and the tract merges directly into the mesothelium of the yolk-sac and chorion. Evidently we have to do in Cebus with an earlier developmental phase than that seen in Hapale and one moreover which provides striking evidence of the unity of origin of the extra-embryonal mesoderm in the Pithecoid. In the Hapale embryo, the derivation of the mesoderm of the connecting stalk primordium from the proliferative area was not open to question, but it remained problematical whether or not the chorionic and yolk-sac mesoderm was of like derivation. In this Cebus embryo, the continuity of that part of the mesoderm which will furnish the connecting stalk primordium with the remainder justifies the conclusion that the whole of the

extra-embryonal mesoderm is derived from one source, viz., the caudo-median proliferative area.

It remains to be mentioned that the yolk-sac vesicle (about 0·2 mm. in length) is much smaller than the amnio-embryonal vesicle. The endoderm forming its roof is composed of a thick layer of columnar cells, whilst its floor was evidently formed of a much thinner layer of more flattened cells, clothed by the layer of mesothelium above described.

As already indicated, the earliest Catarrhine embryo so far obtained is Keim S. of *Nasalis larvatus*, described and figured by SELENKA ('00, Heft 8, p. 189). His beautiful figures (figs. A and B, Taf. 11) convey an excellent idea of the general structure and placental relations of the blastocyst but are somewhat schematic and are not quite accurate in regard to certain details as study of the serial sections, fortunately preserved in the HUBRECHT collection, shows. The sections through the embryo form a fairly complete series and though some of them are imperfect, are in wonderfully good condition, both as regards fixation and the staining of the tissues, as may be judged from Pls. 9 and 10, figs. 59–62, all of which are based on photomicrographs. SELENKA describes his fig. B, Taf. 11 as a "Querschnitt durch den Keim," but the figure quite clearly represents a longitudinal section through the embryo. The actual sections appear to be slightly oblique to the median plane.

The dimensions of the blastocyst and the embryonal primordium are as follows:— Blastocyst, greatest diameter, 1·29 mm.; diameter at its attachment to endometrium, 0·986 mm. Embryonal primordium, 0·219 × 0·119 mm. in diam. Amnio-embryonal vesicle (excluding amniotic prolongation), 0·137 mm. in length × 0·068 mm. in height. Shield-ectoderm, 0·129 mm. in length × 0·04 mm. in thickness. Yolk-sac primordium, 0·086 × 0·051 mm. in diam.

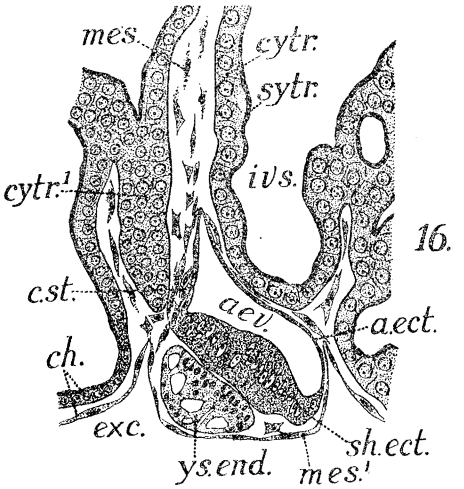
These measurements may be compared with those of blastocyst Lk. of *Semnopithecus pruinosus* (calculated from SELENKA'S fig. 7, Heft 10, p. 334). Blastocyst, greatest diameter, 0·67 mm.; diameter at its attachment to endometrium, 0·5 mm. Embryo, 0·12 × 0·12 mm. in diam.; Amnio-embryonal vesicle, 0·11 × 0·06 mm. in diam.; Shield-ectoderm, 0·109 mm. in length; Yolk-sac vesicle, 0·1 × 0·038 mm. in diam. SELENKA regarded this blastocyst as his earliest stage. The measurements show that it is distinctly smaller than Keim S., but his description of the embryo is not sufficiently detailed to enable one to judge whether it is younger or older than the latter.

The blastocyst of Keim S. is markedly flattened in its polar axis and is implanted by means of the villi arising from its embryonal hemisphere in a bowl-shaped depression in the endometrium, round which the latter is thickened to form a circular cushion-like elevation, whilst the slightly convex anti-embryonal hemisphere of the blastocyst is smooth and projects freely into the uterine lumen (Pls. 9 and 10, figs. 59 and 62).

Its wall (fig. 62) is formed of a thin chorionic membrane, composed of a layer of cytotrophoblast, overlain over the embryonal hemisphere only, by a thin layer of

syncytiotrophoblast and of an inner layer of chorionic mesoderm, much less developed than in Cebus 509 and in the form of a single layer of flattened cells, except where it is prolonged to form the axes of the larger villi. The chorion encloses the exocœlomic cavity and also the embryonal primordium which occupies the base of the large " central " villus, arising from the central or polar region of the embryonal hemisphere (Pl. 9, figs. 59 and 60).

The amnio-embryonal vesicle (Pl. 9, fig. 61, *aev.* and text-fig. 16), in marked contrast with the yolk-sac primordium, is fully established and exhibits a noteworthy agreement with that of Cebus 509 in its general relations, proportions and structure, but is considerably smaller. The shield-ectoderm appears in section as a thick slightly arched plate (of pear-shaped outline according to SELENKA) composed of high and



TEXT-FIG. 16.—*Nasalis larvatus.* Keim S. (SELENKA). Median longitudinal section (combination of two sections) of the embryo (by Dr. J. FLORIAN) × 200. *aev.* amnio-embryonal vesicle. *a.ect.* amniotic ectoderm. *ch.* chorion. *cytr.* cytotrophoblast. *cytr.*¹ the same, cut tangentially. *exc.* exocœlom. *ivs.* intervillous blood-space. *mes.* mesenchyme of villus. *mes.*¹ mesothelium. *sytr.* syncytiotrophoblast. *sh. ect.* shield-ectoderm. *ys.end.* yolk-sac endoderm.

narrow columnar cells with mostly centrally situated nuclei. Marginally it is continuous with the very thin amniotic ectoderm which, as SELENKA describes, is prolonged postero-dorsally, close below the trophoblast of the central villus, in the form of a pointed projection, evidently comparable with the caudal prolongation of the amniotic cavity in Cebus 509.

The very thin chorionic mesothelium on reaching the cranio-dorsal surface of the amniotic ectoderm is reflected down so as to invest the cranial and lateral surfaces of the latter and is then continued on to enclose the yolk-sac primordium, whilst the amniotic ectoderm forming the roof of the primitive amniotic cavity is separated from the trophoblast of the central villus by a correspondingly thin layer of mesoderm which appears to be continuous with the chorionic mesothelium along the line of its downward reflection.

In striking contrast with this thin mesothelial investment of the embryonal primordium, is a very definite tract or band of mesodermal cells which extends upwards from the level of the caudal extremity of the shield-ectoderm, immediately behind and in contact with the amniotic ectoderm forming the caudal boundary of the postero-dorsal extension of the amniotic cavity. The tract is composed of rather plump spindle-shaped cells with large oval nuclei, which are fairly compactly arranged up to four deep and which appear younger and more embryonic than the mesenchyme cells forming the axis of the central villus into which they pass over. In the serial sections, the tract is quite conspicuous in the three or four sections which precede the one in which the last trace of the yolk-sac occurs. It does not appear in the section figured on Pl. 9, fig. 61, but it is shown somewhat schematically in SELENKA's fig. B, Taf. 11, and is also indicated in text-fig. 16. SELENKA regarded this tract as the representative of the " Haftstiel oder später Bauchstiel," and so labelled it in his fig. B. With this identification I am in agreement. Comparison of text-fig. 16 with text-fig. 15 of Cebus 509 and Pl. 9, fig. 56, of Hapale, demonstrates that it occupies a position precisely comparable with that of the mesodermal tract which in these two forms we have seen reason to regard as the mesodermal primordium of the connecting stalk. Moreover, though the condition of the sections just in the critical region does not justify one in making a positive statement, there are fairly definite indications suggestive of the continuity of the tract with the caudal extremity of the shield-ectoderm just at its junction with the amniotic ectoderm as well as with the mesothelium where it dips in to become reflected round the yolk-sac primordium (text-fig. 16). I therefore venture to suggest that it is formed like the comparable tracts in Hapale and Cebus as the result of the proliferative activity of the caudo-median portion of the shield-ectoderm just at its junction with the amniotic ectoderm. If this suggestion is substantiated, the occurrence in common of this proliferating area in Platyrrhine and Catarrhine embryos would afford striking evidence of the essential unity of the Pithecoid type.

It remains to be mentioned that I have seen no evidence in the sections of the layer of mesoderm between the shield-ectoderm and the yolk-sac primordium which SELENKA states is present near the hinder end of the shield and which he depicts in his fig. A, Taf. 11. Nor have I observed the thickenings of the mesothelium, which he shows in his fig. B, underlying the cranial and caudal extremities of the shield-ectoderm. The three cells seen in Pl. 9, fig. 61, below and in front of the apparent cranial end of the shield-ectoderm, are probably displaced cells belonging to the latter, as the slender cell behind them almost certainly is displaced.

The endodermal yolk-sac primordium in this embryo, if my interpretation of its structure is correct, is of unique interest. It may be recalled that SELENKA, in his first description of this blastocyst, which is contained in a short paper dealing with the question of germ-layer inversion in the monkeys ('98, *a*), completely misinterpreted the yolk-sac and regarded the thin layer of chorionic mesoderm as endoderm and the genuine yolk-sac as a " Primitivplatte." In a second communication ('98, *b*), published

some three and a-half months later, he corrected these errors of interpretation and explains that "In dem Präparate, nach welchem die schematische fig. 4, p. 552 [of his first paper] entworfen wurde, ist nämlich der Dottersack derartig mazeriert und bis zur Unkenntlichkeit kollabiert, dass sein Lumen nicht zu sehen ist; er war zu einem napfförmigen Gebilde zusammengefallen, welches eine "Primitivplatte" vortäuscht. In der frischen Keimblase muss aber hier der winzige bläschenförmige Dottersack gelegen haben." He states that he was led to adopt this, undoubtedly the correct, interpretation, through the examination of preparations of an early blastocyst of *Cercocebus cynomolgus* [later designated Keim Ca (Heft 8, p. 197)], which showed essential agreement with that of *Nasalis*, except that the supposed "Primitivplatte" was represented by a hollow yolk-sac vesicle. In his final description ('00, Heft 8), he describes the yolk-sac as a diminutive round vesicle, which he states he had at first overlooked because of its collapsed condition. In his fig. B, Taf. 11, it is depicted, obviously schematically and on the basis of its condition in Cercocebus, as an oval vesicle, with a thicker dorsal wall composed of cubical to low columnar cells and a thinner ventral wall of more flattened cells.

My own study of the sections leads me to put forward an interpretation of the yolk-sac which is quite different from that of SELENKA, to wit, that we have here neither a macerated nor a collapsed yolk-sac vesicle, but a hitherto undescribed stage in the development of the same, viz., the stage when an originally solid endodermal yolk-sac primordium is in course of becoming converted into a hollow vesicle by a process of vacuolization. This may seem a large claim in view of the defective condition of the yolk-sac, but no other explanation, not even that of imperfect fixation, seems to me compatible with the remarkable appearance it presents in section as seen in Pl. 9, fig. 61.

In the serial sections through the embryo, the yolk-sac, or at least its larger dorsal portion, is recognizable in some fourteen sections, commencing with SL. 14, s. 1, and terminating with SL. 16, s. 1. In these two sections, mere traces of the yolk-sac are present; in SL. 14, s. 3, 4 and 5, the primordium is complete except for a slight break in the caudal wall of s. 4; s. 5 is the most instructive in the series, and is depicted in Pl. 9, fig. 61; in the remaining sections, its floor, as well as the investing mesothelium, is lacking, but in the more centrally situated of these sections, *e.g.*, SL. 14, s. 8, sufficient of the yolk-sac remains to show that it had a similar structure throughout its extent.

The primordium in Pl. 9, fig. 61, is seen to lie below the shield-ectoderm, being separated from the same by an artificial cleft, and to have the form of a plano-convex ovalish mass, enclosed by the cœlomic mesothelium. Histologically it appears as a continuous structure in which cell-outlines are not apparent, but we may distinguish in it an upper thick, solid portion containing numerous nuclei, the upper surface of which, during life, was no doubt closely applied to the under-surface of the shield-ectoderm, a middle vacuolated zone and a very thin limiting layer bounding the lower surface of the mass and lying adjacent to the mesothelial investment.

The upper solid zone forms about half the total thickness of the primordium and consists of a light staining cytoplasmic matrix, the upper surface of which possesses a fairly definite smooth contour, but below it is devoid of any definite limit, since it is continued into a few delicate pale-staining strands which, separated by vacuolar spaces, extend across the middle zone to join the lower limiting layer. Its upper third or so is free of nuclei, but in the remainder of its extent there are present numerous nuclei which vary both in size and in shape, but are mostly small and deeply staining, some of them presenting a shrivelled and rather degenerate-looking appearance. The middle zone occupies, I believe, the site of the future yolk-sac cavity. Of the strands which cross it, the two most cranially situated are the best marked. They are separated by a narrow cleft and appear at first sight like columnar cells, each possessing a nucleus situated close to its origin from the upper zone. In front of the most cranial of these two strands, between it and the downward continuation of the upper zone, is a well-marked vacuolar space, whilst behind them is a similar space, bounded by a third strand, wider, but much less prominent than the first two, which starts by a broad base and narrows slightly as it passes down to join the lower layer. Behind this, again, is a quite thin and rather indefinite strand separating the two caudally situated vacuolar spaces. In this section, accordingly, we can recognize four cytoplasmic strands, more or less well defined, and five vacuolar spaces, one small and cleft-like, the others much larger. By the disappearance of these strands and the confluence of the spaces, I suggest the continuous yolk-sac cavity is formed.

The lower limiting layer of the primordium, quite thin and rather irregular in character, contains small oval or spindle-shaped nuclei, less deeply staining than those of the upper zone. It bounds the primordium caudally as well as ventrally, and is in continuity with the upper zone as well as with the cytoplasmic strands of the middle zone. It represents, I suggest, the ventral wall of the future yolk-sac vesicle, whilst the nucleated upper zone is destined to furnish the dorsal wall of the same, that wall in the early embryos of Cebus and Hapale being distinctly thicker than the ventral.

If my interpretations of the structural features of Keim S. are correct, this embryo may well be regarded as constituting one of the most important early Primate developmental stages so far described. But from our present point of view, its chief interest lies not so much in the light it sheds on early Primate ontogeny as in the striking similarity in structural plan it presents to early Platyrrhine embryos as represented by those of Cebus 509 and Hapale 2, and the similarity would be still more striking if the yolk-sac of Keim S. had attained the vesicular condition as seen, for example, in SELENKA'S Keim Ca of *Macacus cynomolgus* (Heft 8, p. 197, *v.* fig. 20*a*, Pl. 21). We have only to compare text-fig. 15 of Cebus 509 with text-fig. 16 of Keim S. to convince ourselves that the two embryos conform to a common structural plan. I need only call attention to the presence in both of an amnio-embryonal vesicle, practically identical in its relations and structure in the two, of an endodermal yolk-sac vesicle (or primordium),

much smaller than the amnio-embryonal vesicle and widely separated from the chorion by an extensive exocœlom, and lastly of a mesodermal connecting stalk primordium with similar relations to the amniotic prolongation, and almost certainly formed in the same way in the two, by the proliferative activity of a caudo-median area of ectoderm, involving the shield-ectoderm and the amniotic ectoderm at the hinder end of the amnio-embryonal vesicle.

These agreements between the two embryos, representative of the Platyrrhines and the Catarrhines, bear striking testimony to the unity of the Pithecoid assemblage, and lend no support to the idea entertained by some authorities of the independent origin of the two groups of monkeys.

We are now in a position to attempt replies to the questions propounded above (*ante*, p. 102, 103).

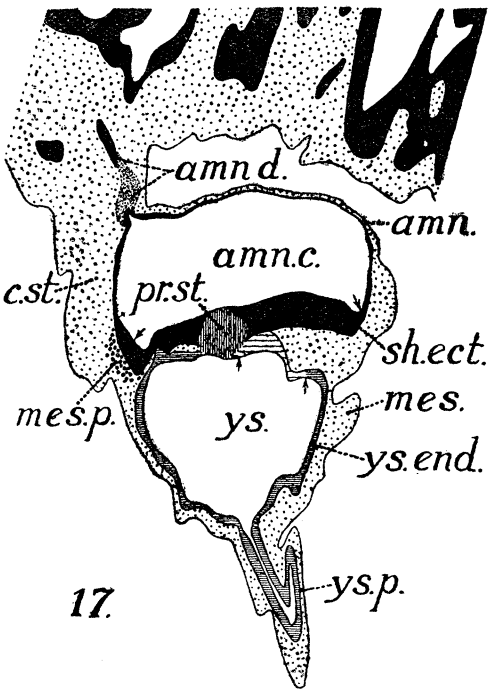
Question 2, as to the occurrence of the caudo-median proliferative area of ectoderm in other Primate embryos, has already been partially answered in our description of the embryo of Cebus 509 and Keim S. We have seen that such an area exists in the former and, with great probability, in the latter, and it now remains to call attention to the recent observations of my colleague, Dr. J. FLORIAN, on this same region in early human embryos. Dr. FLORIAN'S conclusions were arrived at after he had had the opportunity of seeing our sections and figures of Hapale, and of discussing the origin of the primary mesoderm with us, and are of outstanding interest in the present connection. It so happened that Dr. FLORIAN, at the time, was in process of completing with Dr. FETZER a detailed account of the Fetzer embryo (FETZER, '10), and, with their kind permission, I am able to reproduce here a graphic reconstruction of the embryo (text-fig. 17), and to give a summary of their conclusions, which are now in course of publication.*

Whilst studying the sections of this embryo, Dr. FLORIAN had been greatly puzzled by the presence of an area of ectoderm, situated immediately behind the cloacal membrane, and involving the junctional region between the shield and amniotic ectoderm which was in evident proliferative continuity with the adjacent mesoderm of the connecting stalk primordium (text-fig. 17, *mes.p.*). Comparison of this text-figure with Pl. 9, fig. 56, representing a longitudinal section through the Hapale embryo reveals a similarity in the relations in this region in the two embryos, amounting to practical identity. Dr. FLORIAN is now of opinion that the area in question represents the site of origin of the primary mesoderm, but he considers that in this stage, in which the first indication of the primitive streak has appeared, the production of primary mesoderm is on the wane, since appearances suggestive of degeneration are already evident in the area. He has also observed the same proliferating area in the Strahl-Beneke embryo, and search through the literature has led him to believe that in the very early embryo of Peters the same proliferation also occurs, and in much more marked degree than in the Fetzer embryo. He also suspects that the cellular material, designated as

* Since published. FETZER, M. and FLORIAN, J., 'Z. mikr-anat. Forsch.,' vol. 21, 1930.

" zerfallende Epithelwucherung des Amnions " in fig. 9, p. 415, of VON MÖLLENDORF'S description of his embryo OP (VON MÖLLENDORF, '26), represents the degenerate remnant of the proliferating area, and lastly, it may be mentioned that he has shown me an unpublished photo-micrograph given to him by Professor VON MÖLLENDORF of his embryo WO, in which there appears to be present a primary mesodermal proliferation in precisely the same position as that of the Hapale embryo.

The extra-embryonal or so-called " primary " mesoderm of the human blastocyst, it may here be noted, is extraordinarily precocious in its appearance. It is apparently formed so early that it is able to fill up the cavity of the minute blastocyst as a delicate cellular reticulum enclosing fluid-filled spaces. In the earliest-known human blastocyst, the " MILLER " ovum, with an average internal diameter of only 0·35 mm., STREETER



TEXT-FIG. 17.—Idealised median section through the Fetzer embryo (after FETZER and FLORIAN, '30, fig. 53). *amn.* amnion. *amn.c.* amniotic cavity. *amn.d.* amniotic duct. *c.st.* connecting stalk. *mes.* mesoderm. *mes.p.* mesodermal proliferation from hinder margin of the shield ectoderm (*sh.ect.*) and adjoining thickened amniotic ectoderm. *pr.st.* primordium of primitive streak. *ys.* yolk-sac endoderm. *ys.p.* yolk-sac process.

('27) describes it as a mesenchymatous tissue, the meshes of which are filled by an albuminous fluid. It forms a membrane-like layer, lining the trophoblast, whilst a corresponding layer invests the embryonal primordium and suspends it from the chorion, these two " membranes " being connected by irregular " trabeculæ " extending across the central region of the blastocyst. The " primary " mesoderm of the early human blastocyst thus differs widely in its characters from its homologue in the earliest-known

Pithecoid (Keim S.). Up till now we have had no knowledge of how it originates. It has been suggested that it is separated off in the morula-stage (hence the name morula-mesoderm (STIEVE, '26); that it arises from the amnio-embryonal cell mass about the time of formation of the blastocyst-cavity and prior to the appearance of the amniotic cavity, or that it may even be a derivative of the trophoblast (STREETER, '26).

We venture to claim that our own observations and those of FLORIAN provide a possible solution of this much debated problem, but whether that be so or not, they certainly afford a very striking demonstration of an important and fundamental agreement in the details of the early ontogeny of the Pithecoid and Anthropoid Primates.

As concerns our questions 3 and 4, we have already in our description of the Cebus embryo 509 provided cogent evidence in favour of the conclusion that the caudo-median proliferative area gives origin to the whole of the extra-embryonal mesoderm and not merely to that part of it which forms the connecting stalk primordium, and we would accordingly answer the first alternative in our third question in the affirmative. Moreover, quite apart from that evidence, it seems altogether unlikely that in such early developmental stages there should be two distinct and unrelated centres of mesoderm formation, one for the exocœlomic mesoderm and another for that of the connecting stalk primordium.

Coming to question 4, if we are correct in assuming that in Tarsius the hinder end of the primitive streak is the first part to become active and that from it the exocœlomic mesoderm is produced, then we need have no hesitation in homologising the caudo-median proliferative area in the Pithecoids with the precociously differentiated caudal extremity of the primitive streak in Tarsius, even if that area should cease its proliferative activity before the primitive streak is completely differentiated and in spite of the fact that it involves amniotic as well as shield-ectoderm, since the participation of the former is obviously secondary and the result of the evolution of the amnio-embryonal vesicle, and in spite of the further fact that it produces connecting stalk as well as exocœlomic mesoderm. All we need assume is that the developmental acceleration which is evident in the precocious activity of the hinder end of the Tarsius primitive streak has manifested itself here also in the Pithecoid and in still more exaggerated form.

Finally, as concerns our last question (5), although we know of no lower mammal with a comparable caudo-median proliferative area, it is perhaps of interest as evidence of the potentialities possessed by the mammalian germ to recall that PATTERSON ('13, p. 594) has described in the early blastocyst of Tatusia the proliferation of extra-embryonal mesoderm from the embryonal ectoderm of the amnio-embryonal vesicle, just below its junction with the amniotic ectoderm.

The last Platyrrhine stage to which I wish here to direct attention is an embryo of *Chrysothrix sciureus* 467, of Professor BLUNTSCHLI'S collection. It belongs to a

much later developmental stage than the foregoing embryos and is of special interest as showing the early relations of the connecting stalk.

The blastocyst (6 mm. in diam. and very large relatively to the size of the embryo) possessed a circular placental attachment to the ventral wall of the uterus (3·84 mm. in diam. in section) and a corresponding but broader dorsal attachment, the broad ring-like band of chorion læve between the two being thin and smooth.

The embryo lies adjacent to the ventral attachment and is attached by the connecting stalk, forming its caudal continuation, to the chorionic mesenchyme. It has evidently undergone rotation during development or perhaps some displacement during fixation since in the sections the yolk-sac lies adjacent to the chorion and the amnion away from it. In the graphic reconstruction, shown in fig. 18*a*, Pl. 21, the embryo is represented in the position it occupies in the sections. The sectional plane is longitudinal but slightly oblique.

The embryo has a total length from its anterior margin to the caudal tip of the amnion of 1·84 mm., whilst from the anterior margin of the shield-ectoderm to the posterior end of the primitive streak it measures just under 1 mm. (0·978 mm.). It possesses a flat medullary plate, a short head-process and a primitive streak measuring about 0·2 mm. in length.

The amnion is now completely established and of great extent and possesses a long narrow caudal prolongation which runs back along the connecting stalk, to terminate in close proximity to the placental trophoblast. So close indeed is it to the latter that but slight growth on its part would result in the establishment of a secondary connection between amnion and chorion, with the resulting formation of an amniotic stalk or duct such as SELENKA ('03, p. 341) has found in a complete form in three out of thirteen embryos (including an embryo of Hylobates) examined by him and in a reduced condition in others and such as is also well known in early human embryos (text-fig. 17, *amn.d.*), where it appears as a more or less luminated or solid strand which, when well developed, passes up in the connecting stalk from the caudal extremity of the amnion to join the chorionic trophoblast and sometimes even opens on the surface as in the case of the embryo (Cu) of *Macacus cynomolgus* described by SELENKA ('03, p. 340) and of the human embryo (H 381) described by STUMP ('29). This amniotic strand or duct is clearly a purely secondary structure which owes its existence to the presence of the caudal prolongation of the amnion along the primitive connecting stalk, but its common occurrence in the Catarrhine Monkeys, Anthropoid Apes and Man is, nevertheless, of considerable interest.

The yolk-sac has a length of 1·17 mm. and is dorsoventrally flattened, a feature often seen in much later embryos. Its mesothelial layer is quite thin, as also is its endodermal lining. From its posterior end, shortly behind the termination of the primitive streak and just behind the possible site of the cloacal membrane, a very short tubular diverticulum (0·056 mm. in length) penetrates into the mesoderm of the connecting stalk (Pl. 10, fig. 63, *all.d.*), but it is not possible to determine from this

one stage whether or not it represents the endodermal allantoic canal. It certainly occupies the right position, but its endoderm does not appear to be definitely thickened.

The connecting stalk in this embryo shows a very definite advance on that of the early Hapale embryo and is now beginning to assume its definitive condition. Two regions may be distinguished in it (fig. 18*a*, Pl. 21, and Pl. 10, fig. 64, *c.st.*^{1}, *c.st*^{2}): (1) an anterior thicker part, situated directly behind the posterior extremity of the yolk-sac and composed of compact mesoderm which can be traced forwards into direct continuity with the primitive streak mesoderm, and (2) a posterior thinner less compact part underlying the caudal prolongation of the amnion and in direct continuity with the chorionic mesenchyme. We suggest this posterior part is derived from what we have termed the connecting stalk primordium in the early Hapale embryo, whilst the anterior part represents a later addition of direct primitive streak origin. If that be so, then we would seem to have represented here, the intermediate stage in the evolution of the connecting stalk between the Tarsioid and the Anthropoid. In the Tarsioid, the mesoderm of the connecting stalk appears to be derived directly by proliferation from the primitive streak just as is the allantoic mesoderm in the lower mammals. In the Pithecoid, as represented by the Platyrrhine, the primordium of the stalk consists in the first instance of primary (extra-embryonal) mesoderm, derived from the precociously established proliferating area of ectoderm at the hinder end of the amnio-embryonal vesicle and this is supplemented later by a definite and large contribution of primitive streak mesoderm. In the Anthropoid as represented by the human embryo, the primary mesoderm reaches a greater development than in the Pithecoids and it would seem to take a larger share in the formation of the primitive connecting stalk than in them. In the early blastocyst (text-fig. 17), prior to the appearance of the primitive streak mesoderm, the primitive connecting stalk is already well differentiated and is distinguishable into two parts, a short, cylindrical, distal part which is continuous above with the chorionic mesenchyme and a longer proximal part which is attached to the amniotic ectoderm forming the posterior wall of the primitive amniotic cavity and which extends down to the level of the proliferating area of ectoderm (*mes.p.*). From this area, we have suggested the whole of the primary (extra-embryonal) mesoderm (including that part of it which forms the primitive connecting stalk) is derived, and though it is not possible to speak with certainty, it does appear as if the contribution of the primary mesoderm to the stalk was larger in the Anthropoid than in the Pithecoid. But whether this be so or not, the important facts remain that in both the primitive connecting stalk consists at first of so-called primary mesoderm, and that this is later reinforced by the addition of mesoderm proliferated from the primitive streak.

As in Tarsius and the Anthropoids, the endodermal constituent of the connecting stalk in the Pithecoids normally appears to have the form of a slender tubular (allantoic) canal with a thickish epithelial wall, which terminates blindly in the mesenchyme of the proximal portion of the stalk. In the 3·2 mm. embryo of Cebus 475, it measures in diameter 0·2 × 0·085 mm. But it is a curious and interesting fact that in the 6 mm.

embryo of Hapale jacchus, as I have elsewhere recorded ('19, *cf.* also '28) the allantoic canal is represented by a flattened cavity, 2·5 mm. in length by 2 mm. in width, with a quite thin lining of endoderm, which extends along one side of the connecting stalk and whose outer wall is likewise extremely thin. At this stage, accordingly, the connecting stalk of Hapale may be described as possessing an allantoic cavity and as semi-vesicular. It is thus of interest as presenting us with a condition which is in some degree intermediate between the primitive vesicular allantois of the Lemur and the almost solid connecting stalk of the other higher Primates. But the condition here described is only a transient one since the umbilical cord of the fœtus of Hapale H.C.1 (G.L. 34 mm., Pl. 10, fig. 67) exhibits the normal Primate structure.

There is one other feature in the connecting stalk of this Chrysothrix embryo which is deserving of brief mention here and that is the presence of vascular primordia in its mesoderm and also in the chorionic mesenchyme adjoining its attachment, when as yet there is no trace of a corresponding differentiation in the mesoderm of any other part of the embryo or chorion. The primordia in question take the form of strands of spindle-shaped cells and of small endothelially lined spaces, some of them in process of formation, others well differentiated and occupied by primitive blood-cells (Pl. 10, figs. 63 and 64, *cp.*[1]). This same precocious and independent appearance of vascular primordia in the mesoderm of the connecting stalk long before they appear in the body of the embryo is a phenomenon we have already encountered in Tarsius (*ante*, p. 79) and it is one well recognised by the human embryologist (*cf.* GROSSER, '27; M'INTYRE, '26).

According to M'INTYRE, in the human embryo, "differentiation to angioblastic tissue occurs at about the same time in the yolk-sac, body-stalk and chorion, while it appears at a slightly later stage in the villi" (*loc. cit.*, p. 110), but in Tarsius and very probably also in Chrysothrix, angiogenesis first begins in the connecting stalk. Its object is, of course, to enable the circulation to be established in the chorion and its villi at the earliest possible moment and it is very interesting to find that the Tarsioid and the Pithecoid in respect of this feature also have already anticipated the Anthropoid.

In the present connection it may be noted that BRYCE ('24, p. 556) has expressed the view that the reason for the precocious development of the extra-embryonal mesoderm in the human embryo is that "it is primarily an angioblastic tissue," and we may well agree that its angiogenetic function is certainly a most important contributory reason for its early appearance.

This phenomenon, moreover, provides us with yet another example of developmental adaptation and acceleration, all the more striking when we remember that the direct ingrowth of the allantoic vessels into the chorion in the Lemuroids was in itself a very great advance in chorionic vascularisation on the primitive Mammalian plan.

As concerns the later embryonic and fœtal stages of the Pithecoids, SELENKA, in his interesting paper "Die Gleichartigkeit der Embryonalformen bei Primaten" ('01) calls attention to the striking conformity in the configuration of the embryonic body

in the forms studied by him and states that in the further course of development, the embryos of the Catarrhine monkeys, the anthropoid apes and man resemble each other "ganz erstaunlich." KEIBEL ('04, '06) also, after a detailed study of SELENKA'S material remarks on the great similarity which is noticeable between the young embryos of different species of monkeys and between these and the corresponding embryos of man, but he lays stress on the fact that differences (exclusive of the development of the tail) very early manifest themselves as well in the development of the single species of Catarrhines as between the embryos of the latter and those of man.

BLUNTSCHLI ('13, p. 199) in his preliminary account of his material makes some very interesting remarks on Platyrrhine embryos. He states that comparison of the ontogeny of the Platyrrhines with that of man yields in regard to general features quite fundamental similarities (Analogien), but that in detail, differences already exist in quite early stages, even before the limb-primordia appear, for example, the Cebus embryo of this stage is characterised by its wide mouth-bay and its enormous heart. So also in Hapale (as I have myself observed in the 6 mm. embryo) and in Chrysothrix, the extremely voluminous heart remains for long an outstanding characteristic, and with this feature is associated the relative smallness of the head in proportion to the trunk as in all monkeys and in contrast with the human embryo. The development of the head, he states, proceeds relatively more rapidly in the Platyrrhine monkeys than in man, perhaps because of its smaller size. Its fore-brain region, though smaller than that of the human embryo of the corresponding stage, as in all monkeys, is of much the same shape as in the latter, whilst its diencephalic and mesencephalic regions exhibit a much greater difference, being shorter as well as narrower.

On Pl. 10, figs. 65–68, I have provided four figures of fairly comparable fœtal stages of Galago, Tarsius, Hapale and Homo to illustrate the fact that in spite of obvious differences, they exhibit a very decided family resemblance to each other and are all unmistakably members of the Order Primates.

A.—*Pithecoid Stage—Placentation.*

The general course of the development and the structure of the placenta in the Platyrrhines and Catarrhines is now fairly well known, thanks to the labours of a large number of investigators from the time of BRESCHET (1845) onwards, and including amongst others, TURNER ('77), SELENKA ('99, '00, '03), STRAHL ('03), STRAHL and HAPPE ('05), WISLOCKI ('29), though we are still ignorant of the earliest stages in the attachment of the Catarrhine blastocyst.

The double discoidal type of placenta is of common occurrence in both groups, but its accessory member is subject to generic and even specific variation, for example, amongst the Catarrhines, the placenta is double in Nasalis ; it is usually double in Macacus, but occasionally single in *M. rhesus* and in *M. cynomolgus* (*irus*) ; in Semnopithecus (Pithecus) it is also normally double, but out of five examples of *S. cruciger*, SELENKA records three with the bidiscoidal condition and two with a single placenta ; in Papio,

on the other hand, the placenta is single. Amongst the Platyrrhines, the double placenta is usual in Cebus, Ateles and Chrysothrix (Saimiri), but in one example of *Chrysothrix nigrivittatus* (816) in Professor BLUNTSCHLI'S collection, there is only a single dorsal placenta (BLUNTSCHLI, '13); in Mycetes (Alouatta) it is normally single but STRAHL and HAPPE record one instance of the occurrence of the bidiscoidal condition in this genus; whilst in Hapale it is always single.*

But apart from this general agreement in placental form, there are such noteworthy differences in the development and structure of the placenta in the two existing Pithecoid groups that we must regard them as representing divergent lines of evolution. The Platyrrhines would seem to have branched off quite early from the primitive Pithecoid stock, retaining and perhaps elaborating its type of placental development, whilst the Catarrhines took a short cut and went on to develop their placenta along lines which led directly to that of the Anthropoids.†

The differences in question are due in large measure to a difference in the behaviour of the trophoblast in the two groups and partly also to correlated differences in the endometrial reactions in the two.

In Tarsius, as we have seen, the ectoplacental trophoblast after effecting a very localised attachment to the endometrium, transformed itself completely (and at a very early stage in the development of the blastocyst) into a rounded mass of peculiar trophoblast which then had to depend on its own inherent powers of growth to meet the demands made upon it to provide at one and the same time a covering for the ingrowing processes of the chorionic mesenchyme and a lining for the maternal blood-lacunæ.

The Pithecoid stage shows us certain definite advances on that condition. In the first place, the ectoplacental trophoblast exhibits from the first a relatively broad attachment to the endometrium, which rapidly expands with the growth of the blastocyst and uterus. Then, in the second place, the originally single-layered ecto-placental trophoblast, practically immediately it has destroyed the hypertrophied and thickened uterine epithelium (which, judging from Hapale, appears to be the first reaction to the primary attachment) proceeds to thicken and to give off cells on its outer side. These run together to form a syncytial layer, which is capable of invading and destroying the maternal endometrial or decidual tissue, with which it comes into contact. In other words, the trophoblast undergoes differentiation into a basal, cellular layer, the cytotrophoblast, and a superficial syncytial layer, the syncytiotrophoblast. And the important point is that here the cytotrophoblast retains its individuality for a longer or shorter time during the development of the placenta, longer in the Catarrhines than

* In his paper on the placentation of the Primates, WISLOCKI ('29) has provided two most useful tables in which are collected the known facts relating to the form of the placenta in the higher members of the Order, to which the reader is referred for further details.

† WISLOCKI ('26), I find, has also reached much the same conclusion. He writes (p. 479), "the placental arrangements of catarrhines and platyrrhines derive from a common stem characterised by a labyrinthine placenta, with the existing platyrrhines less removed from that stem."

in the Platyrrhines and so continues to produce syncytiotrophoblast until it is finally completely transformed into the latter.

Moreover, the syncytiotrophoblast here in the Pithecoid exhibits other and quite different characters and properties to that of the Tarsioid. There, it was relatively passive and inert in its relations to the maternal tissues. Here it is endowed with much more potent cytolytic properties and is capable of active proliferative growth and of burrowing into the vascular decidual tissue in the form of an irregular network. It erodes and destroys that tissue and opening up its capillary vessels, its lacunar spaces very early become filled by maternal blood. In this way it provides a richly vascularised bed into which sprout-like processes of the cytotrophoblast of the chorion, occupied by chorionic mesenchyme carrying the fœtal capillaries, can grow and branch.

Now it is just in the development of the syncytiotrophoblast that we find a marked difference in the two groups of monkeys. As STRAHL ('06) was the first to show and his observations have been fully confirmed by ourselves (*cf.* HILL and SANSOM ('23)), and by WISLOCKI ('29), the Platyrrhines are characterised by the extraordinary profuseness of their trophoblastic proliferation, the syncytiotrophoblast reaching an extent and massiveness out of all proportion to that of the Catarrhines and that distinction conditions, as we shall see, certain characteristic differences in the mode of development and in the structure of the placenta in the two groups, the Platyrrhine placenta recalling that of Tarsius, the Catarrhine foreshadowing in the most unmistakable fashion that of the Anthropoids.

B.—*The Placentation of the Platyrrhina.*

The following account of the development of the Platyrrhine placenta is largely based on a study of the rich material of Chrysothrix and Cebus contained in Professor BLUNTSCHLI's collection, supplemented by my own material.

Neither STRAHL nor WISLOCKI had any very early stages at their disposal; we are more fortunate. The earliest stage of attachment so far known is that represented by our Hapale 2 blastocyst, but whether the conditions obtaining there hold also for the Cebidæ can only be determined when early material of the latter becomes available.

In our Hapale 2, the embryo of which has already been described (*ante*, pp. 100–102), the first reaction of the endometrium to contact with the trophoblast of the opposite polar regions of the fused blastocysts is a profuse proliferation on the part of the uterine epithelium and its continuation into the neck-portions of the uterine glands, accompanied by an increase in the number and size of the sub-epithelial capillaries. This proliferation occurs not only over the areas of contact, but also for a short distance outside these (Pl. 8, fig. 57) and results in the epithelium assuming the form of a thick stratified layer, the superficial cells of which tend to be somewhat loosely arranged. This is the condition presented by the epithelium where it lies in contact with the trophoblast of the anti-embryonal pole and also where it is in contact with the marginal zone of the attaching or ectoplacental trophoblast of the upper or embryonal pole and for a short

distance outside both these regions. Over the more central portion of the ectoplacental area, however, the proliferated epithelium has disappeared as a distinct layer, being represented by irregular groups of small intensely staining pycnotic nuclei (Pl. 9, fig. 56, *cf.* also Pl. 8, figs. 57 and 58, *ep.n.*).

The ectoplacental trophoblast itself, over its more central region, lies in the most intimate contact with the irregular masses of pycnotic nuclei or where these are absent, with the subepithelial tissues (Pl. 9, fig. 56, *tr.pl.*). It appears as a thinnish somewhat irregular layer containing numerous nuclei, but in which cell-limits are not obvious. It varies, however, both in thickness and in its detailed characters in different parts of its extent. Marginally where it passes over into the trophoblast of the free wall of the blastocyst, it is thicker than over the central region (Pl. 8, fig. 57), whilst in places it presents the curious appearance of discontinuity illustrated in Pl. 8, fig. 58. Its cytoplasm is often vacuolated and frequently encloses spherical masses of varying size and homogeneous aspect. Altogether, the condition of the ectoplacental trophoblast in these fused blastocysts of Hapale is by no means strikingly suggestive of its future potentialities as revealed in later stages.

It may be recalled that in Tarsius, a comparable proliferation of the uterine epithelium is the concomitant of the attachment of the blastocyst, whilst SELENKA ('00, '03) has described even more marked proliferative activity on the part of the uterine epithelium outside the area of attachment in his early Catarrhine stages (*Nasalis larvatus*, Keim S, *Semnopithecus pruinosus*, Lk.).

Our next stage (Pl. 11, figs. 69, 70) is furnished by *Chrysothrix sciureus* [*Saimiri sciurea*] 505, of the BLUNTSCHLI collection. The sections show only the area of attachment to the anterior wall of the uterus and a folded portion of the blastocyst wall, no embryo being present. From macroscopic examination, Professor BLUNTSCHLI thought that the blastocyst was invested in a closed capsularis, but of this there is no evidence in the sections. The stage is of great interest and importance, since the ectoplacental trophoblast is now a well-defined layer which is just beginning to form syncytiotrophoblast on its outer or attached surface. It is thus unfortunate that we cannot characterise it accurately by reference to the developmental stage of the embryo, but so far as trophoblastic differentiation is concerned, it is clearly younger than Cebus 509, the embryo of which is distinctly more advanced than SELENKA'S Keim S of *Nasalis larvatus*.

The area of attachment has a diameter of approximately 2 mm. and the ectoplacental trophoblast over it is thrown into folds, filled or in some cases lined by chorionic mesenchyme, which dip down into the already much altered decidual tissue, the uterine epithelium having completely disappeared. Some of these folds are quite shallow, others reach a depth of up to 0·27 mm. (Pl. 11, fig. 69). The trophoblast (Pl. 11, fig. 70), which is beautifully fixed, measures about 0·048 mm. in thickness, and is distinguishable into a basal thicker and lighter staining layer of cytotrophoblast, forming roughly about two-thirds of the thickness of the entire trophoblast, and a superficial,

more deeply staining layer of syncytiotrophoblast, forming the remaining third. The cytotrophoblast is composed of large, plump, cubical to columnar cells, often arranged two deep, with large oval or rounded nuclei and not infrequently in mitosis. In between the cytotrophoblast cells there occur, at irregular intervals, single, darkly staining, narrow elements which pass into continuity with the syncytiotrophoblast, and which are evidently in process of being added to the latter. The syncytiotrophoblast consists of an irregular layer of darkly staining cytoplasm, in which are situated similarly staining nuclei, rounded or ovalish in form, and smaller than those of the cytotrophoblast. It closely follows the uneven surface of the latter. As yet these are only occasional indications of sprout-like processes passing from it into the subjacent endometrial tissue, nevertheless the latter already exhibits a very pronounced reaction to the trophoblastic attachment. This is manifested in the superficial zone of the endometrium by the presence of numbers of enlarged capillaries, the endothelial walls of which are distinctly thickened, and especially by the occurrence of numerous darkly stained rounded masses or " nests " together with strands of variable size and shape which are very conspicuous in the sections (Pl. 11, figs. 69 and 70). They are syncytial in character, consisting of a cytoplasmic matrix, densely crowded with small nuclei, extremely rich in deeply staining chromatin granules. Most of the nests are solid, but some few are luminated. Study of the sections shows that these structures are to be interpreted as degenerating remains resulting from the proliferation of the epithelium of the neck-portions of the uterine glands.

In the superficial part of this subtrophoblastic zone the stroma cells, though enlarged, are mostly spindle-shaped, but in its deeper part, which appears more uniform in character under low-power examination, the cells are beginning to take on the appearance of epithelioid elements, the future decidual cells. Intermingled with them are degenerating cells as well as rounded masses, less degenerate and less deeply staining than the masses referred to above, both clearly of gland-epithelial origin. Examination of the later stage represented by Chrysothrix 467 suggests that the deeper part of the superficial zone gives origin to the pars compacta of the decidua basalis of later stages, whilst the upper part becomes engulfed by the actively ingrowing syncytiotrophoblast and in this way undergoes resorbtion.

The remaining and very much thicker part of the endometrium underlying the thin superficial zone contains the persisting more basal portions of the uterine glands and is destined to form the very conspicuous and greatly developed pars spongiosa of the later stages. Already the glands are becoming irregularly enlarged and tortuous, whilst their lining epithelium, especially in the region of their blind upper extremities, is profoundly modified, being irregularly thickened and in active process of disintegration. In the Platyrrhine, there can be no doubt, the epithelium of the uterine glands is a highly important source of histiotrophic material.

The succeeding stage of Chrysothrix (Chrysothrix 467) is that to which the flat embryo described on pp. 112–115 (fig. 18*a*, Pl. 21) belongs. Judged by the stage of development

of the embryo, it is very distinctly older than Cebus 509, but it falls much better into line with the stage of Chrysothrix just dealt with than does the latter, and so may be briefly described here. It provides us with an extremely interesting and important phase in the further differentiation of the trophoblast (Pl. 11, figs. 71, 72, and Pl. 12, figs. 73–75). Professor BLUNTSCHLI'S photograph of the opened uterus shows the primary placental area on the anterior wall of the uterus with the embryo in relation to it and on the opposite wall, the secondary placental area, both beautifully displayed. The exposed or inner surfaces of both areas present a characteristically pitted appearance, which in the sections is seen to be due to the presence of foldings of the cytotrophoblast occupied by prolongations of the chorionic mesenchyme and similar to those noted in the preceding stage. Over the cephalic portion of the primary area the folding is only slight, but centrally and caudally in the region of the connecting stalk, where the trophoblast is thickest, the folds are much more marked, having the form of more or less flattened outgrowths, varying in depth and in width. They may attain a depth of about 0·5 mm. and a width at the surface of from 0·25 to 0·34 mm., some of them reaching as far as the basal decidual tissue (Pl. 11, figs. 71, 72).

The primary placental area is distinctly larger than in Chrysothrix 505, its diameter being about 3·8 mm., but more striking than this increase in the surface area of the attaching trophoblast is its increase in thickness, for at its maximum it is now just about ten times as thick as that of the preceding stage, its depth over the central region of the area being about 0·5 mm. The cytotrophoblast is of very much the same thickness in the two stages, so that the increase here is in the syncytiotrophoblast and is to be regarded as the result, on the one hand, of the continued activity of the parent cytotrophoblast in producing new syncytium, and on the other, of the growth of the syncytiotrophoblast itself, as is evidenced by its penetration into the subjacent decidual tissue and its engulfment of constituent elements of the same.

The cytotrophoblast essentially resembles that of the preceding stage and is actively engaged in the production of syncytium, many of its cells being in mitosis. The syncytiotrophoblast, in the region of attachment of the connecting stalk and caudally thereto, appears as a darkly staining layer of very variable thickness owing to the penetration into it of the folds of the cytotrophoblast above mentioned, whilst its under surface is very irregular owing to the presence of prolongations of variable size and shape which pass off from it into the subjacent decidual tissue. It consists of a continuous cytoplasmic matrix in which are situated numerous oval nuclei and also numerous spaces of varying size and shape. These spaces cause it to have the appearance in places of a very irregular coarse reticulum (Pl. 11, figs. 71, 72), but only exceptionally and over small areas (fig. 73) does it exhibit the finely reticular character which is distinctive of the syncytiotrophoblast of Cebus 509, presently to be described. Of the just mentioned spaces, some, smaller, more irregular and less definitely contoured, are simply of the nature of vacuolar spaces or lacunæ in the syncytial matrix and in many of them, normal maternal red blood corpuscles as well as " vesicular " corpuscles are

already present in small numbers, others contain a granular material, possibly a coagulation product or detritus.

Yet others of these spaces, more definitely contoured than the lacunæ, are actually enlarged maternal capillaries with their endothelial walls intact which have been surrounded and enclosed by the syncytiotrophoblast in its growth into the endometrial tissue. They can often be traced into direct connection with enlarged capillaries situated at the surface of the basal decidual zone, at its junction with the syncytiotrophoblast (Pl. 11, figs. 71, 72). Such intra-syncytial or intra-placental maternal vessels are not destroyed but persist into quite late stages. They increase greatly in size, their endothelial walls become supported by a clear homogeneous layer which is deposited around them and eventually definite gaps or perforations appear in their walls through which the maternal blood can pass directly into the lacunæ or in later stages into the intertrabecular blood spaces formed from them.

These intra-placental capillary vessels were first described by KLEIN ('10) in the placenta of Mycetes and my own observations show that they are present not only in Mycetes but also in Hapale, Cebus and Chrysothrix, so that we may anticipate that they will be found to be of general occurrence in all Platyrrhine placentas. In that event we should be justified in regarding them as constituting one of the most characteristic features of the Platyrrhine placenta, since in no other Primate placenta are such intra-placental vessels known to occur.

Comparison of Pl. 11, fig. 69, of Chrysothrix 505 with Pl. 11, fig. 71, of the present stage suggests that the upper part of the superficial zone of the endometrial tissue of the former has been completely resorbed by the ingrowing syncytiotrophoblast with the exception of its enlarged capillaries, whilst the deep part of the same zone has persisted to form the thick cellular layer seen underlying the syncytiotrophoblast in figs. 71, 72, 73. This layer which we may now distinguish as the pars compacta of the decidua basalis consists of polyhedral decidual cells intermingled with degenerating cells and their products, but it is far from being everywhere so definite and well marked as in the figures referred to, since it is invaded and even interrupted by more or less extensive sprout-like prolongations of the syncytiotrophoblast. These may extend right through it and are active in engulfing and resorbing the syncytial masses and degenerating cells derived from the gland-epithelium. Pl. 12, fig. 74, provides a very striking picture of a small area from the more cephalic, thinner region of the placenta where such resorption is actively in progress. But not all the syncytial masses are directly resorbed in this way, others of them degenerate directly and their products become disseminated through the deep part of the compact zone (Pl. 11, fig. 72). In the pars spongiosa underlying the latter zone, the changes already initiated in the preceding stage are still more accentuated (Pl. 11, fig. 71 ; Pl. 12, figs. 73, 74). The uterine glands are greatly enlarged and their contours are extremely irregular. Their basal portions are still lined by an intact epithelium, but in their upper enlarged portions, the epithelium is greatly altered, being irregularly folded and thickened. Syncytial nests and free cells formed by proliferation

from it are more abundant than in the preceding stage, indeed, the nests are so numerous that they form quite thick patches below the compact zone, in between the upper ends of the gland lumina (figs. 73, 74). In the latter, free rounded cells in all stages of degeneration occur in considerable numbers, together with occasional large syncytial masses densely crowded with deeply staining nuclei. These latter masses can be traced into continuity with the syncytiotrophoblast, but whether they represent prolongations of the latter or direct derivatives of the gland epithelium is difficult to determine. In any case, the amount of histiotrophic material available for resorption in this stage is very considerable. On the other hand, maternal blood extravasations are so rare and so slight as to be negligible (Pl. 11, fig. 72).

The stage represented by *Cebus macrocephalus* 509, the embryo of which (described on pp. 103–105, text-fig. 15) is very much younger than that of Chrysothrix 467, is of interest inasmuch as it provides us with an even more striking demonstration than does the latter, of the capacity of the Platyrrhine trophoblast for rapid and exuberant growth. Moreover, its trophoblast shows certain differences in detail from that of Chrysothrix.

Although the primary area of attachment has a diameter of only 2·6 mm. as compared with 3·8 mm. in Chrysothrix 467, the trophoblast has already attained a thickness of at least 1·36 mm.* as compared with 0·5 mm. in the latter, the difference being entirely due to the greater thickness of the syncytiotrophoblast. The latter (Pl. 13, fig. 77) further differs from that of Chrysothrix in that it is composed of anastomosing cytoplasmic strands, for the most part thin, in which are situated ovalish or rounded nuclei, more dispersed and less abundant than in Chrysothrix and which enclose lacunar spaces of variable size and shape and much more conspicuous than those of the latter. Consequently the syncytium here presents a much more uniform appearance and a more definitely reticular character than in Chrysothrix. The lacunæ already contain maternal blood corpuscles in fair abundance so that evidently maternal capillaries have been opened up during the growth of the syncytium into the endometrial tissue. How that may happen is beautifully shown in Pl. 12, fig. 76, where a hollow syncytial sprout growing out from the marginal region of the syncytium, is seen in process of penetrating into the lumen of a capillary.

As in Chrysothrix 467, other capillaries have become included in the syncytiotrophoblast, with their endothelial walls complete and thickened, but they are here still small and consequently much less conspicuous than in that stage (fig. 77, *icp.*).

The cytotrophoblast (Pl. 13, fig. 77) presents a wavy uneven contour and is produced into fold-like outgrowths like those of the preceding stage, but owing, no doubt, to the greater thickness of the syncytiotrophoblast, they appear more extensive and some of them penetrate deeply into the latter, a specially large prolongation with indications of secondary outgrowths, being situated almost directly opposite to the embryo (*cf.* text-fig. 15). In early Catarrhine blastocysts, SELENKA (*v.* figs. 19*a* and 20*a*, Pl. 21) has

* The serial sections available do not include the subtrophoblastic decidual tissue of the central part of the placenta.

recorded the presence of a specially large villus (his " Zentralzotte ") at the root of which the embryo is situated so that it occupies a precisely corresponding position to this large villus-like outgrowth in Cebus.

In the marginal region of the placental area, it may be noted, the cytotrophoblast has not produced reticular syncytiotrophoblast but instead has given origin to curious thick finger-like syncytial processes which penetrate into the endometrial tissue and even extend deeply into the gland lumina.

From these early preparatory stages in placental development we pass to the much later stage represented by Cebus 475, with a curved embryo 3·2 mm. in length (BLUNTSCHI, '13, fig. 4). In the interval, very definite advance has been made and we see in progress in this stage that penetration of localised outgrowths of the chorion, carrying the umbilical capillaries, into the thick bed of syncytiotrophoblast, vascularised by the maternal blood, which is the prelude to the formation of the definitive placenta.

Though much later than Cebus 509, the present stage links up with it without difficulty and provides us with an even more striking demonstration than it does of the massive character of the trophoblastic proliferation in this genus. In Pl. 13, fig. 78, by far the greater bulk of the fœtal portion of the placenta which is apparent as the darkly stained lobulated mass underlying the embryo (seen in transverse section), is formed of coarsely reticular syncytiotrophoblast, invested on its surface by a thin layer of cytotrophoblast. Overlying the latter is a layer of chorionic mesenchyme in which small umbilical vessels are now present, quite abundantly indeed in the region of attachment of the connecting stalk.

From the figure it will be seen that the irregularly lobulated character of the mass is due to the presence at intervals of light staining strands which penetrate more or less deeply into the syncytial mass. They appear at first sight to be formed exclusively by prolongations of the chorionic mesenchyme but more careful examination shows that the mesenchymal axis is everywhere separated from the syncytiotrophoblast by a thin layer of cytotrophoblast prolonged in from the surface layer and which, like the latter, is in proliferative continuity with the strands of the syncytial network (Pl. 13, figs. 80, 82). It is clear then that these prolongations must have been formed by the correlated growth activity of both the cytotrophoblast and the mesenchyme of the chorion, involving localised areas of the latter that, in other words, they are to be regarded as localised chorionic outgrowths, carrying the umbilical capillaries which penetrate into the thick bed of syncytiotrophoblast, the lacunæ of which already contain maternal blood. They are clearly of the same nature as the fold-like formations and outgrowths described in connection with the cytotrophoblast and mesenchyme in the earlier stages, but here they have acquired much greater definiteness, they have increased both in size and in number, and arising as they do at more or less regular intervals, they have induced the appearance in the placental mass of the characteristic lobulation referred to above, which, it is interesting to note, persists through later stages and is more or less distinctly visible in the mature placenta.

The question arises, how are we to designate these chorionic derivatives ? They are clearly the homologues of the chorionic villi of the Catarrhine and Anthropoid placenta, defining the placental villus as a localised, eventually branched, outgrowth involving both the cytotrophoblast and the mesenchyme of the chorion and if that homology be accepted, there can be no valid objection to terming the outgrowths in question " chorionic villi," even though they exhibit certain characteristic differences from those of the Catarrhines and Anthropoids.

The villi are seen in their simplest condition in the secondary placenta (Pl. 13, figs. 79, 80) where they appear as simple unbranched processes varying in length and in thickness, the longest of them extending through about the upper two-thirds of the syncytiotrophoblast and so failing to reach the basal decidual tissue. In the primary placenta, they attain a much more extensive development (fig. 81). Not only do they reach a greater length but many of the larger villi have given off branches which are in process of penetrating into the syncytium of the deeper parts of the lobules. They are destined to form the trabeculæ of the mature placenta and already, indeed, some few of them have formed direct anastomoses with corresponding branches of other villi, but such fusions are rare, the great majority simply terminating in the syncytium.

As regards the structure of the trophoblast, the cytotrophoblast, as may be seen from Pl. 13, fig. 82, representing the growing tip of a villous branch, is formed by a single layer of large, plump, mostly cubical cells with large nuclei, occasionally seen in mitosis. At intervals it is in definite proliferative continuity with the strands of the syncytium and in between these spots its outer surface is clothed by a thin layer of syncytium, forming the immediate boundary of a lacunar space. The syncytiotrophoblast appears as a nucleated reticulum composed of coarse anastomosing strands and masses between which are wide lacunæ containing maternal blood corpuscles (Pl. 13, figs. 79–82).

Imbedded in the syncytiotrophoblast are numbers of enlarged intraplacental capillaries with their endothelium hypertrophied and resting on a thin homogeneous supporting layer, the nature of which remains to be determined. In the secondary placenta these capillaries are mostly situated in or close to curious streak-like tracts of the syncytiotrophoblast which run more or less horizontally through the mid-regions of the lobules (Pl. 13, figs. 79, 80 *st.*). Also in proximity to them, there occur here and there small isolated masses of quite healthy looking decidual cells. These tracts do not extend continuously throughout the width of the placenta but, after coursing through two or more lobules, they are found to curve down and to pass into continuity with the basal part of the syncytium overlying the decidua basalis. Possibly they mark the junctional line between the syncytium first produced and the decidual tissue, the superficial zone of the latter having been undermined and all but completely resorbed by the later formed syncytium on the deep side of the tracts.

In this connection it is worthy of remark that the syncytiotrophoblast on the upper side of these tracts differs somewhat from that on the deep side, inasmuch as its strands

tend to exhibit a radiating arrangement as they run out to pass into continuity with the cytotrophoblast, and are rich in nuclei, whereas on the deep side the strands form an irregular network and their nuclei are more scattered.

In the primary placenta, irregular areas corresponding to these tracts and containing intraplacental capillaries are seen near the centres of the lobules, whilst round them the syncytial strands exhibit an even more marked tendency to assume a radiating arrangement than is the case in the secondary placenta (Pl. 13, figs. 78, 81). Isolated patches of decidual cells are also occasionally met with in the syncytium.

The decidua basalis, in contrast to that of Chrysothrix 467, may now be said to have attained its definitive condition, inasmuch as its constituent parts, the pars compacta and the pars spongiosa, are established (Pl. 13, fig. 79).

The pars compacta appears as a somewhat irregular layer, mostly thin, but varying in thickness as well as in its detailed histological characters in the different parts of its extent. Polygonal, rather darkly staining decidual cells, compactly massed together and occasionally in mitosis, form its main basis, but throughout its extent there are present in it other cells exhibiting all stages of degeneration down to the condition of angular non-nucleated eosinophil flakes. Such cells may occur singly in amongst the decidual cells, or they may be grouped in nests replacing the latter; moreover, on the deep surface of the layer, where it is joined by the gland-septa, large numbers of free rounded cells are present, also showing all stages of degeneration (Pl. 13, fig. 79). The precise origin of these cells is still uncertain, but they are possibly derived from the enlarged polygonal cells which form the axes of especially the upper parts of the gland-septa, and which resemble the decidual cells, except that they have light staining cell-bodies. Whatever their origin, their abundance indicates that they are an important source of histiotrophic material.

The syncytiotrophoblast furnishes an irregular thin layer clothing the upper surface of the pars compacta, and from it sprout-like processes penetrate into the latter, and may aid in the resorption of the products of cell-degeneration.

In the pars spongiosa (Pl. 13, fig. 79) the gland-lumina are enormously enlarged and contain a finely granular material. They are separated by gland-septa of varying thickness, and are lined in their upper parts by a low flattened to cubical epithelium (evidently regenerated), only their basal ends, adjacent to the muscularis, possessing a columnar epithelium.

The next older stage in the BLUNTSCHLI collection is that furnished by *Chrysothrix nigrivittatus* 600, with an embryo of G.L. 6·8 mm. Although it does not link up with Cebus 475 quite so well as does Cebus 528 with an embryo of G.L. 10 mm., it provides a very interesting further stage in placental development, and is most conveniently dealt with here.

A low power view of a portion of the primary (ventral) placenta is shown in Pl. 14, fig. 83. We observe the same lobulation in the superficial portion of the placenta as in Cebus 475, but, as compared with the latter, the chorionic mesenchyme is much thicker,

the umbilical vessels are larger and more numerous, and the chorionic villi are more strongly developed and much more conspicuous. They appear as very definite outgrowths penetrating into the syncytiotrophoblast, where they sooner or later branch and subdivide. As in Cebus 475, direct anastomoses between the branches of adjoining villi do occur, but the great majority appear to end freely. Most of the main villous stems extend through the greater part of the thickness of the syncytiotrophoblast to terminate in the proximity of the pars compacta, and some of them indeed actually reach the latter, and are attached thereto by means of their cytotrophoblast (Pl. 14, fig. 83), and so form "anchoring" villi comparable with those of Catarrhine and Anthropoid placentas, but "cell columns" comparable with those of the early villi of the latter are not developed.

The villi (Pl. 14, fig. 84) show an advance histologically on those of Cebus 475. Their axes are no longer formed of simple undifferentiated mesenchyme, but consist of a fairly compact variety of embryonic fibrous connective tissue, in which the umbilical capillaries, as yet small, ramify. The cytotrophoblast, though still in the form of a continuous cellular layer over most of its extent, is less regular in character, and in places on the villi, and especially on the chorion, is flattened and in process of transformation into syncytium, or is actually replaced by such (Pl. 14, fig. 84). This syncytium I shall refer to as the "villous syncytium." It is the equivalent of the "Zotten- oder Resorptions-syncytium" (GROSSER) of the human placental villi.

The interspaces between the main villous stems and their branches are partially occupied by darkly staining syncytiotrophoblast in the form of irregular strands and masses connected together so as to form quite irregular coarse networks, enclosing large lacunar spaces, whilst similar spaces also occur between the syncytium and the surfaces of the villi. I propose to speak of the syncytium in this position as the "intervillous syncytium." The spaces occupied by maternal blood, in relation to it, are destined to form what we shall speak of as the "intervillous" or "intertrabecular" spaces in later stages. They represent the continuous intervillous blood-space of the Catarrhines and Anthropoids.

As may be seen from figs. 83 and 84, the intervillous syncytium exhibits a very loose and irregular relationship to the cytotrophoblast of the main villous stems and is only connected with the same at quite irregular intervals, much as is the case in Cebus 475 (Pl. 13, fig. 80), but, whereas in the latter, the cytotrophoblast appears to be actively contributing to the syncytium, here the appearances suggest that it has largely given up its proliferative activity. Moreover, in numerous places throughout its extent, the syncytium already shows definite signs of degeneration, isolated patches in the syncytium and even small entire masses of it having already undergone conversion into so-called "fibrinoid," staining deeply with eosin.

The structural relations of the syncytiotrophoblast in this stage suggest (1) that the villous syncytium of later stages is not derived primarily from the intervillous syncytium

but is formed largely by the transformation of the cytotrophoblast, and (2) that the intervillous syncytium is destined in greater part to undergo " fibrinoid " degeneration and to take no active part in the constitution of the mature placenta, except in so far as it may contribute in some degree to the villous syncytium and persists as a cementing material linking up the free villous branches into a trabecular system. The primary functions of the early trophoblastic proliferation which later forms the intervillous syncytium are (1) to effect the implantation of the blastocyst in the endometrium and (2) to provide a thick, spongy, syncytial bed, vascularised by the maternal blood, into which the chorionic villi can grow and branch, so as to bring the fœtal blood into the closest possible relation with the maternal. Once those functions have been achieved, its usefulness is over and it undergoes degeneration.

That portion of the intervillous syncytium which is related to the surface of the pars compacta in the Platyrrhine placenta has been termed by STRAHL ('03) the " basal syncytium." I propose to speak of it as the " peripheral syncytium." In this stage it is hardly deserving of separate designation and appears simply as the very irregular boundary zone of the syncytium. It varies very greatly in thickness, being in places greatly attenuated, in others quite thick. Its under surface is quite uneven owing to its being produced into coarser and finer sprout-like processes containing small flattened deeply staining nuclei, which may extend through practically the entire thickness of the pars compacta. In our Hapale 1 stage (with an embryo of G.L. 6 mm.) corresponding but much coarser processes are given off from the peripheral syncytium which anastomose to form a very obvious but quite irregular network in the pars compacta. These syncytial processes, as was indicated above, are doubtless destructive as well as absorptive in function and would seem to correspond to what FLORIAN ('28*b*) has termed the " Proliferationsplasmodium " in the early Human placenta (*v.* Pl. 18, fig. 104, *p.syn.*). The pars compacta (fig. 83, *p.c.*) is very similar to that of Cebus 475, but it is thicker, its cells are smaller and mitoses are not infrequent. Cellular degeneration is very evident, large tracts of degenerating cells (*dg.e.*) being present on its deep surface.

The composite zone in this and the preceding stage which results from the penetration of the just mentioned syncytial processes and sprouts into the superficial compact zone of the decidual tissue (pars compacta), constitutes what we may term the " junctional zone " or, following GROSSER, the " penetration zone." As WISLOCKI ('29) has pointed out, it corresponds to the composite layer which occupies a corresponding position in the Catarrhine and Anthropoid placentas and which STRAHL ('03) has termed the " chorio-basalis."

Chrysothrix nigrivittatus 599 with an embryo of G.L. 8·1 mm. and *Chrysothrix sciureus* 642, with an embryo of 8·6 mm. exhibit no very striking advance on the conditions seen in Chrysothrix 600, and the same holds true for *Cebus macrocephalus* 528 with an embryo of 10 mm. All of them show, however, an increase in the branching of the chorionic villi and in their blood supply and further progress, especially noticeable in

Cebus 528, in the replacement of the cytotrophoblast by villous syncytium. In all three, the intervillous syncytium is still extremely prominent and in Cebus 528 in particular, its strands still tend to possess the same radiating arrangement round the intraplacental capillaries situated near the centres of the lobules, as was indicated in Cebus 475. Pl. 14, fig. 85, illustrating the sectional appearance of the dorsal (secondary) placenta of Cebus 528, should be compared with Pl. 13, fig. 81, illustrating that of Cebus 475. Pl. 14, fig. 86, shows the uterus of Cebus 528 opened up so as to display the inner (chorionic) surfaces of the two placentæ, with the umbilical vessels ramifying over them, the ventral (primary) placenta, 24 mm. in diameter, being on the left, and the dorsal (secondary) placenta, about 18 mm. in diameter, on the right.

From the nature of the lacunar system in these earlier stages, one would surmise that the circulation of the maternal blood through the placenta must be a very slow process and that that is actually the case is borne out by the occurrence of thrombi in the large lacunæ situated adjacent to the basal syncytium in Cebus 528 (Pl. 14, fig. 85, *th*) and also, in slighter degree, in Chrysothrix 642.

As concerns the general course of the circulation through the placenta, it may again be emphasised that the maternal blood reaches the intervillous spaces through the intraplacental arterial capillaries. The arteries, like the veins, run in the interglandular septa. They penetrate the pars compacta (junctional zone) and the peripheral (basal) syncytium and, passing up through the villous system as huge capillaries, they proceed to divide a short distance below the chorion, the blood reaching the intervillous spaces through the gaps that are formed in their walls. From these spaces the blood is drained away by veins which take origin from the large spaces abutting on the peripheral syncytium.

Attention may be called here to a curious condition affecting the maternal blood in the placental lacunæ and that is the occurrence, often in large numbers, of red corpuscles which have lost their hæmoglobin and have swollen up to form relatively huge vesicular structures. At first I was inclined to regard these " vesicular " corpuscles as artifacts, due to post-mortem change or to the action or want of action of the fixatives employed, but the following considerations indicate that that explanation is unlikely: (1) they appear to be widely distributed in early Primate placentas, occurring not only in the Platyrrhines but also in Tarsius, in Papio amongst the Catarrhines as well as in the early human placenta; (2) they occur in material otherwise quite adequately fixed and along with perfectly normal corpuscles. Possibly they owe their origin to a lowering of the density of the blood-plasma, as the result of absorptive activity on the part of the syncytium.

If we pass now to the much later stage represented by Chrysothrix nigrivittatus 648 with an embryo of G.L. 25 mm., we find that the placenta (ventral (primary) 22 mm. in diam., dorsal (secondary) 21 mm.), apart from a very evident increase in thickness, presents in section a very different aspect from that of Cebus 528, as comparison of Pl. 14, fig. 87, with Pl. 14, fig. 85, at once demonstrates. Whereas in the latter the intervillous

yncytium is conspicuous and immediately catches the eye, in the former, the syncytium appears markedly reduced and by far the greater bulk of the placenta is seen to be constituted by the villous stems and their branches.

The intervillous syncytium is best marked below the chorion and on the surface of the pars compacta (junctional zone) where it now forms a readily distinguishable layer, the peripheral (basal) syncytium; elsewhere it is represented by irregular strands and masses, distributed between the villi and serving to some extent to connect them together (Pl. 15, fig. 88). Everywhere throughout its extent, below the chorion, in the peripheral syncytium and at the margin of the placenta adjacent to the origin of the chorion læve, streaks, patches and masses of "fibrinoid," stained bright red with eosin, are present in it. Not infrequently small villous branches are more or less completely surrounded by intervillous syncytium and in such cases one can observe below it a thin layer of villous syncytium and sometimes remains of the cytotrophoblast.

The general appearance presented by the villous branches as seen in a transverse section through the placenta is depicted in Pl. 14, fig. 88. They do not by themselves form an obvious trabecular system (though in the sections there is evidence of the occurrence as in earlier stages of direct anastomoses between them), but are connected quite irregularly by strands of intervillous syncytium. They are invested by a thin layer of villous syncytium, the mostly small flattened nuclei of which contrast with the larger oval or rounded nuclei of the intervillous strands. The cytotrophoblast has largely disappeared, having undergone conversion into villous syncytium, though traces of it still remain in the form of light staining cells with plump ovalish nuclei underlying the more darkly staining syncytial covering.

In this stage we encounter for the first time a very remarkable, possibly unique, phenomenon in the Platyrrhine placenta and that is the formation inside enlarged capillaries situated in the mesenchymal axes of the villous branches, of fœtal non-nucleated red blood corpuscles from parent cells, identical in character with those of normal hæmopoietic centres (Pl. 15, fig. 88, and Pl. 16, fig. 92). That this process is not an occasional happening but is of fundamental importance is indicated by the abundance of these hæmopoietic capillaries throughout the entire extent of the placenta, by their occurrence in later stages and by their presence not only in the placenta of Chrysothrix but in those of all the other genera I have examined (Hapale, Cebus, Mycetes). It seems probable that these blood-forming foci begin to be established soon after the stage represented by Cebus 528, and it is worthy of remark that their appearance would seem to coincide with the replacement of the nucleated red corpuscles of the fœtus by non-nucleated, for in this stage such nucleated corpuscles as occur in the larger umbilical vessels are few in number as compared with the non-nucleated and, judging from the condition of their nuclei, are in process of degeneration.

I believe this to be the first authentic record of the normal occurrence of hæmopoiesis

or more strictly erythropoiesis in the Mammalian placenta,* though GOORMAGHTIGH ('25) in a case of congenital œdema in a new-born child has recorded its occurrence in the villi of the related placenta. I have already made reference (*ante*, pp. 88, 89), to HUBRECHT'S contention, which was subsequently supported by DE GROOT ('19) that in the placenta of Tarsius (as well as in that of Tupaia), maternal red corpuscles are formed from the fragmented nuclei of fœtal as well as maternal constituents of the placenta, but the evidence he produced is entirely unconvincing and his contention has never met with general acceptance.

It is also deserving of note that in this stage the maternal red corpuscles present in the intervillous spaces are for the most part quite normal in character. Vesicular corpuscles are still present here and there and they also occur in numbers in the spaces adjoining the peripheral syncytium and in some of these, as well as in the hypertrophied intraplacental vessels, thrombi are still in evidence; nevertheless it would seem that a proper placental circulation is in process of being established. The intraplacental vessels just referred to are both numerous and large (Pl. 14, fig. 87, *icp.*) and are in open communication with the intervillous spaces by gaps in their walls.

The peripheral syncytium (fig. 87, *p.sytr.*), is distinct as an irregular layer of very variable thickness which is in continuity on its upper side with the strands of the intervillous syncytium and on its under side with a fine reticulum which pervades the pars compacta (junctional zone). Its cytoplasmic basis has undergone a curious change, possibly indicative of commencing "fibrinoid" degeneration in that it encloses what seems to be a network of fine channels occupied by strands of material with a quite different staining reaction to that of the cytoplasm. The pars compacta presents a loose open appearance and shows extensive areas of quite degenerate cells on its deep surface.

Following on Chrysothrix 648, the BLUNTSCHLI collection contains two stages of Cebus, viz., *Cebus macrocephalus* 703, with a fœtus of crown-rump length (C.R.L.) of 40 mm. and a dorsal contour length (D.C.L.) of 78 mm., and *Cebus gracilis* 474, with a fœtus measuring in C.R.L. 82 mm. and in D.C.L. 130 mm.

The primary placenta on the dorsal uterine wall in Cebus 703 measures 24 mm. in diameter by about 9 mm. in thickness, the secondary on the opposite wall 24 mm. by about 6·5 mm. Remarkably enough, in Cebus 528, with an embryo of only 10 mm. G.L., the primary (ventral) placenta also measures 24 mm. in diameter.

Unfortunately, no measurements of the placenta of Cebus 474 are available, but in *Chrysothrix nigrivittatus* 816 (fœtus, C.R.L. 80 mm., D.C.L. 153 mm.), the dorsal placenta (which is alone present) measures 3·8 by 3·4 cm. in diameter, whilst in *Cebus macrocephalus* (?) 33, with a fully haired fœtus, the primary (dorsal) placenta measures 6·1 by 5·7 cm. in diameter and the secondary (ventral) 6 by 4·5 cm. Lastly, in the case of *Cebus apella* 624 (with a haired fœtus, C.R.L. 10·3 cm. and D.C.L. 22·5 cm. (Pl. 17, fig. 99)), the primary (dorsal) placenta measures 4·9 by 4·3 cm. in diameter, and the

* Preparations of Platyrrhine placentas showing erythropoiesis were exhibited by me at the Liége meeting of the Association des Anatomistes in 1926.

secondary, 5·6 by 4·1 cm. (Pl. 17, fig. 98). It is evident from these data that the Platyrrhine placenta undergoes its greatest growth in what are relatively late fœtal stages, and it is an interesting fact that during this period also, as the sequel will show, it attains its maximum grade of functional efficiency, so far as that may be judged from its structural condition.

Apart from a definite increase in thickness, due to the growth and branching of the villi, the placenta of Cebus 703 shows no very great advance on that of Chrysothrix 648. The villous branches, though varying greatly in size, still tend to be coarse and very variable in form. Remains of the cytotrophoblast are even more abundant than in Chrysothrix 648, whilst the intervillous syncytium is still prominent, as irregular anastomosing strands and masses, connecting the villous branches and ramifying between them. It tends to be greatly thickened around the intraplacental vessels and in the deep part of the placenta where large blood spaces are present it may form networks connected with the basal syncytium. Below the chorion it is represented by irregular bands and masses of " fibrinoid " and similar masses are common throughout the placenta and especially in the peripheral syncytium. The latter varies greatly in thickness and over most of its extent is already extremely degenerate, much more so than in the succeeding stage, 474. The intervillous spaces are mostly well filled with normal corpuscles. In some of the large spaces adjoining the basal syncytium fibrin occurs, but vesicular corpuscles are largely confined to the intraplacental vessels and are not numerous.

The placenta of Cebus 474 (Pl. 15, fig. 89) exhibits very definite progress as compared with that of 703. It is now just about twice as thick as the latter and, notwithstanding that increase, its villous branches, seen in section (Pl. 15, fig. 90) appear on the whole to be more compactly arranged ; they present a more uniform appearance, are more numerous and of smaller diameter than in it, clear proof that growth and subdivision of the villi have been actively proceeding. Consequent on that growth the intervillous spaces appear reduced, vesicular corpuscles are now fairly abundant in them, whilst fibrin occurs not only in some of the large basal spaces, but also in the intraplacental vessels, so that possibly the placental circulation may have been temporarily slowed up.

The intervillous syncytium (fig. 90) is much less conspicuous than in Cebus 703, and where it does occur in any bulk, *e.g.*, below the chorion, around the intraplacental vessels, in the basal part of the placenta and at odd spots throughout the thickness of the latter, it is more or less completely converted into " fibrinoid," presenting a laminated, fibrous or amorphous appearance. Occasional coarsely reticular areas of syncytium still occur in connection with the peripheral (basal) syncytium, whilst between the villi thin strands and small masses of unaltered syncytium are present, which are in continuity with the villous syncytium and so serve to connect the villous branches.

The peripheral syncytium (Pl. 15, fig. 91, *p.sytr.*), though on the whole less degenerate in Cebus 703, is an extremely irregular layer, variable in its characters and in its thickness in the different parts of its extent.

Erythropoiesis is still in active progress in both Cebus 703 and Cebus 474 (Pl. 16, fig. 92).

Subsequently to the stage represented by Cebus 474, placental differentiation evidently proceeds with considerable rapidity for the next older placentas available, those of Chrysothrix 816 and *Chrysothrix nigrivittatus* 31*a*, present a markedly different aspect in section to that of the former and have almost attained their definitive condition.

Chrysothrix 816 is exceptional in possessing only a single (dorsal) placenta. It has a diameter of 3·8 by 3·4 cm. and is exceptionally thick (about 1·5 cm.), no doubt as the result of compensatory growth. The fœtus measures in C.R.L. 80 mm. and in D.C.L. 153 mm. Chrysothrix 31*a* has the normal double placenta, the primary (ventral) measuring 3·2 cm. in diameter and the secondary (dorsal) 3·1 cm. A low power view of the primary placenta is shown in Pl. 16, fig. 93, and should be compared with the corresponding figure of the placenta of Cebus 474 (Pl. 15, fig. 89).

The alteration in the appearance of the placenta as seen in section in these two specimens of Chrysothrix is the result of the continued branching and subdivision of the villi, accompanied by a very striking reduction of the intervillous syncytium and the cessation of active erythropoiesis in the fœtal capillaries. Remains of the erythropoietic foci are still to be found, but they are rare, very small, and their cells quite degenerate.

The branching of the villi has resulted in an enormous increase in the number of the villous branches and a marked reduction in their size. They now appear as relatively thin, irregularly branched strands invested by a quite thin layer of syncytium and provided with an axis of fine fibrillar connective tissue in which are abundant capillaries, often situated immediately below the syncytial covering. Over large areas of the placenta they are connected together so as to form a trabecular network of quite irregular character, enclosing meshes of very varying size, but mostly small (Pl. 16, fig. 94). The connections between them are effected by lateral or terminal fusions of their syncytial coverings, by quite short bridges or longer and narrower strands of presumably intervillous syncytium, and no doubt also by direct anastomoses, though such are not easy to demonstrate. In places the trabecular network is compact, with quite narrow meshes ; in other places it is much more open, and in yet other places one is not justified in speaking of a trabecular network at all, inasmuch as the branched villi or trabeculæ lie more or less completely free of each other in a continuous intervillous blood-space (Pl. 16, fig. 95). In such places we see a very close approximation to the villous condition characteristic of the Catarrhines and Anthropoids which has resulted from a relatively slight change, viz., the disruption of the syncytial connections between the villous branches.

Apart from the connecting bridges and strands between the villous branches, remains of the intervillous syncytium are represented by occasional masses and layers of " fibrinoid " below the chorion and here and there throughout the placenta, especially in relation to the irregular spaces which represent the lumina of the intraplacental

vessels. The peripheral syncytium has been completely transformed into an irregular layer of "fibrinoid" and the pars compacta is largely degenerate.

In Pl. 16, fig. 96, is shown a small area from the slightly more advanced primary placenta of Chrysothrix 31*b* (primary (dorsal) placenta, 3·9 cm. in diam., secondary (ventral) placenta, 3·6 by 3·5 cm.) in which the villous branches, finer than in Chrysothrix 816, are seen to be connected up into a very distinct trabecular system, but other areas can readily be found where the villi present precisely the same appearance as those shown in fig. 95 of Chrysothrix 816.

If fig. 96 be compared with Pl. 8, fig. 54, of Tarsius 405, the similarity of the trabecular networks in the Platyrrhine and the Tarsioid will at once be apparent. In the absence of a knowledge of the antecedent stages, it might readily be assumed that the two organs are directly and genetically related, that in other words, the Tarsius placenta is the direct precursor of that of the Platyrrhine. Comparison, however, of the details of placental development in the two, as set forth in this lecture, demonstrates, it seems to me, that that assumption is untenable and that we have to do here, as I have already pointed out (*ante*, p. 94), with a striking example of developmental parallelism, *i.e.*, the attainment of a comparable developmental end in two somewhat different ways, and if you ask what lies at the back of that phenomenon, I can only vaguely reply that it is doubtless the outcome of some particular configuration inherent in the germinal constitution of the ancestral stock.

The most mature Platyrrhine placentas I have been able to examine are those of *Cebus apella* 624 from my own collection (Pl. 17, fig. 98) and *Cebus macrocephalus* 33 from the BLUNTSCHLI collection, both with haired fœtuses, probably nearing term, a lateral view of that of *Cebus apella* being shown in fig. 99 (for measurements of the placentas, see *ante*, pp. 131, 132).

Apart from the more compact arrangement of the villi in *C. apella* (due perhaps to greater contraction during fixation), the placentas in the two specimens closely agree in the details of their structure and may be dealt with quite briefly. Pl. 17, fig. 97, illustrates what may be regarded as an average portion of a section of the placenta of Cebus 33. The simple and irregularly branched villi are largely free of each other and are seen lying in what is to all intents and purposes a continuous intervillous blood-sinus occupied by perfectly normal maternal corpuscles, but other areas can readily be found where the villi are more compactly grouped and more connected with each other, as well as others where they exhibit an even more dispersed condition than that shown in the figure.

The process of disruption of the syncytial connections between the villi, already initiated in the preceding stages, has made further progress with the result that the villi have acquired a much greater measure of independence and have largely lost the fine net-like trabecular character they exhibited in certain areas in preceding stages (Pl. 16, figs. 94, 96).

We thus arrive at the conclusion that the fœtal portion of the mature Platyrrhine

placenta as exemplified by that of Cebus (and the same holds true for that of Hapale) cannot adequately be described as formed simply by a trabecular network; rather is it a villous placenta in which the greatly branched and relatively slender villi are not completely free but are connected to a variable and inconstant extent by direct fusions and syncytial junctions. Over extensive areas of the villous field, however, these latter connections break down and disappear with the result that the villous branches become isolated from each other and lie free in a continuous intervillous blood-space. Thus, in the end, the Platyrrhine placenta attains a condition which is not so very different from that of the Catarrhine organ, a remarkable and highly significant fact. And, here, we may direct attention to another very interesting parallel between the Platyrrhine and Catarrhine placentas. In recent years, certain Catarrhine placentas have been described which, in the presence of syncytial strands and plates connecting the villi so strikingly recall the Platyrrhine condition that certain authorities have regarded them as representing the transitional stage in the evolution of the Catarrhine organ from a Platyrrhine-like type. Study of developmental stages shows, however, that these syncytial connections in the Catarrhines arise relatively late as sprout-like outgrowths of the villous syncytium and that, accordingly, they do not represent the remains of an originally profuse intervillous syncytium, such as occurs in the Platyrrhines and so are of no genetic significance (see later, pp. 149–153).

We conclude then that the main difference between the Platyrrhine placenta and that of the Catarrhine is one of degree, so far as the villi are concerned. In the former, the villi grow into a massive vascularised bed of syncytiotrophoblast and never wholly acquire the independence and freedom which characterise those of at least the majority of Catarrhines. Not only is the primary trophoblastic proliferation in the Platyrrhine immensely more massive than that of the Catarrhine, but it persists for a much longer period, with the result that the development of the Platyrrhine placenta is a slow and cumbrous process involving so much time that it only reaches a condition of what we may call structural efficiency at a quite late period in gestation and as a compensation much more use appears to be made in the earlier stages of histiotrophic materials derived from the maternal tissues than is the case in the Catarrhine.

The Catarrhine, on the other hand, by abbreviation and acceleration of the developmental processes, has speeded up the development of its villous placenta in the most remarkable way. The earliest stages in the attachment of the blastocyst are unknown, but the available evidence indicates that attachment is effected when the blastocyst is smaller and less advanced than that of the Platyrrhine, and that the primary trophoblastic proliferation (implantation syncytium) is, relatively, insignificant in bulk compared with that of the latter, since in the earliest stages known, practically all that remains of it is a thin irregular peripheral zone adjoining and invading the endometrial tissue. But though small in amount, it is evidently endowed with more active cytolytic and invasive properties than that of the Platyrrhine, for in the early stages referred to, the maternal capillaries have already been opened up and maternal blood is present

in the space originally occupied by the syncytium. Already in these early stages (*cf.* SELENKA's Nasalis, Keim S, p. 138), we find that the chorion of the placental area has given origin to independent villous outgrowths which are situated not in a syncytial network as in the Platyrrhine, but in the space above referred to, which constitutes a continuous intervillous sinus occupied by maternal blood, in which the villi are free to branch. The result is that the Catarrhine placenta is capable of carrying on its full functions immediately the fœtal circulation is established and it does so not only much earlier but in what would seem to be a much more efficient manner (judging from the structural relations) than is the case in the Platyrrhine.

C.—*The Placentation of the Catarrhina.*

The earliest stage of placental development in the Catarrhines known to us is provided by two blastocysts described by SELENKA ('00, '03), viz., his Keim S of the Proboscis Monkey (*Nasalis larvatus*), the embryo of which has already been dealt with at some length (*ante*, p. 105), and his blastocyst Lk. of *Semnopithecus* (*Pithecus*) *pruinosus*. Both are in very much the same stage of placental development, though blastocyst Lk. is distinctly the smaller of the two. In both cases the primary placental primordium, situated on the ventral uterine wall, is alone definitely established, and in both the attachment of the blastocyst has resulted in a very decided endometrial reaction, the implantation site, now occupied by the villous field of the primary placenta, being surrounded by a circular cushion-like thickening of the endometrium, definitely elevated above the general uterine surface (SELENKA, Heft 8, Keim S, figs. 25 and 26, p. 189, and Taf. 11, fig. A; Heft 10, Blastocyst Lk, figs. 2 and 7, p. 334).

The following account of the placenta of Keim S is based on SELENKA's description and my own study of the sections. As the stage is one of great importance, I have provided three new illustrations (Pl. 9, figs. 59, 60, and Pl. 10, fig. 62), based on photomicrographs which show the details of the placenta rather more clearly than does SELENKA's beautiful but somewhat schematic fig. A, Taf. 11.

Pl. 9, figs. 59 and 60, show low and higher power views of a section of the blastocyst and the related endometrium, which just shaves the embryonal primordium. The blastocyst is very markedly flattened, and is seen to be implanted by means of the villi arising from its lower or embryonal hemisphere in a shallow, bowl-shaped depression in the endometrium, bounded on either side by a raised cushion-like thickening, which is part of the circular endometrial swelling referred to above. The embryo (*emb.*) lies in the base of the large centrally-situated branched villus (SELENKA's " Zentralzotte "), and is shown under higher magnification in Pl. 9, fig. 61.

The chorion of the upper or anti-embryonal hemisphere of the vesicle-wall is slightly convex, and projects freely into the uterine lumen. It is smooth and devoid of villi, but towards one margin, eccentrically situated, there occurs a small localised circular

thickening of its trophoblast, composed in its thickest part of narrow columnar cells with their nuclei at different levels, which SELENKA suggests is the " Anlage der sekundären Placenta " ; it is marked V in his fig. A. SELENKA states that the sections through the dorsal uterine wall showed no evidence of a " Haftfleck."

In Pl. 10, fig. 62, it will be seen that the margins of the blastocyst are downwardly recurved and attached to the margins of the implantation depression, actually to the free inner edges of the epithelium of the endometrial cushion. Beyond this attachment the wall of the blastocyst projects freely for a short distance over the endometrial cushion, and to a greater extent on the left than on the right. Measured from the extremities of these projections, the maximum diameter of the blastocyst is 1·29 mm., whilst its diameter measured from its attached margins is 0·98 mm.

The endometrial tissue, apart from the endometrial cushion and that part of it directly underlying the villous field of the blastocyst, consists of a dense small-celled matrix in which the blood vessels and uterine glands are situated (figs. 59, 60, 62). The glands are large, greatly convoluted, and are lined by a perfectly normal low columnar epithelium. Altogether, they present a distinct resemblance to those of the pre-menstrual human uterus, and are quite unlike those of Platyrrhines, like Cebus or Chrysothrix. They open freely on the surface, with the possible exception of the gland situated below the blastocyst, directly in line with the central villus (fig. 59), and the one on its right, both of which appear to end blindly. Both these glands are almost completely filled by maternal blood ; the others contain a fine granular material. The glands underlying the endometrial cushion, on nearing the same, become greatly reduced in diameter, and, penetrating through it as narrow straight ducts, open on its surface.

The endometrial cushion (Pl. 9, figs. 59, 60), as SELENKA describes, is formed mainly as the result of the proliferative activity of the uterine epithelium. From the latter there arise numerous club-like ingrowths, solid with the exception of a few round the periphery which are luminated. They extend down into the underlying connective tissue, and there break up into rounded or ovalish " cell-nests." The connective tissue between them is loose, and contains numerous capillaries. Such cell-nests are present below, and centrally to the marginal attachment of the blastocyst, but are absent below the central region of the latter ; if they were ever present in this position, they were probably destroyed by the trophoblast along with the uterine epithelium during the formation of the implantation depression. SELENKA describes and figures what he believes to be similar cell-nests in *Semnopithecus pruinosus* Lk and in *Cercocebus cynomolgus* (*Macaca irus*), and states that they occur also in the Gibbon, but I have failed to find any description of them in that Anthropoid.

The remarkable precocity in placental development which characterises the Catarrhine blastocyst is well illustrated by the present stage. Whereas in our Hapale 2 blastocyst, the embryo of which is distinctly more advanced than Keim S, placental development is only just commencing; in the latter it is already far advanced, chorionic villi,

surrounded by a continuous intervillous blood-space filled by maternal blood, having already been differentiated as definitely individualised structures.

The chorionic wall of the blastocyst consists over its extent of (1) an outer layer of trophoblast composed of a single layer of cubical cells, overlain on the lower or embryonal hemisphere wall only, by a thin layer of syncytiotrophoblast containing sparse flattened nuclei, and (2) an inner layer of chorionic mesoderm, lining the extra-embryonal cœlom, in the form of an extremely attenuated membrane, composed of a single layer of flattened cells. It is somewhat thickened, however, where it is prolonged to form the axes of the central and some of the other larger villi.

The chorionic villi arising from the embryonal hemisphere number, according to SELENKA, about fifty (about twenty large and thirty small). The largest villus of all, the central villus, in whose base the embryo is situated, has a diameter of about 0·2 mm., and very soon divides into a number of smaller branches of varying size. The remaining villi also vary considerably both in thickness and in length, the shortest lying at the periphery of the villous field where the implantation depression is shallowest, and the longest (up to 0·49 mm. in length) more centrally. They vary also in the extent to which the chorionic mesoderm has penetrated into them. Though there appear to be no villi completely devoid of mesoderm, in the case of some of the smaller the penetration is only slight, whilst in the larger it rarely, if ever, exceeds more than about two-thirds of their length, so that each villus possesses a solid terminal or distal portion of variable length which serves to connect the more extensive mesoderm-containing proximal portion with the floor of the intervillous blood-space. Each such terminal segment consists of a solid cellular core, composed of cells with nuclei similar to those of the cytotrophoblast, and in favourable sections seen to be in direct continuity with that layer, and of an investment of syncytiotrophoblast forming the direct prolongation of that enclosing the proximal segment of the villus. Thus the latter segment consists, like the chorion of which it is an outgrowth, of an investing layer of trophoblast (differentiated into a basal cellular layer of cytotrophoblast (Langhans layer) and a thin superficial layer of syncytiotrophoblast), and a very slender axis of mesoderm, whilst the distal segment is solid and formed of a compact core of cytotrophoblast and a thin covering of syncytiotrophoblast.

Now the interest of this condition lies in the fact that the chorionic villi of the early human blastocyst exhibit a precisely comparable structure, their distal segments being formed of solid so-called " cell-columns " (Zellsäulen) of cytotrophoblast, invested by syncytium (Pl. 18, fig. 104). The whole distal segment represents the remains of the hypothetical solid " primary villus " of the human embryologist and the proximal segment, the so-called " secondary villus," destined to lengthen *pari passu* with the growth of the mesoderm into the " primary " portion of the villus. These " cell-columns " are not mentioned by SELENKA in his description of Keim S. He simply states that the chorionic ectoderm (Langhans layer) enlarges at the ends of the villous branches to " einem vielschichtigen Vollgewebe."

The " cell-columns " can be traced quite clearly in many instances into connection with the loose endometrial tissue flooring in the intervillous blood-space and sometimes indeed spindle-shaped endometrial cells may extend for a short distance into their tips. Their investing syncytial layer at the same time, with or without previous thickening, passes into direct continuity with a quite irregular discontinuous layer of syncytiotrophoblast which lies on the surface of the endometrial tissue and sends prolongations into the same (Pl. 10, fig. 62). Over a narrow zone, round the periphery of the intervillous space, it appears as a relatively thin, uniform layer which passes above into continuity with the syncytiotrophoblast of the chorion, but over the rest of the floor it takes the form of a quite irregular layer, which in places is coarsely vacuolated or reticular in character. Moreover, it is not everywhere perfectly continuous, there being small areas where the endometrial tissue directly bounds the intervillous space. It contains sparse nuclei, varying in size but mostly large, ovalish and vesicular.

That this peripheral syncytial layer possesses invasive and cytolytic properties is clearly indicated by the fact that processes of it penetrate into the underlying endometrial tissue and by the characters of the latter. As can be seen in Pl. 10, fig. 62, the narrow superficial zone of endometrial tissue underlying the syncytial layer presents quite a different appearance to that of the deep zone, being less uniform, looser and distinctly œdematous in character.

In it there are present numbers of enlarged capillaries, the endothelial walls of which are more or less altered. Adjacent to the intervillous space, the endothelium has largely disappeared with the result that the capillary lumina are in more or less free communication with that space through the gaps in the peripheral syncytium, whilst the more deeply situated endothelium has hypertrophied to form an irregular layer of large ovoidal or irregularly cubical cells, many of them in process of degeneration. In the large capillary (*cp.*[1]) which lies directly below the central villus in Pl. 10, fig. 62, the endothelium over its upper end has broken down, whilst over the rest of its extent it has undergone hypertrophy. On the right of this capillary is a second, much more irregular in outline, into the lumen of which a vacuolated mass of syncytium directly projects (*cp.*[2]). Its endothelium is in active process of degeneration.

This peripheral syncytial layer obviously corresponds to the so-called " basal syncytium " of the Platyrrhine placenta but it would seem to possess more potent cytolytic properties than it does. It is probably to be regarded as the persisting peripheral portion of the primary trophoblastic proliferation which originally filled the implantation depression prior to the formation of the villi and the intervillous blood-space and which has been distinguished by GROSSER as the " Implantationssyncytium " in the early human blastocyst (MILLER, BRYCE-TEACHER I., KLEINHANS and others), in contrast to the " Resorptionssyncytium " which is formed later from the trophoblast of the chorion and the villi (" villous syncytium ").

The intervillous blood-space is extensive and largely filled by normal maternal blood-corpuscles, though " vesicular " corpuscles in small numbers are also present. It is

deserving of mention that there are slight traces of delicate syncytial strands passing from the villous syncytium into the intervillous space which may represent a further remnant of the implantation syncytium.

The blastocyst Lk. of the Langur, *Semnopithecus pruinosus* [*Pithecus obscurus*] described by SELENKA ('01, '03) presents an essentially similar implantation picture to that of KEIM S. but with certain interesting differences in detail (fig. 19*a*, Pl. 21).

The blastocyst has a greatest diameter, estimated from SELENKA's sectional fig. 7, of 0·67 mm., though in the text he speaks of it as " die 1 mm. grosse Keimblase," whilst its diameter, measured from its attached margins, is only 0·5 mm. A single central villus arising directly opposite the embryo and consisting of a central stem, with indications of lateral branches, is alone developed. Its tip reaches to near the floor of the maternal blood-space, is " mehrschichtig " and is connected with the latter by syncytium. The peripheral or basal syncytium is thicker, more compact and more complete than in Keim S. and it is a point of interest that a fair amount of what may possibly be implantation syncytium is present in the intervillous space. Round the blastocyst is an endometrial cushion similar to that of Keim S., only not quite so massive, and SELENKA records the interesting fact that a corresponding cushion is also present on the dorsal wall of the uterus, to which the anti-embryonal pole of the blastocyst was attached. No details of the attachment are available but SELENKA figures a portion of a section through the secondary cushion (his fig. 8, p. 334) in which the uterine epithelium is seen to have thickened to form a stratified layer, two or more cells in thickness and with an irregular free surface (*cf.* the uterine epithelium of Hapale 2 (Pl. 8, fig. 57)), whilst club-shaped ingrowths are shown arising from its deep surface.

It will be evident from these two blastocysts that the early placental development in the Catarrhine differs in certain important respects from that of the Platyrrhine. In the first place it would appear that the attachment of the Catarrhine blastocyst is effected when that structure is quite minute and at a very early stage in the development of the embryo, prior indeed to the attainment by the yolk-sac of the fully vesicular condition. Following on the fixation of the blastocyst, the next event of importance would seem to be the formation from the ectoplacental trophoblast of the embryonal hemisphere of a vacuolated or reticular mass of syncytiotrophoblast (implantation syncytium) which actively invades and destroys the uterine epithelium and the subepithelial endometrial tissue with which it comes into contact. The result is the formation of a crater-like depression or implantation pit at first occupied by the syncytium and the concomitant opening up of maternal capillaries and the escape of maternal blood into the lacunar spaces of the syncytium. Then, in the second place, we have the precocious development from the chorion of independent outgrowths, the chorionic villi and the accompanying reduction of the implantation syncytium and its replacement by a continuous intervillous space, filled by maternal blood. These features represent a very distinct advance on the condition in the Platyrrhines and are to be regarded as the outcome of marked acceleration in the developmental processes. The trophoblast

in particular becomes active at an earlier period than in the Platyrrhine and is endowed with more potent invasive and cytolytic properties, whilst the chorionic villi are formed directly and precociously and are bathed by maternal blood practically as soon as they are formed. In all these respects the Catarrhine foreshadows the Anthropoid.

The very early formation of a large branching central villus, at the base of which the embryo is situated, is regarded by SELENKA as characteristic of all the Catarrhines, but it should be emphasised that such a villus has only been observed in the primary placenta and it is, accordingly, tempting to suggest that its formation may be associated with the occurrence in the immediate neighbourhood of the embryo of a localised thickening of the mesoderm such as might result from the presence of a mesodermal proliferating area at the caudal end of the shield ectoderm as seen in our Hapale 2 embryo and possibly also in Keim S. In this same connection it may be recalled that the embryo of Cebus 509 is also situated at the base of a very extensive villous-like outgrowth.

A distinctly later stage in the differentiation of the Catarrhine placenta is seen in the blastocyst of the Kra Monkey, *Cercocebus cynomolgus* [*Macaca irus*], Keim Ca, figured but only briefly described by SELENKA ('00, p. 196, figs. 27–31). His fig. 28 is reproduced here as fig. 20*a*, Pl. 21. What I take to be the sections of this blastocyst are preserved in the Hubrecht Collection (*Cercocebus cynomolgus*, 236*a*).

The blastocyst measures $2{\cdot}6 \times 1{\cdot}5$ mm. in diam. and the embryo about $0{\cdot}4 \times 0{\cdot}3$ mm., whilst the primary placenta has a diameter of about $2{\cdot}7$ mm. and the secondary about $1{\cdot}6$ mm. (measurements based on SELENKA'S figures).

In addition to the primary placenta on the dorsal wall, a smaller less advanced secondary placenta is now present on the ventral wall. The villi are simple with only indications of branching, except in the case of the large central villus of the primary placenta which is definitely branched, four of the branches being connected with the floor of the intervillous space, the remaining two ending freely. Apart from these, the tips of all the villi of the primary placenta and most of those of the secondary placenta are figured as being connected with the floor of the intervillous space. The chorionic mesenchyme is now a well-defined thickish layer and is prolonged to form the axes of the proximal halves or thereabouts of the villi of the primary placenta. The distal portions of the same villi which connect with the floor of the intervillous blood-space are shown in SELENKA'S figure as dark strands enclosed by fine lines, the latter representing the syncytium which is labelled, but the strands are not referred to in the text. They are clearly the same as the " cell-columns " of Keim S. as well as those of DUCKWORTH'S early placenta of *Macacus nemestrinus* presently to be referred to.

The villi of the secondary placenta are all simple and unbranched, they are much shorter than those of the primary and only indications of " cell-columns " are shown in the figure, though a " zusammenhängende Syncytium-Platte " (basal syncytial layer) is indicated as forming the floor of the intervillous space. That floor is only slightly depressed below the level of the surface, *i.e.*, there is no definite implantation depression such as exists in the primary placenta.

Though there are no endometrial thickenings around the placentas, apart from a slight œdematous swelling round the primary, SELENKA figures and describes numerous cell-nests in the endometrial tissue below and around the secondary placenta as well as below the margins and more sparsely below the central region of the primary, many of which have become syncytial. He regards them as of similar origin to the nests in Keim S. and blastocyst Lk., but in view of the fact that the neck portions of the uterine glands shown in his fig. 28 have disappeared, the possibility that some of them at least may be of gland epithelial origin cannot be excluded.

It will be evident from the foregoing that our knowledge of the placentation of blastocyst Ca is not of a very detailed character. It is therefore fortunate that we have available another early Catarrhine stage, viz., the early placenta of *Macacus nemestrinus* described by Dr. W. H. L. DUCKWORTH ('07) in 1907 which appears to be, if anything, just a little older than that of Keim Ca. Through the great kindness of Dr. DUCKWORTH I have been enabled to study his sections of this important stage and to provide four new figures (figs. 100–103) to illustrate the details of its structure. The following account is based on Dr. DUCKWORTH'S description, supplemented by my own observations. I shall refer to the specimen as *Macacus placenta* (DUCKWORTH).

When the uterus came into the hands of Dr. DUCKWORTH it had already been opened, the embryo was no longer present and only the placenta on the posterior wall was available for examination. Dr. DUCKWORTH states (*loc. cit.* p. 299) that the placenta appeared as a small hemispherical projection, measuring 2·2 mm. in diam. (in section its maximum diameter is 2·08 mm.). It is thus intermediate in size between the primary and secondary placentas of Keim Ca and from its general characters, the presence of relatively short villi and the impossibility of distinguishing a main central villus, I am inclined to think that it is the secondary one. The uterus was fixed by the late Dr. CHARLES HOSE, presumably in formol, and its state of preservation is quite good.

A low power view of a section through the presumed secondary placenta is shown in Pl. 17, fig. 100, from which it will be seen that it forms a projecting knob-like mass, the superficial part of which is formed by the placenta fœtalis, comprising the chorion, its villi and the intervillous blood-space, whilst its deeper part is formed of a very irregular zone of endometrial tissue underlying the latter and reaching down as far as the level of the constriction marking the margin of attachment of the chorion and its reflection to form the thin chorion læve (figs. 100 and 103). Below this level is the deeper part of the endometrium containing the long, straight and occasionally branched uterine glands. Those below the central region of the placenta appear to end blindly, whilst those more peripherally situated bend outwards to open on the surface around the placenta. Beyond the placental margin the endometrium is in no way specially thickened. The uterine epithelium is intact and composed of a low columnar epithelium, exhibiting no signs of proliferative activity. On its surface, the underlying uterine glands open freely into the uterine lumen. It is evident then that the ring-shaped

endometrial thickening, so characteristically developed in Nasalis, Keim S., and in Pithecus, Lk., does not occur in all Catarrhines. Moreover, as DUCKWORTH has emphasised, there is here no implantation excavation such as we encountered in the primary placental primordium in the two forms mentioned; on the contrary, the endometrial tissue flooring in the intervillous blood-space is elevated above the general level of the uterine surface. It is possible, however, that this elevation may be due, in part at least, to the fact that the uterine wall around the placental site has been artificially folded back during fixation and it may also be recalled that in Macacus Ca, the secondary placenta had no definite implantation depression.

The chorion, like that of Keim Ca, possesses a well developed thick layer of mesenchyme, whilst its trophoblast as well as that of the proximal segments of the villi is clearly distinguishable into a basal cytotrophoblast and a superficial layer of syncytium which is thicker and less uniform than that of Keim S. (Pl. 17, fig. 101).

The villi, as already noted, are relatively short; except for a few which are quite small, and " free," they are connected with the floor of the intervillous space and are mostly simple, thin and unbranched, though a few are thicker and branched (Pl. 18, fig. 102). DUCKWORTH states (*loc. cit.* p. 300) that " the mesoderm has not yet reached the majority of these villi." I find, however, that the larger villi are well penetrated by chorionic mesenchyme, but the smaller show only a relatively slight penetration involving about one-third of their length. In the case of all the attached villi, their distal segments are formed by solid cellular strands of varying length, each of them invested by a syncytial layer continuous with that of the proximal mesoderm-containing segment (" secondary villus "). These strands are clearly related to those we identified as trophoblastic " cell-columns " in SELENKA'S Keim S. as well as to the strands which terminate the villi in his Macacus blastocyst Ca. In Keim S. we had no hesitation in regarding them as composed of cytotrophoblast and here there can be no doubt that their proximal parts at least are also formed of the same cell-layer, but the constitution of their distal parts is not so readily determinable. If the villi depicted in figs. 101 and 102 be examined (see especially the villus situated towards the left side of fig. 101), it will be seen that the cells forming the proximal part of the strand are in direct continuity with the cytotrophoblastic layer of the " secondary villus " and that they are compactly arranged, possess fairly definite outlines and contain nuclei ovalish or rounded in form and fairly uniform in size, whereas the cells composing the distal part tend to be more loosely arranged, are less well delimited and more vacuolated, whilst their nuclei are more variable both in form and size and are occasionally seen in mitosis. They are thus to some extent transitional between the undoubted trophoblast of the proximal part of the strand and the looser tissue forming the superficial zone of the endometrium into which they merge below, there being no definite line of demarcation between them. The question accordingly arises, is this distal part formed from trophoblast or from endometrial tissue ? After careful study of the sections and taking into account the condition in later stages, I am inclined to hold that the distal, like the proximal parts of these

strands or " columns " are composed of cytotrophoblast and that their junctions with the endometrial tissue lie about on a level with the deep extremities of the irregular bays into which the floor of the intervillous blood-space is produced. In this connection, it may be noted that WISLOCKI and HARTMAN ('29), in their description of the placenta of the 7·5 mm. embryo of *Macacus rhesus*, state that " the basal portions of the villi are composed almost solely of solid masses of cytotrophoblast or Langhans cells."

The bays just referred to vary in size and in depth, with the result that the floor possesses an extremely rugged, uneven contour. Their presence suggests that the endometrial tissue has undergone active erosion as the result of the activity of the syncytium which lines them.

This syncytium (the peripheral (basal) syncytium) clothes the entire extent of the floor and forms a practically continuous boundary to the intervillous blood-space, which is only interrupted by the openings of the maternal capillaries. It is in direct continuity with the syncytial covering of the " cell columns," that layer tending to become irregularly thickened over the terminal ends of the latter.

The peripheral syncytium here (figs. 101–103) generally resembles in its characters that of Keim S., but is on the whole more strongly developed. In parts of its extent, it appears as a fairly uniform homogeneous layer containing sparse, flattened, ovalish or spherical nuclei ; in other parts it is thickened and possesses a coarsely vacuolated character as in fig. 102 where a large vacuolated mass of syncytium is seen bounding a space, really the lumen of an enlarged capillary, which some sections further on opens into the intervillous blood-space. As DUCKWORTH has described, similar masses are to be met with in the superficial zone of the endometrium which either bound or have actually penetrated into the lumina of enlarged capillaries, whilst more exceptionally a syncytial mass prolonged from the peripheral syncytium, can be seen actually penetrating the blind end of a uterine gland, as is shown in DUCKWORTH'S figs. 9–11. Figs. 101 and 103 also provide evidence of this invasive activity of the peripheral syncytium and that it also possesses potent destructive properties is shown by the degenerative changes that are evident in the endometrial tissues and more especially in the blood-vessels and uterine glands. The superficial zone of the endometrium as far down as the level of the constriction round the base of the placental knob exhibits the greatest alteration and in Pl. 17, fig. 100, it will be seen that the uterine glands below the central region of the villous field end blindly just about this level. Their neck portions have disappeared, there being no evidence of any of them opening directly into the intervillous space, but rounded or oval masses of enlarged cells, staining more deeply than the stroma-cells, occur above, as well as adjacent to the terminations of the glands. The appearances suggest that such masses are derived from the gland epithelium which is frequently distinctly thickened. They are more numerous in the peripheral region of the placenta than centrally, but are nowhere so abundant as the cell-nests figured by SELENKA in the endometrium of his stage of Macacus Ca ; nevertheless, as I have already pointed out (p. 142), the possibility cannot be excluded that some at least of the " cell-

nests " in that specimen are likewise of gland-epithelial origin. It is worthy of mention that the epithelium at the terminal end of the long gland seen on the right in Pl. 17, fig. 100, has broken down and the gland-lumen leads into what appears to be an enlarged capillary, bordered by spindle-shaped cells. The lumen of this particular gland contains only a granular coagulum, but in others, as DUCKWORTH has recorded, the lumina are more or less completely filled by maternal blood corpuscles (Pl. 18, fig. 103, *gl.*[2]).

The alterations in the blood-vessels are even more striking than those in the glands. In the superficial endometrial zone, there are present fairly numerous capillaries, many of them greatly enlarged, and with their endothelium in varying stages of hypertrophy and degeneration. In some of them, the endothelium in their deeper parts appears intact and only slightly thickened, whereas in their more superficial parts, it is in process of degeneration and may have largely disappeared. In others, it has hypertrophied to form large oval cells which project irregularly into the lumen (figs. 101 and 102). These enlarged capillaries can be followed up as irregular channels and clefts, devoid of a continuous lining, until they open into the intervillous blood-space through gaps in the peripheral syncytium, prolongations of which not infrequently project into them or border them on one side. Some of these capillaries can be traced into continuity with the fine straight vessels (venules) which run down in the deep endometrial tissue between the uterine glands. In this same position are situated small arterioles, characterised by their spiral course, thick walls and minute lumina. Even before they reach the level of the blind ends of the uterine glands, their endothelium has become hypertrophied and the enlarged cells becoming detached, largely block up their lumina as is the case also in the corresponding arterioles in the endometrium of Keim S. They seem to contain little or no blood, but can be followed up into the superficial zone as quite irregular channels with a discontinuous lining of oval or spindle-shaped cells.

The endometrial tissue of the superficial zone presents a very heterogeneous appearance, since in addition to its own proper elements, there are present in it endothelial and glandular epithelial derivatives, as well as small blood extravasations, numerous disseminated leucocytes, mainly polymorphonuclears, and patches of serous coagulum. Its stroma cells are enlarged and vacuolated, and intercellular clefts are present between them, so that they contrast sharply with the compactly arranged, spindle-shaped cells of the deep zone of the endometrium.

The just described Macacus placenta (DUCKWORTH) and that of SELENKA's Keim S. are the earliest Catarrhine placentas known of which we possess anything approaching a detailed knowledge, and in the present connection their value lies in this that they afford a definite basis for comparison with the early Anthropoid placenta as exemplified by that of the early human embryo. Thanks to the kindness of Dr. FLORIAN, I am able to provide a figure of a section (Pl.18, fig. 104) of the placenta of his Bi I human embryo (FLORIAN, '28*a*, '28*b*, Tafelabb. 1). This embryo, according to FLORIAN, comes very near in its stage of development to the embryo Beneke (STRAHL-BENEKE, '10).* Its

* *v.* also FLORIAN-BENEKE, '30/'31.

embryonal shield measures 350 μ. in length by 343 μ. in breadth; the primordia of the primitive streak and the cloacal membrane are already established. The chorionic vesicle, measuring in internal diameter 2·13 × 2·12 × 2·3 mm. is shown *in situ* in Pl. 20, fig. 112.

If we compare fig. 104, Pl. 18, of the placenta of Bi I with fig. 101, Pl. 17, of the Macacus placenta (DUCKWORTH), the general similarity of the two is seen to be extraordinarily striking, so much so, indeed, that we should have no hesitation in at once grouping them together as belonging to the same placental type, even though they present obvious differences in detail. That similarity centres on the presence in both of chorionic villi of the same sharply individualised type situated in a continuous intervillous blood-space and composed each of a short proximal segment penetrated by a core of chorionic mesenchyme and a longer distal segment formed by a solid " cell-column," connected below with the floor of the intervillous space. The trophoblast investing the proximal segments is identical in the two and consists of a basal cellular layer (Langhans layer, cytotrophoblast) and a superficial layer of syncytiotrophoblast which is continuous with the similar layer investing the " cell-columns." The latter in Bi I are even more obviously cytotrophoblastic in constitution than are those of Macacus and it is worthy of note that in both, the cytotrophoblastic cells composing them are larger than those of the Langhans layer of the proximal villous segments. The Bi I cell-columns, however, differ from those of Macacus in that they spread out below and join together to form a very irregular layer of very varying thickness which encloses prolongations of the intervillous space. This layer is the primordium of the relatively thick layer which in somewhat later stages temporarily forms the floor of the intervillous space and which is known to the human embryologist as the " basal ectoderm " or " Trophoblastschale " (*cf.* GROSSER, '27, p. 277).

Such a trophoblastic " shell " has, so far, only been described in the early human placenta, but in later Catarrhine placentas what appears to be a comparable but much less developed layer of cytotrophoblast is found clothing the surface of the superficial zone of the decidua basalis, immediately below the layer of peripheral syncytium, the two layers fœtal and maternal intermingling where they meet. It appears to be formed in much the same way as the trophoblastic shell by the growth and extension of the cytotrophoblast investing the distal terminal portions of the attaching villi. Here the cytotrophoblast is markedly thickened and persists long after it has disappeared from the remainder of the villous stems. The composite layer which results from the intermingling of the fœtal cytotrophoblast with the maternal endometrial tissue, constitutes, as already noted (*ante*, p. 128), the " chorio-basalis " of STRAHL ('03) (see also later, p. 148). WISLOCKI and HARTMANN (*loc. cit.*) in their Macacus placenta also describe the cytotrophoblast of the expanded ends of the attaching villi as spreading out in sheets and intermingling with the elements of the endometrium to form the " chorio-basalis."

In the placenta of Bi I, FLORIAN ('28*a*) describes the trophoblastic shell as consisting

of enlarged Langhans cells and of syncytial elements in the form partly of multinucleate masses of variable form and size, partly of darkly staining elongated elements containing pycnotic nuclei. These syncytial structures he regards as being formed directly from the Langhans cells of the " shell " and the cell-columns. It is to be noted also, that in places (Pl. 18, fig. 104), the cytotrophoblast of the " shell " is separated from the subjacent decidual tissue by irregular discontinuous masses of syncytium, some of them being greatly vacuolated. These masses thus occupy a comparable position to that of the peripheral (basal) syncytium in the early Macacus placenta but, according to FLORIAN, they can only in small part be regarded as remnants or derivatives of the original implantation-syncytium, in greater part they would appear to be formed directly from the cytotrophoblast of the " shell." In addition, FLORIAN has described the presence, in the decidual tissue of the Bi I placenta, of elongated spindle-shaped elements, sometimes connected together to form networks ; they constitute what he terms the " Proliferations-elements oder plasmodium " and according to him represent invasive elements, prolonged from the syncytial masses occupying the position of the peripheral syncytium (Pl. 18, fig. 104, *p.syn.*).

In the Macacus placenta (DUCKWORTH) the only comparable structures present are the irregular prolongations of the peripheral syncytium, which penetrate into the endometrial tissue. Lastly, it may be noted that whereas in this early human placenta the stroma cells of the endometrium are already beginning to undergo enlargement to form decidual cells, in the Macacus placenta that differentiation can hardly be said to have commenced.

But leaving the differences in detail on one side (and they are mainly associated with the presence of the trophoblastic " shell " in the early human placenta, the great development of which is probably to be associated with the interstitial type of implantation), the striking similarities in the form and constitution of the villi, and indeed of the entire placenta, in these early stages of the Catarrhine and the Anthropoid, taken in conjunction with the fundamental agreements in the details of their early ontogeny, so strongly insisted on by SELENKA, provide, in my opinion, ample justification for the conclusion that the Anthropoids took origin from a primitive Catarrhine stock.

It is not necessary for our present purpose to follow in detail the later history of the Catarrhine placenta. WISLOCKI and HARTMAN ('29) have recently provided an account of the placenta of the 7·5 mm. embryo of *Macacus rhesus*, whilst STRAHL and HAPPE ('05) have described at some length the more important of the older placental stages in SELENKA'S collection. I therefore content myself with providing a figure of the placenta of *Semnopithecus* [*Pithecus*] *femoralis* (fœtus, G.L., 35 mm.) (Pl. 18, fig. 105), for comparison with Pl. 19, fig. 106, illustrating the placenta of a human fœtus of G.L. 29 mm., in order to emphasise the close general resemblance of the two, and especially the presence in both of the same arborescent type of villus, the main stem of which subdivides usually into a number of secondary stems, some or all of which are attached

by their apices to the decidua basalis, whilst from them numerous finer lateral offshoots arise which undergo further subdivision, the terminal branches projecting more or less freely into the continuous intervillous blood-space (Pl. 19, fig. 107). But whilst there is this fundamental agreement in the form and, it may be added, in the constitution of the villi, the Catarrhine placenta presents certain peculiarities of its own which distinguish it from that of the Anthropoid. Let us see what these peculiarities amount to. They concern the peripheral (basal) syncytium, the so-called chorio-basalis, and the relations to each other of the villous branches.

STRAHL and HAPPE (*loc. cit.*, p. 499) point out that whereas in the Platyrrhines the peripheral or, as they term it, the " basal " syncytium is " mehrschichtig," or, more accurately described, takes the form of a continuous thick layer containing numerous superimposed nuclei, in the Catarrhines the corresponding layer is " einschichtig," *i.e.*, it appears as a relatively thin layer, with its nuclei usually in a single row, though, as WISLOCKI ('29, p. 67) points out, it varies slightly according to the species, and in the relatively young placenta of *S. femoralis* shown in Pl. 18, fig. 105, it appears irregularly thickened and vacuolated, whilst in the Anthropoids, in the corresponding position, there is no such continuous layer, but only isolated patches of syncytium, either layer-like or in the form of small irregular masses.

In the Platyrrhines, as we have already seen, the peripheral syncytium is clearly none other than the peripheral portion of the original massive trophoblastic proliferation, but in the Catarrhines the evidence at the moment is not sufficient to justify a positive statement as to its mode of origin. We do not know whether it is formed exclusively by the growth of the peripheral persisting portion of the implantation syncytium or partly from that, partly by the extension of the villous syncytium, though the latter seems the more probable. In the Anthropoids the discontinuous pieces of syncytium present in this position, are presumably derived in part from the growth of the villous syncytium, in part, as FLORIAN has suggested, by the syncytial transformation of cells of the trophoblastic shell. It is perhaps worthy of remark that the intervillous blood-space of the Catarrhine placenta, unlike that of the Anthropoid, is bounded by a practically continuous layer of syncytium, and possibly, as a consequence, the laminated layers of " fibrinoid " which form such a conspicuous feature in the roof and floor of the Anthropoid placenta are in the Catarrhine organ much less marked, judging from the full-term placenta of *Papio porcarius*.

As concerns the " chorio-basalis," that term, as already mentioned (*ante*, p. 128), has been applied by STRAHL ('03, *cf.* also WISLOCKI and HARTMAN ('29) and WISLOCKI ('29, p. 67)* to the composite zone of tissue which, in the Catarrhines, lies immediately below the peripheral syncytium, between that and the subjacent compact zone of the decidua basalis, from which it is usually fairly definitely marked off. This latter zone, it may be noted, is not fibrous, as is suggested by the designation " pars fibrosa " applied to it by STRAHL and HAPPE ('05), but consists of somewhat enlarged spindle-shaped

* *Cf.* further, WISLOCKI ('30, p. 189).

stroma-cells, really forming the decidual cells which, in the Catarrhines, never attain the size of those of the Anthropoids.

STRAHL recognised the existence of a "chorio-basalis" in the Catarrhine and Anthropoid placenta, but not in that of the Platyrrhines, though it is clear, as WISLOCKI has also pointed out, that in the latter it is represented by the superficial compact zone of the decidua basalis into which penetrate prolongations of the peripheral syncytium.

The name "chorio-basalis" is not a very appropriate one even in the case of the zone in the Catarrhines, inasmuch as the whole of the chorion is not involved, but only its trophoblast, whilst in the Anthropoids, as GROSSER ('27, p. 307) has pointed out, the zone is not confined to the decidua basalis, but is also present in relation to the decidua capsularis. In the earlier histiotrophic stages of the human placenta, GROSSER ('27, p. 306) has proposed to term it the "penetration zone" (Durchdringungszone). In the Pithecoids it represents a persistent junctional zone, composed partly of fœtal elements (syncytial in the Platyrrhines, cellular in the Catarrhines) and partly of maternal decidual elements.

As already indicated (*ante*, p. 146), it arises in the Catarrhines by the spreading out on the surface of the pars compacta of the decidua basalis of the thickened cytotrophoblast investing the distal portions of the attaching villi. These latter are so close set that the cytotrophoblastic extensions can readily join with each other so as to form a continuous layer of varying thickness, the cells of which intermingle with those of the compact zone along their line of junction. In this way there is produced a well-defined composite zone (Pl. 19, fig. 107, *zj*) underlying the peripheral syncytium which varies in its detailed characters in the different species, and which, once established, persists in a readily recognisable, though more or less degenerate, condition through the later stages, right up to the full-term placenta, whereas only remnants of it are described as persisting in later stages of the human placenta.

In this connection it may be recalled (for the fact is well known) that in the human placenta of such a stage as that represented in Pl. 19, fig. 106 (fœtus, G.L. 29 mm.), the cytotrophoblast of the greatly-reduced "cell-columns" of the attaching villi may be found spreading out on the surface of the decidua basalis, round their bases of attachment, in the form of irregularly ring-shaped zones which thin out peripherally. Such isolated areas of cytotrophoblast are no doubt to be regarded as remnants of the trophoblastic "shell" of earlier stages, that "shell" itself being represented in the Catarrhine placenta by the cytotrophoblastic layer of the "penetration" or "junctional" zone (chorio-basalis).

Finally, as concerns the relations of the villous branches to each other, it has been shown by several observers in recent years, first by COVENTRY ('23) in 1923 in the placenta of *Cynocephalus* [*Papio*] *papio* (fœtus, C.R.L. 122 mm.), then by GROSSER ('25, '27) in 1925, in the shed placenta of Cercopithecus (?) and by WISLOCKI ('29, p. 64) in placentas of *Colobus abyssinicus caudatus* (fœtus, C.R.L. 143 mm.), *C. abyssinicus ituricus* (fœtus, C.R.L. 134 m.m), and the Macaque (fœtus, C.R.L. 163 mm.), that the villi in

parts of the placenta are connected together by nucleated syncytial strands or plates so that they form a more or less well developed network, recalling the villous trabecular system of the Platyrrhine placenta.

According to COVENTRY* (*loc. cit.*, pp. 239–240) the syncytium covering the villi gives origin to " numerous syncytial processes projecting freely into the intervillous space " as well as to syncytial buds. In addition, it " forms also a peculiar network between the villi. This is unevenly developed, being much more marked in some areas than elsewhere ; such a region is shown in fig. 5. These intervillous strands are of two forms : the first, and much less usual, is thin cords of cylindrical section ; the other consists of wide, flat bands of syncytium sometimes extending through ten or more sections each 10 μ thick."

In *Colobus caudatus*, WISLOCKI (*loc. cit.*, p. 64) states that " the chorionic trabeculæ are connected by abundant, slender, richly nucleated strands of syncytium (figs. 7 and 14). The number of connections in no way compare with their abundance in Platyrrhines, for in COVENTRY'S and my own specimens there are, as well, numerous free villi. Moreover, the intervillous space in these forms is much wider and more confluent than the intertrabecular sinuses of Platyrrhines."

GROSSER ('25, '27, p. 173, fig. 163) in the case of the shed placenta of Cercopithecus (?), describes the villous branches as being connected by syncytial plates with the result that the intervillous space is subdivided into small cleft-like interconnected channels. In addition to such intervillous syncytial plates, he states that there are also present free ends of syncytial plates and syncytial sprouts. His figure conveys the impression that the syncytial connections are more richly developed in his specimen than in those described by COVENTRY and WISLOCKI (see COVENTRY'S figs. 5 and 6, Pl. 2, and WISLOCKI'S fig. 7, Pl. 2, and figs. 14 and 15, Pl. 3).

All the placentas examined by the investigators above named belong, it should be noted, to relatively late developmental stages.

Both GROSSER and WISLOCKI are inclined to regard the interconnected net-like condition of the villi in these Catarrhines as of significance in relation to placental evolution. In GROSSER'S opinion, the condition would seem to represent the transition between the labyrinth type of placenta and the villous type characteristic of the higher Primates. He writes ('28, p. 2, *cf.* also '26, p. 7) : " Die beiden im histologischen Bild so stark von einander verschiedenen Gruppen [villous and labyrinth placentas] standen sich lange Zeit unvermittelt gegenüber ; erst in den letzten Jahren sind von zwei amerikanischen Forschern, COVENTRY und WISLOCKI, und von uns selbst Affenplacenten beschrieben worden, die Ubergänge darstellen und den Weg zeigen, auf dem die Placenta olliformis des Menschen entstanden sein mag. Besonders merkwürdig erscheinen dabei diejenigen Placenten, bei denen ein dem menschlichen ähnlicher Zottenbaum durch Syncytiumblätter, die zwischen den Zweigen ausgespannt sind, ergänzt wird,

* I am much indebted to Dr. COVENTRY for his kindness in sending me sections as well as portions of his Cynocephalus placenta for examination.

so dass kein zusammenhängender intervillöser Raum ensteht, sondern ein Labyrinth von kleineren, vielfach platten Räumen."

WISLOCKI, also, tentatively entertains a somewhat comparable idea of the significance of this condition. He writes ('29, p. 64): "Moreover, to one familiar with the labyrinth in Platyrrhines this type appears logically to represent a transition between the Platyrrhine and Catarrhine placenta." He is careful to add: "However, until complete developmental series of one or other of these species has been obtained, including the early stages, their exact relationship will not be known." Nevertheless, he goes on to remark: "Bearing in mind the possibility of such a transition amongst the Simiæ, the present series has been studied with the result that other species have been found which give evidence of such a transition." That evidence is to the effect that in *C. abyssinicus ituricus* and in the Macaque, "a large number of the villi do not end in free tips, but have strands of syncytium connecting them. Moreover, buds or sprouts of pure syncytium are seen upon the villi in the Macaque. The latter are also observed in the gibbon, gorilla and man, whereas actual syncytial trabeculæ are very infrequent." He goes on to remark that "these observations suggest that the buds and sprouts in Anthropoids represent the last remnant of a previous phylogenetic condition which is in process of disappearance." To me, they suggest no such conclusion but simply that the villous syncytium in the Catarrhines and the Anthropoids is endowed with a like capacity to proliferate and to form localised sprout-like outgrowths and to a higher degree in the former than in the latter.

After a survey of the placenta in some ten species belonging to four genera of Catarrhines (*Macaca, Pithecus, Cercopithecus, Papio*) and of five developmental stages of *Papio porcarius*, I find myself unable to accept either the point of view of GROSSER or the tentative suggestion of WISLOCKI regarding the significance of these syncytial connections. The most striking examples of the latter I have encountered are furnished by the primary placenta of *Macacus cynomolgus* [*Macaca irus*] 737 (fœtus, H.L. 3 cm.), (Pl. 19, fig. 108) and by sections of a late placenta labelled "*Semnopithecus* sp." from the collection of the late RICHARD ASSHETON, of which no history is available (Pl. 19, fig. 109).

The primary placenta of Macacus 737 (Pl. 19, fig. 108) shows a very rich development of syncytial sprouts, especially in its deeper zone. They take the form of fairly coarse irregular strands often of considerable length, which contain numerous nuclei mostly closely aggregated along their axes. The strands branch and anastomose with each other in a quite irregular fashion or they may fuse directly with the syncytial coverings of adjoining villi and so in these ways serve to link up the villous branches into a more or less interconnected system. In places they are present in such abundance as to reduce the intervillous space to what appear in section as irregular spaces and clefts. On the other hand, in the superficial zone of the placenta, below the chorion, the villous branches are for the most part free, being connected only here and there by syncytial strands, whilst they possess relatively few, quite small sprouts.

The secondary placenta of this specimen is much smaller and less advanced than the primary and throughout its extent, it is important to note, much the same condition prevails as in the superficial zone of the latter. The villous branches are mostly free and possess well-marked sprouts, especially in the deeper zone, though they are not very numerous. Occasional sprouts may be seen arising also from the peripheral syncytium.

The placenta of *Semnopithecus* sp. (R.A.) relates to a much later stage of development than that of Macacus 737, judging from the small size and fairly uniform character of the villous branches and the very degenerate condition of the junctional zone. Over extensive areas of the villous field, the villous branches are connected by syncytial junctions, mostly quite short and densely crowded with small darkly staining nuclei, so that they appear as villous networks (Pl. 19, fig. 109), which strikingly recall those of the Platyrrhines (*cf.* Pl. 16, fig. 96) and which in their degree of completeness surpass that shown in GROSSER'S figure of Cercopithecus (?) (*loc. cit.*, fig. 163). But there are other areas where the junctions are much less numerous and yet others where the villous branches are largely free and independent. In marked contrast to the condition in this specimen, I may mention that in a well advanced placenta of *Semnopithecus* [*Pithecus*] *hosei*, 749 (Pl. 19, fig. 107), syncytial sprouts and connections are not at all abundant and this is the case also in the much earlier placentas of three other species of Semnopithecus I have examined.

Crucial evidence in regard to the significance of these syncytial sprouts can only be obtained by the examination of a developmental series as WISLOCKI has pointed out, and this I have been able to do in the case of *Papio porcarius*.* I find that in the early placentas (embryos G.L. 2·65 mm. and 5 mm.), syncytial sprouts are beginning to make their appearance, whilst syncytial connections between the villi are of rare occurrence; in the placenta of an embryo of G.L. 16·5 mm., syncytial sprouts are now more numerous and syncytial connections are met with here and there; in the placenta of a fœtus with a C.R.L. of 6·5 cm., syncytial sprouts and syncytial connections are now quite common and in places the latter may be so numerous as to produce the appearance of a coarse villous network which, however, is nothing like so fine or so complete as in *Semnopithecus* sp. (R.A.); lastly, in the full-term placenta in which the villous branches are now much finer, there is abundant evidence of the presence of syncytial connections (mostly short and thin) between them, but they are not so numerous as to produce the appearance of a villous network. Syncytial sprouts, mostly small and bud-like, are also present in fair numbers.

The evidence set forth above leads me to the conclusion that the intervillous syncytial trabeculæ, variable in their degree of development in different Catarrhines, are purely secondary formations, of no phylogenetic significance, which arise in the first instance as free-growing outgrowths or sprouts from the villous syncytium and which subsequently

* Thanks to the very fine collection of developmental material of this species, made by Dr. S. ZUCKERMAN, Anatomist to the Zoological Society, in connection with his work on the menstrual cycle in the Primates.

unite with similar outgrowths from other villi or fuse directly with their syncytial coverings. Such syncytial sprouts are well known on the human placental villi and that they occur also on those of Anthropoids has been observed by WISLOCKI. Moreover, localised fusions of the syncytial coverings of adjoining villi are not infrequent in the human and gorilla placentas (Pl. 20, figs. 116 and 117).

It is thus evident that the peculiarities which distinguish the Catarrhine placenta from that of the Anthropoid are to be regarded as mere differences in detail or degree, such as we might well expect to find in the divergent branches of a common stock; the marvel is they are not greater than they are. It is also clear that they in no way detract from the significance of the striking and fundamental similarities in the constitution of the two organs which have been stressed by all previous observers, TURNER ('77), WALDEYER ('90), KOLLMANN ('00), STRAHL and HAPPE ('05) and others, and on which I have laid emphasis in the preceding pages.

CHAPTER IV.

ANTHROPOID STAGE.

In this final stage, in which we group together the Anthropoid Apes and Man, we see the culmination of developmental adaptation, so far as the Primates are concerned. Unfortunately we have no knowledge of the earliest stages in the development of the Anthropoid Apes but, thanks to the labours of SELENKA and STRAHL, we know enough of their later stages and placentation to justify the belief that their development conforms in all essentials to the human type, so that for the details of early Anthropoid ontogeny we depend on the work of the human embryologist. The outstanding feature of the early human blastocyst is the extraordinary directness and precocity it exhibits in its developmental processes as exemplified, for example, in the relations it very early acquires to the uterine lining and in the remarkably early differentiation of its trophoblast and its extra-embryonal mesoderm. It is no longer content to undergo its development in the uterine lumen as does that of all the lower Primates, but whilst still quite minute (possibly — 0·3 mm. in diameter) burrows its way through the uterine epithelium and implants itself in the vascular subepithelial endometrial tissue. Therein it forms for itself a space or so-called decidual cavity in which it undergoes its subsequent development. Its cytotrophoblastic wall early gives origin to a complete investing mantle of syncytiotrophoblast, endowed with potent cytolytic and invasive properties and penetrated by an intercommunicating system of lacunar spaces. Under its influence the endothelial walls of the maternal capillaries are destroyed, the maternal blood escapes into its lacunæ and soon begins to circulate and so the blastocyst continues its development under ideal conditions, with maternal blood actually circulating through the spaces in its trophoblastic wall. In this way the Primate germ reaches the acme

of its endeavour to maintain itself in the uterus and to obtain for itself an adequate supply of nutriment at the earliest possible moment.

The actual process of implantation has never been observed in the case of the human blastocyst, but it is no doubt effected as TEACHER ('24), STREETER ('26) and others have suggested, along comparable lines to that of Cavia, the only other mammal in which this so-called interstitial mode of imbedding has been described in detail. There, as F. GRAF SPEE ('01) was the first to show, and his results have been confirmed more recently by SANSOM and HILL ('29),* the minute blastocyst so orientates itself in the uterine lumen that its thickened lower pole comes to lie in contact with the uterine epithelium. It adheres thereto, perhaps through the agency of pseudopodia-like processes which SPEE ('83) has described as arising from the thickened polar trophoblast, and very soon a small, sharply defined gap is formed in the uterine epithelium, into which the lower polar region of the blastocyst insinuates itself. The remainder of the blastocyst gradually follows, the gap at the same time widening and so eventually it disappears beneath the surface and becomes completely imbedded, the margins of the gap through which it passed gradually closing in to complete the uterine epithelium over it. During implantation, the blastocyst is growing in size and it simply makes room for itself in the soft stroma tissue, no destruction of the latter taking place.

But there is one very obvious difference in the details of implantation in Man and Cavia. Whereas in the latter the lower, or anti-embryonal pole, constitutes the implantation pole and is the first part to enter the endometrium, it is a very interesting and significant fact that, just as the first attachment of the Pithecoid blastocyst is effected by the trophoblast over the embryonal pole, so in the human blastocyst (*cf.* TEACHER, '24) that pole is normally the first to enter, as is shown by the fact that in the great majority of the early human blastocysts which have been examined, the embryo is attached to the chorion of the deep wall of the vesicle, opposite or nearly opposite the site of entry, as is seen very clearly in Pl. 20, fig. 112, which I owe to the kindness of my colleague, Dr. J. FLORIAN. The figure represents a section through the decidual swelling in which lies imbedded an early blastocyst (Bi I, FLORIAN, '28, *b*, fig. 1). The embryonal primordium is attached to the chorion forming the deep wall or floor of the exocœlomic blastocyst cavity, whilst at the surface of the swelling, almost opposite the embryonal primordium, the point of entry of the blastocyst is marked by a plug of syncytiotrophoblast (*op.tr.*), the so-called "Verschluss- oder Ektodermpfropf," TEACHER'S operculum deciduae. The reason for this precise and almost constant mode of entry is not far to seek, since as the result of it the embryo comes to lie in immediate proximity to the site of formation of the definitive placenta and it is for a precisely comparable reason that the Cavia blastocyst imbeds itself anti-embryonal pole first, since in this way the ectoplacental trophoblast is left in a superficial position as near as possible to the future placental site.

The earliest well-preserved, normal human blastocyst, known to us is the Miller

* See also 'Trans. Zool. Soc.,' vol. 21, 1931.

" ovum," originally described by J. W. MILLER ('13) in 1913. Unfortunately only five sections of the series through it were preserved, but of these STREETER ('27) has more recently provided an excellent detailed account, illustrated by very fine photomicrographs, so that we now possess a fairly adequate knowledge of this most interesting stage in human ontogeny, estimated as belonging to the 10th or 11th day after ovulation. I refer to it here because it provides us with an extraordinarily striking and concrete illustration of that developmental precocity which characterises the earlier stages in human development.

The blastocyst is completely implanted, but the facts that the outer margin of its trophoblastic wall lies only 0·17 mm. below the uterine surface and the further fact that its presence has induced so far very little alteration in the surrounding endometrial tissue, lead STREETER to conclude that it can only recently have become imbedded. Its average internal diameter (measured from the inner surface of the trophoblast) is only 0·35 mm., nevertheless its trophoblast is already well differentiated. It has an average thickness of 0·22 mm. and consists of a well-marked basal layer of cytotrophoblast in proliferative continuity with an irregular layer of sponge-like syncytiotrophoblast composed of coarse anastomosing nucleated trabeculæ enclosing lacunar spaces of variable size. Peripherally, the syncytiotrophoblast is in contact with the surrounding endometrial tissue and has already commenced to erode the endothelial walls of its capillaries, though maternal blood corpuscles have not yet penetrated into its lacunae. Beyond this erosion, the endometrial tissue is very little altered, many of the stroma cells in the neighbourhood of the blastocyst are beginning to enlarge and mononuclear leucocytes have invaded it to some extent, but the glands are still quite normal, and their epithelium is intact even where the syncytiotrophoblast directly abuts against it. STREETER failed to find any evidence of the destruction or ingestion of stroma cells by the syncytium so that in imbedding itself the blastocyst would appear to make room simply by pushing the soft and no doubt œdematous stroma tissue outwards, just as happens during the implantation of the Cavia blastocyst. Accordingly the syncytium has not yet acquired the active cytolytic properties it exhibits in slightly later stages. Whether the syncytium is differentiated before or only after implantation is, of course, not known, though STREETER is inclined to regard the latter alternative as the more probable.

Equally striking is the condition attained by the extra-embryonal mesoderm in this early blastocyst. It lines the inner surface of the cytotrophoblast as a delicate membrane, one or two cells in thickness, and so we are justified in regarding the primordium of the chorion as already established ; it is prolonged to form a correspondingly thin layer investing the embryonal primordium, and it also fills the central cavity of the blastocyst as a very delicate spun-out mesenchymal network, connected on the one hand with the chorionic mesoderm and on the other with the layer investing the embryonal primordium. The presence of such a network seems to be distinctive of the human blastocyst, and is doubtless to be accounted for by the small size of the latter

and the remarkably early formation of the extra-embryonal mesoderm. The sections unfortunately yield no information as to the origin of the latter. STREETER suggests that "it must have either separated from the inner cell-mass [? amnio-embryonal vesicle] during the formation of the segmentation cavity, or have been derived from the trophoblast." He considers the latter derivation the more probable, but see *ante*, p. 110.

The embryonal primordium itself consists of an amnio-embryonal vesicle (0·087 × 0·06 mm. in diameter), with a thick floor of embryonal ectoderm and a thinner roof of amniotic ectoderm, which is attached to the cytotrophoblast of the chorion by the intervening mesoderm, and of a small solid triangular mass of cells which lies below and adjacent to the embryonal ectoderm, and which STREETER is inclined to believe is the endoderm of the yolk-sac; but owing to the lack of the adjacent sections, it is impossible to say whether or not it is solid throughout. The embryonal primordium is clearly much earlier than that of SELENKA's Keim S., and so, if our interpretation of the latter is correct, the yolk-sac endoderm here might very well be represented by a solid mass.

The structure of the fully-established embryonal primordium in Man is illustrated in Pl. 20, fig. 113. The figure is a photomicrograph (by kind permission of Dr. FLORIAN) of a transverse section through the Beneke embryo (STRAHL-BENEKE, '10), a short distance in front of the primitive streak, and serves to demonstrate very clearly the cardinal fact that the early human embryo, just like that of the Pithecoid, is formed of two superimposed vesicles, the amnio-embryonal and yolk-sac vesicles, enclosed by an investing layer of mesoderm and situated close below the chorion in an extensive exocœlomic cavity. The primordium is suspended from the chorion by the connecting stalk, which, as we have already seen (*ante*, p. 102, and text-fig. 17*), has precisely the same relations and, in all probability, the same mode of development as that of the Pithecoid. This fundamental similarity in the constitution and relations of the early embryo in the Pithecoid and Anthropoid types provides, it seems to me, indisputable evidence of their direct genetic relationship.

Certain features, distinctive of the Anthropoids, are to be regarded as the direct outcome of the interstitial mode of implantation of the blastocyst, and consequently as purely secondary specializations of adaptive significance. These include the following:—

(*a*) The differentiation of a decidua capsularis from the decidual tissue covering the blastocyst. The primordium of the capsularis is clearly seen in Pl. 20, fig. 112, of Bi I, FLORIAN, and that it exists in the lower Anthropoids in a condition precisely comparable to that in Man is demonstrated by the observations and figures of SELENKA ('00) and STRAHL ('03). I reproduce on Pl. 20, figs. 114, *a* and *b*, SELENKA's figures (figs. 19 and 20, Heft 8, p. 183) of the opened pregnant uterus and the chorionic vesicle *in situ* of *Hylobates Rafflesi*, Embryo Ab.,

* See also the median reconstruction of the Beneke embryo in FLORIAN–BENEKE ('30/'31, fig. 1).

and on Pl. 19, figs. 111, *a* and *b*, STRAHL's figures (figs. 10 and 12, Heft 12, p. 434) of the opened pregnant uterus and the isolated chorionic vesicle of his Orangutan 2. More recently WISLOCKI ('29) has recorded the presence of remains of the capsularis in the placenta of a Gorilla fœtus of C.R.L. 88·5 mm. (*v.* his figs. 34 and 36, Pl. 7).

(*b*) The formation round the early blastocyst of a complete enveloping network of syncytiotrophoblast which possesses in even more marked degree than that of the Pithecoids destructive and invasive properties, and which is well seen in, for example, the Miller " Ovum " (STREETER, '26) and the TEACHER-BRYCE blastocyst No. 1 ('08).

(*c*) The development from the chorion of the slightly older blastocyst of a more or less uniform covering of chorionic villi as illustrated in the Bi I blastocyst of FLORIAN (Pl. 20, fig. 112), in the chorionic vesicle of STRAHL's Orang 2 (Pl. 19, fig. 111), and of SELENKA's Hylobates Ab. (Pl. 20, fig. 114), and in the human chorionic vesicle figured on Pl. 19, fig. 110.

Apart from these adaptive specializations, the Anthropoid develops along the lines laid down in the Catarrhine stock, and, as the result of the atrophy of the chorionic villi originally related to the decidua capsularis and the growth of those related to the decidua basalis, forms a single discoidal placenta (Pl. 20, fig. 115), which is the homologue of the primary placenta of the Catarrhine, and which differs from it in no fundamental respect, but only in detail and possibly in its somewhat higher degree of functional efficiency, its intervillous blood-sinus being probably more extensive than that of any Catarrhine. In a very interesting paper, in which he discusses the significance of the intervillous blood-space, GROSSER ('29) contrasts the labyrinth-type of hæmochorial placenta (characterised by " enge mütterliche Blutbahnen, strömendes mütterliches Blut, rasche Erneurung, aber geringe Beeinflussung desselben ") with the villous type as exemplified in the human placenta (characterised by " weite unregelmässige Bluträume, stagnierendes Blut, mit weitergehender Auswertung desselben "). He regards the latter type as the more complete of the two, since it is capable by itself alone of providing for the nutrition of the fœtus, and concludes that " morphologisch und physiologisch ist die menschliche Placenta das Product einer extrem einseitigen Entwicklung."

What the course of that development has been, I have attempted to trace in this lecture, and the conclusion I have arrived at is that the Anthropoid placenta represents the end-product of an independent developmental trend which, starting out from the simple and primitive conditions obtaining in the Lemuroids, steadily progressed through Tarsioid and Pithecoid phases to its final culmination in the highly-efficient organ we see in the Anthropoids.

As concerns the Anthropoid placenta itself, we now know sufficient of its structure in the Anthropoid Apes (the Chimpanzee excepted) to justify the statement that it

differs in no essential respect from that of Man. In summarising the results of his detailed examination of the placental material of the Gibbon and the Orang contained in the Selenka collection, STRAHL ('03, p. 491) wrote as follows : " Die uteri gravidi des Menschen, des Orang-utan und des Gibbon gehen während der Graviditätszeit im allgemeinen den gleichen Entwickelungsgang," and further, " die fötalen Teile der Placenten sind, abgesehen von der Grösse der Chorionzotten, im Prinzip sehr übereinstimmend gebaut und die Unterschiede somit bedingt durch Verschiedenheiten im Bau der Decidua basalis."

WISLOCKI ('29, p. 75) also, after a study of the placenta in the Gibbon and the Gorilla, states that " except for minor points of difference, the form and finer architecture of the mature placenta in these species is practically identical with that of Man " and concludes that " placentation—a genetically important factor—speaks for a very close kinship of the anthropoids and man."

Figs. 116 and 117, Pl. 20, provide confirmation of the conclusions of these investigators. They show the sectional appearance of the chorionic villi of the full-term human placenta and those of an advanced placenta of the Gorilla respectively and demonstrate very clearly their striking structural similarity.

Finally, it only remains to state my conviction that the developmental evidence herein set forth leaves no room for question or doubt as to the close genetic relationship of the Anthropoid Apes and Man and of the origin of these from an ancestral Catarrhine stock.

Summary.

Starting with the relatively simple developmental conditions met with in the Lemuroidea, the attempt is made to show how the much more specialised and cænogenetically modified developmental relations found in the higher Primates may be supposed to have arisen as the result of continued adaptative specialisation, involving more especially acceleration and abbreviation in the developmental processes. A broad survey of the early development and placentation in representatives of the chief subdivisions of the Order has led to the recognition of four main stages in its evolutionary history, viz., a Lemuroid, a Tarsioid, a Pithecoid and an Anthropoid developmental stage.

1. *Lemuroid Stage.*—The existing Lemurs are regarded, from the developmental point of view, as the remnant of that basal Lemurine stock from which the higher Primates took their origin. In their development they exhibit a combination of primitive features with others which are certainly advanced and which foreshadow conditions characteristic of the higher types. Primitive features are evinced in the constitution of the blastocyst and its central type of development, in the disappearance of the covering trophoblast and consequent exposure of the embryonal ectoderm, in the origin and mode of spreading of the mesoderm, in the formation of the amnion by folds and in the development of the allantois as a free vesicle ; while amongst the advanced

features may be included the relatively early establishment of a complete chorion and its direct and complete vascularisation by the ingrowth into it of the allantoic vessels and the reduction of the yolk-sac and its vessels. Their placentation is regarded as genuinely primitive and the attempt is made to show how the more specialised hæmochorial type of the higher Primates may have been substituted for it.

2. *Tarsioid Stage.*—In this stage, as exemplified by the existing Tarsius, we observe :—

(1) The retention of certain lowly features characteristic of the Lemuroids, *e.g.*, the exposure of the embryonal ectoderm and the development of the amnion by fold-formation.

(2) The realisation of certain developmental tendencies already foreshadowed in them, *e.g.*, the still more precocious differentiation of the extra-embryonal mesoderm, cœlom and chorion, and the replacement of the vesicular allantois by the almost solid connecting stalk, all of them features in which Tarsius anticipates the Pithecoids.

(3) Certain definite advances on the Lemuroid, in particular the acquisition by the early blastocyst of a direct attachment to the uterine lining and the resulting formation of a massive discoidal placenta of the deciduate hæmochorial type. The development of the placenta is discussed and it is shown that the trophoblast is unique, both in its histological characters and in its behaviour. On these grounds the conclusion is reached that the Tarsius placenta is too specialised to have been the actual forerunner of that of the Pithecoids, but would seem to have developed along lines of its own, as a parallel formation. It is emphasised that the acceptance of this conclusion in regard to the placenta in no way lessens the significance of the Tarsioid phase as the most important transitional stage in the evolution of the developmental processes in the Primates. We have only to suppose that the Pithecoids took origin from another branch of the Tarsioid stock in which the attempt at the formation of a hæmochorial placenta proceeded along lines more comparable with those which we find in the existing Pithecoids, than does that of Tarsius.

3. *Pithecoid Stage.*—The justification for the recognition of this stage rests on the occurrence in the Platyrrhine and Catarrhine Monkeys of certain striking resemblances in their early development, all of them of the nature of definite developmental advances on the Tarsioid condition.

(1) The amnion no longer develops by fold-formation, since its cavity, the primitive amniotic cavity, arises as a closed space, in the ectodermal cell-mass of the very early blastocyst.

(2) The primary attachment of the blastocyst to the uterine wall is always effected by the trophoblast over the embryonal pole. A second attachment is also usually formed at the anti-embryonal pole, in which case the placenta is bi-discoidal.

(3) The extra-embryonal mesoderm and cœlom and the mesodermal primordium of the connecting stalk are formed even more precociously than in the Tarsioid. The extra-embryonal mesoderm (the so-called primary mesoderm of the early human

blastocyst) though homologous with that of the Tarsioid, is no longer of direct primitive streak origin, but appears to arise as in Hapale and Cebus as a proliferation from the hinder margin of the shield-ectoderm and the adjoining amniotic ectoderm.

(4) The trophoblast always becomes clearly distinguishable into cellular and syncytial layers. The syncytiotrophoblast exhibits erosive and destructive properties, and has the capacity of proliferating and of penetrating more or less deeply into the maternal decidual tissue in the form of an irregular network. The existence of certain well-marked differences in the behaviour of the trophoblast and in the structure of the placenta in the two groups of monkeys and the very striking similarities in the development of the placenta in the Catarrhines and the Anthropoids suggest the conclusion that the Platyrrhines separated very early from the parent stem to pursue a path of their own, whilst the Catarrhines furnished the stock from which the Anthropoids originated.

4. *Anthropoid Stage.*—In this final stage in which we group together the Anthropoid Apes and Man, we see the culmination of developmental adaptation, so far as the Primates are concerned. Unfortunately, we have no knowledge of the earliest stages in the development of the Anthropoid Apes, but, thanks to the labours of SELENKA and STRAHL, we know enough of their later stages and placentation to justify the belief that their development conforms in all essentials to the human type, so that for the details of early Anthropoid ontogeny we depend on the work of the human embryologist. The outstanding feature of the early human blastocyst is its extraordinary precocity as exemplified, for example, in the relations it very early acquires to the uterine lining and in the remarkably early differentiation of its trophoblast and its extra-embryonal mesodern. It is no longer content to undergo its development in the uterine lumen as does that of all the lower Primates, but, whilst still quite minute, burrows its way through the uterine epithelium and implants itself in the very vascular subepithelial decidual tissue of the uterus. Therein it forms for itself a decidual cavity and undergoes its subsequent development, completely embedded in the maternal tissue. In this way the Primate germ reaches the acme of its endeavour to maintain itself in the uterus and to obtain an adequate supply of nutriment at the earliest possible moment. And it is an interesting and significant fact that just as the Pithecoid blastocyst always attaches itself by the embryonal pole, so here that pole is normally the first to enter, so that the embryo lies on the deep side of the blastocyst in immediate proximity to the site of formation of the definitive placenta. Certain features, distinctive of the Anthropoids, are to be regarded as the direct outcome of this process of interstitial implantation and consequently, as purely secondary specialisations. These include (*a*) differentiation of a decidua capsularis from the decidual tissue covering the blastocyst; (*b*) formation round the very early blastocyst of a complete enveloping network of syncytiotrophoblast, possessing in even more marked degree than that of the Pithecoids, destructive and penetrative properties; (*c*) development from the chorion of the older blastocyst of a more or less uniform covering of chorionic villi. In the blastocyst itself, formation of the extra-embryonal mesoderm apparently takes place at such an early period that it

is able to fill the minute cavity of the blastocyst completely as a delicate cellular tissue in which only later the exocœlomic cavity appears.

Apart from these adaptative specialisations, the Anthropoid develops along the lines laid down in the Catarrhine stock, and as the result of the atrophy of the chorionic villi originally related to the decidua capsularis and the growth of those related to the decidua basalis, forms a single discoidal placenta, the homologue of the primary placenta of the Catarrhine and differing from that only in minor details.

Of the genetic relationship of the Anthropoid Apes and Man, and of these to the Catarrhine stock, there can be no question on embryological grounds.

Conclusion.

In this lecture I have attempted to extend and to review our knowledge of the developmental processes in the Primates so far as these relate to the earlier stages of development and the formation of the placenta and now, in conclusion, I propose to indicate quite briefly what seem to me the chief conclusions and inferences as to the evolutionary history of the Order that may legitimately be drawn from the embryological data now available.

As the outcome of a survey of the development in representatives of the several subdivisions of the Order, I have distinguished four well-defined developmental stages or grades within it, which I have designated the Lemuroid, the Tarsioid, the Pithecoid and the Anthropoid stages. These coincide only in part with the subdivisions recognised by the systematist. The facts and considerations I have adduced in the body of this lecture demonstrate, in my opinion, conclusively, that these four grades represent successive stages in the developmental evolution of the Primates, *i.e.*, in the evolution of those developmental features, generally recognised as distinctive of the group and that being so, I venture to suggest that they may represent also actual phyletic stages in the evolution of the Order.

The basal or Lemuroid stage (typified by the existing Lemuroidea) is characterised developmentally by a combination of generalised or primitive features such as are met with in the development of lower (non-primate) Mammals (including what I hold to be a primitive type of diffuse, non-deciduate placenta), together with certain other features which I regard as progressive and anticipatory of conditions which become fully manifest in the next higher or Tarsioid grade. The developmental plan, presented to us by the Lemuroids, devoid as it is of extreme specialisation, is of just that generalised type we should expect in a basal group and, moreover, it provides just the requisite basis for the manifestation of those adaptive modifications in the developmental processes which characterise in such distinctive fashion the evolutionary history of the higher groups of the Order.

From the standpoint of development, accordingly, I am led to regard the Lemuroidea

as the persisting representatives of the primitive Lemuroid stock which lay at the base of the Primate radiation.

The developmental gap between the Lemuroid and the Pithecoid stages is so great that in the absence of any knowledge of the development of the Tarsioidea, we should have been forced to postulate the existence of an intermediate stage between the two, and it is worthy of remark that the extent of that gap does not appear to have been realised by those who would derive the Pithecoids directly from Lemuroid ancestors.

Fortunately, that remarkable creature, Tarsius, has come down to us as the sole survivor of a race widely distributed over Europe and N. America in Eocene times and the knowledge of its development we now possess (and which we owe entirely to the initiative of A. A. W. HUBRECHT) enables us to affirm that it is characterised by a remarkable combination of features, partly Lemuroid, partly advanced and anticipatory of the Pithecoid and partly specialised and peculiar to itself. That combination justifies us in regarding Tarsius as the representative of what was by far the most important as well as the most critical transitional stage in the developmental history of the Primates and in holding that the Tarsioids, on the one hand, took origin from the basal Lemuroid stock and, on the other, gave origin to the Pithecoid grade. But the peculiar features which Tarsius itself displays in its placental development indicate quite definitely, in my opinion, that it is to be regarded as a specialised terminal member of the group and that the Pithecoid Monkeys took origin from some other more generalised branch of the Tarsioid stock.

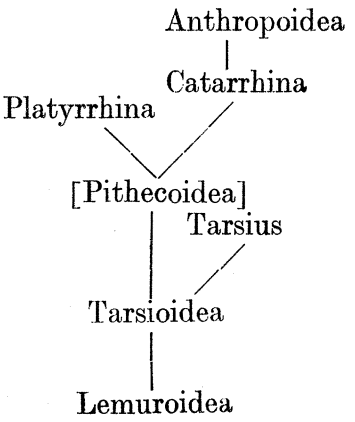
The fundamental agreements that exist in the details of the early developmental processes in the existing Platyrrhine and Catarrhine Monkeys justify the postulation of a common ancestral stock from which both took origin. For this hypothetical stock I have adopted the designation Pithecoid. The resemblances in question lend no support whatever to the idea that these two groups of Monkeys are of diphyletic origin and were evolved quite independently, the Platyrrhines from a Lorisiform stock in N. America and the Catarrhines from Lemuriform ancestors in the Old World. Such an origin takes no cognisance of the enormous developmental hiatus that exists between the Lemuroid and the Pithecoid and implies developmental parallelism of an unprecedented order and, moreover, for such to occur in two groups so closely allied by their major morphological characters that systematists by common consent place them together in the same sub-order, seems to me in the highest degree improbable.*

Assuming the existence of this common stock and from my point of view, it is immaterial whether we designate it Pithecoid or primitive Platyrrhine, the developmental evidence suggests that from it the existing groups of New and Old World

* In communications published since the delivery of this lecture, Dr. C. TATE REGAN has vigorously supported the conception of the diphyletic origin of the two groups of Monkeys (' Nature,' vol. 125, p. 125, January 25, 1930, and ' Ann. and Mag. Nat. Hist.,' Series 10, vol. 6, p. 383, October, 1930), whilst my colleague, Professor G. ELLIOT SMITH, has re-affirmed his belief in their monophyletic origin (' Nature, vol. 125, p. 270, February 22, 1930).

Monkeys evolved along two divergent lines of descent. The Platyrrhines would seem to represent the direct, though no doubt somewhat modified, descendants of the ancestral stock and remained on a lower developmental plane than the Catarrhines, as a kind of by-product of the evolutionary stream, in the comparative isolation of the S. American continent. The Catarrhines, more progressive, branched off on a line of their own and, as the result of acceleration and abbreviation of their developmental processes, so perfected their placental arrangements that one or other of their early branches proved capable of giving origin to the final grade in Primate evolution, the Anthropoid, as I have designated it, comprising the Anthropoid Apes and Man.

The following scheme indicates the way in which I would arrange the sub-divisions of the Primates in a phyletic series, on the basis of the known facts concerning their development :—



It is no part of my task in this lecture to attempt to correlate the developmental with the morphological and other evidence bearing on the large and complex question of the phylogeny of the Primates. I am well aware, however, that certain morphological facts do not, at the moment, appear to fit in with the phylogenetic scheme here envisaged, *cf.* for example, the striking observations of my colleague, THORNTON CARTER ('22) on the structure of the enamel in the Primates which, taken at their face value, seem to support the conception of the diphyletic origin of the Old and New World Monkeys rather than the monophyletic view I have been led to adopt. The significance of these and other like facts must remain over for future determination and discussion,* but meantime I venture to claim that the views herein put forward on developmental grounds are by no means lacking in support from the morphological side. I content myself with calling attention to the conclusions of my colleague, ELLIOT SMITH, as expressed in his writings† and graphically in the phylogenetic scheme constructed by

* See the communications of TATE REGAN and ELLIOT SMITH (*loc. cit., supra*), in which THORNTON CARTER'S results have already formed the basis of a discussion on the classification of the Primates, by these authorities.

† See especially his contribution to the discussion on Tarsius (' P.Z.S.,' 1919).

him now some years ago ('24)* on the basis of his extensive researches on the brain of living and fossil Primates ('02, '03, '08), which are in fundamental agreement with my own, and also to the conclusions of W. K. GREGORY arrived at after comprehensive surveys of the morphological and palæontological evidence and summarised in his tentative scheme of the phylogeny of the Primates ('27, fig. 10) which likewise afford striking confirmation of the views I have reached quite independently.

Nevertheless, I fully recognise that there are many matters, both of fact and theory, still to be elucidated before the problem of the phylogeny of the Primates ceases to be of interest to the student of Mammalian descent. Our problem, like that which exercised the learned Dr. CROONE,† when he found as he supposed, the embryo Chick fully formed, inside the new-laid egg is " one which we can nowhere with any certainty or only after a long time attain to perfect knowledge."

EXPLANATION OF PLATES.

LIST OF COMMON REFERENCE LETTERS.

B.C., BLUNTSCHLI Collection.

a.ect., amniotic ectoderm.
aev., amnio-embryonal vesicle.
all.c., allantoic cavity.
all.d., allantoic canal.
all.m., allantoic mesoderm.
amn., amnion.
amn.c., amniotic cavity.
amn.cd., caudal prolongation amniotic cavity.
art., arteriole.

blc., blastocyst.
bl.ex., blood extravasation.

c.c., cell-column.
cg., coagulum.
ch., chorion.
ch.l., unattached chorion (chorion læve).
ch.m., chorionic mesoderm.
ch.v., chorionic villus.
ch.ves., chorionic vesicle.

H.C., HUBRECHT Collection.

cl., artificial cleft.
c.n., cell nest or epithelial proliferation destined to form same.
cp., capillary.
c.st., connecting stalk.
c.tr., covering trophoblast.
cytr., cytotrophoblast.

d.b., decidua basalis.
d.c., decidua capsularis.
dec., decidual strands and masses (Tarsius).
d.ep., degenerate remains of epithelium.
dg.c., degenerating gland cells.
d.p., decidua parietalis.

e.a., embryonal area.
ecu., endometrial cushion.
e.ect., embryonal ectoderm.
emb., embryo.
end., endoderm.

* *Cf.* also ' Nature,' February 22, 1930, fig. 1, in which the group Pithecoidea is recognised.

† W. CROONE (CROUNE). The name of Dr. CROONE is perpetuated for all time by this annual Croonian lecture, founded in memory of him. He was the author of a memoir " De formatione pulli in ovo," of which an abstract appeared in the ' Phil. Trans.,' vol. 7, p. 5080, 1672. See also BIRCH's " History of the Royal Society of London," vol. 3, pp. 30–40, London, 1757.

I have to thank my friend, Professor F. J. COLE, F.R.S., for directing my attention to Dr. CROONE'S memoir, for the above references and also for the loan of a translation of the copy of the original Latin MS. which is preserved in the Library of the Society. The quotation above is taken from the translation.

List of Common Reference Letters—*continued.*

ep., uterine epithelium.
ep.n., degenerate epithelial nuclei.
er., erythropoiesis in fœtal capillary.
exc., exocœlom.

fb., fibrinoid.

gl., uterine gland.
gl.[1], degenerate gland.
gl.cn., gland-cell-nest.
gl.d., degenerate gland epithelium.
gl.e., gland epithelium.
gl.o., gland opening.

icp., intraplacental capillary vessel.
i.pl.v., interplacental vessels.
ivs., intervillous blood-space.
iv.syn., intervillous syncytium.

l., lacuna.

m.bl., maternal blood corpuscles.
mes., mesoderm, mesothelium.
mes.v., mesodermal "villus."
m.n., multinucleate mass.
msc., muscularis.
m.v., maternal vessel.

op.tr., operculum deciduæ.

p.c., pars compacta, junctional zone.
pl., placenta.
p.pl., prochordal plate.
pr.pl., primary placenta.
pr.st., primitive streak.
p.sp., pars spongiosa.
p.syn., syncytial network (Proliferationsplasmodium, Florian).
p.sytr., peripheral (basal) syncytium.

sec.pl., secondary placenta.
sh.ect., shield-ectoderm.
sta., placental "stalk" (Tarsius).
str., stroma of endometrium.
sy.sp., syncytiotrophoblastic sprout.
sytr., syncytiotrophoblast.
sytr.d., degenerate trophoblast (Tarsius).

tr., trophoblast.
tr.m., trophoplacental mass.
tr.pl., ectoplacental trophoblast.

u.art., umbilical artery.
u.c., umbilical cord.
u.cp., umbilical capillary.
u.e., uterine epithelium.
u.m., uterine mucosa.
u.vl., umbilical vessel.
u.vn., umbilical vein.

v., villus.
v.a., attaching villus.
vbl., vesicular blood corpuscle.
v.br., villous branch (trabecula).
v.c., central villus.
ven., venule.
vit.vl., vitelline vessel.
v.st., stem of villus.
v.syn., villous syncytium.

ys., yolk-sac.
ys.c., yolk-sac cavity.
ys.end., endoderm of yolk-sac.
ys.p., yolk-sac process.
y.spl., yolk-sac splanchnopleure.

z., zona.
z.c., compact decidual zone.
z.j., junctional zone (chorio-basalis).
z.r., superficial zone of the decidua destined to be resorbed.

PLATE 1.

FIGS. 1–4.—Ovarian Oocytes of Loris (from a preparation by Professor C. R. NARAYAN RAO), Tarsius, *Hapale jacchus* and *Macacus rhesus*. Fig. 1, × 366. Fig. 2, × 567. Fig. 3, × 456. Fig. 4, × 470.

FIG. 5.—Loris 4. Section of 4-celled egg (Egg A). × 484.

FIGS. 6 & 7.—Nycticebus 241. H.C. Sections of blastocyst from the Fallopian tube. × 430.

FIG. 8.—Loris 45. Section of blastocyst here seen occupying a bay in the endometrium. × 337.

FIG. 9.—Nycticebus 264. H.C. Section of blastocyst. × 237.

FIG. 10.—Nycticebus 190. H.C. Section of uterus with blastocyst *in situ*. *e.a.* embryonal area. × 19.

FIG. 11.—Nycticebus 190. H.C. Section passing through embryonal area. *p.pl.* prochordal plate. × 280.

FIG. 12.—Loris 5. Section of uterus with blastocyst (A) *in situ*. The folded embryonal area (*e.a.*) is seen on the right upper side of the figure and, on the left, a developing chorionic vesicle (*ch.ves.*). Below is an absorptive area (*a.a.*), with thickened and folded trophoblast. × 18.

PLATE 2.

FIG. 13.—Loris 5. Section through embryonal area of blastocyst. × 115.

FIG. 14.—Loris 5. Section through the bilaminar omphalopleure and the uterine wall, showing the mode of attachment of the trophoblast (*tr.*) to the uterine epithelium (*ep.*). See text, p. 52. × 515.

FIG. 15.—Loris 5. Tangential section through the trophoblast of the bilaminar omphalopleure to show the presence of terminal bars (*t.b.*) separating the outer ends of its cells. × 267.

FIG. 16.—Loris 5. Section through a developing chorionic vesicle. Note its position opposite the common opening (*o.gl.*) of a group of uterine glands, the presence of secretion in its concavity and the vacuolated trophoblast cells (*tr.*) which line it. × 120.

FIG. 17.—Loris 8. Section passing through the yolk-sac wall (*y.spl.*) with its vitelline vessels (*vit.vl.*), the extra-embryonal cœlom (*exc.*), the chorion, in the mesenchyme (*ch.m.*) of which are situated the umbilical vessels (*u.vl.*), and the superficial portion of the endometrium. The trophoblast (*tr.*) of the chorion and the uterine epithelium (*ep.*) are here artificially separated. × 138.

FIG. 18.—Loris 9A. Trans. section of embryo showing the freely projecting, thick walled allantois, *all.c.* allantoic cavity, *all.m.* allantoic mesoderm. × 63.

FIG. 19.—Loris 8. Embryo *in situ* in the opened uterine horn. Note the outline of the four subequal accessory allantoic lobes, and the rounded chorionic vesicles, showing through the fœtal membranes (*cf.* text-fig. 3, p. 58). × 6·4.

FIGS. 24, 25, 26 & 27.—Loris 33. Sections through the bilaminar omphalopleure and the adjoining portion of the endometrium, showing the occurrence of cells at the free surface of the trophoblast, destined to degenerate (figs. 26 & 27) and their probable mode of origin (figs. 24 & 25). Fig. 24, × 365. Fig. 25, × 310. Fig. 26, × 310. Fig. 27, × 350.

PLATE 3.

FIGS. 20 & 21.—Nyticebus 302. H.C. Trans. sections through the embryo and its fœtal membranes, fig. 20 being at the level of the opening of the yolk-stalk (*o.v.d.*) into the yolk-sac and fig. 20 at the level of the opening of the allantoic canal (*o.all.c.*) into the primary sac or main lobe of the allantois (*all.m.l.*). Note the chorion (*ch.*), the allanto-chorion (*all.ch.*), the allantois (*all.m.l.* main lobe, *all.l.* accessory lobe), amnion (*amn.*), the yolk-sac splanchnopleure (*y.spl.*) and the exocœlom (*exc.*), and in fig. 21, the direct passage of umbilical vessels (*umb.vn.* umbilical vein, *l.umb.a.* left umbilical artery) from the inner or cœlomic wall of the allantois into and from the chorion (*ch.*). *tr.* trophoblast (in fig. 21, artificially separated from the underlying allantochorionic mesenchyme). *l.umb.a.*, *r.umb.a.*, left and right umbilical arteries, *umb.vn.* umbilical vein. *vit.a.* vitelline artery. *vit.n.* vitelline vein. × 31.

FIG. 22.—Loris 19. Total view of portion of the placenta from the region of the cornual septum. The chorion has been turned back towards the right in the figure, exposing its villi (*ch.v.*) and the honeycomb-like system of crypts (*cr.*) in the endometrium, into which they fit. × 7·3.

FIG. 23.—Loris 19. Section of the placenta, showing the chorion (*ch.*) with its villi (*v.*) and a single chorionic vesicle (*ch.ves.*), with a narrow spout-like opening and its lining produced into sparse, slightly branched processes and also the thin uterine wall, the glands (*gl.*) of the endometrium and the muscularis (*msc.*). Note between the villi the extremely thin walls of the uterine crypts. × about 24.

FIG. 28.—Tarsius 405. H.C. Total view of the placenta seen from the fœtal surface. Placenta 15 × 12 mm. in diameter × 7·5 mm. in thickness. Fœtus D.C.L. 8·7 cm. H.L. 2·8 cm. Note the umbilical cord (*u.c.*) cut across, the umbilical vessels on the placental surface, the yolk-sac (3·5 × 2 mm. in diameter) with its stalk, and the reflection of the chorion (*ch.*) from the lower border of the placenta. *u.art.* umbilical artery. *u.vn.* umbilical vein. × 4.

FIG. 29.—Tarsius 72. H.C. Total view of a section through the placenta. Placenta, 10 mm. in diameter × 3 mm. in thickness. Fœtus G.L. 20 mm. Note the constricted base of attachment of the placenta (*pl.*) to the uterine wall (decidua basalis, *d.b.*), the umbilical cord (*u.c.*) seen in section and to the right of it the folded yolk-sac (*ys.*). Between the amnion (*amn.*) and the chorion (*ch.*) is a dense mass of coagulum (*cg.*) occupying the exocœlom. × about 5·5.

PLATE 4.

FIG. 30.—Tarsius 110*b*. H.C. Blastocyst, shortly after attachment to the endometrium; combination figure from two sections (*cf.* HUBRECHT, '99, Pl. 7, fig. 55). Two trophoblastic sprouts (*tr.sp.*) are seen arising from the trophoblast (*tr.*) of the blastocyst (*blc.*). They penetrate through the uterine epithelium (*ep.*) which is thickened, to terminate in contact with the uterine gland epithelium. The neck portions of the uterine glands (*gl.*) are enlarged and their epithelium thickened, whilst immediately below the blastocyst some of them appear already to be solid and are here separated by thin deeply staining connective tissue strands. × 108.

FIG. 31.—Tarsius 617. H.C. Blastocyst (combined from two sections) and the related portion of the endometrium to which it is attached (*cf.* HUBRECHT, '99, Pl. 7, fig. 56). The blastocyst is attached by its lower pole to the bottom of an endometrial groove. Note the shield-ectoderm (*sh.ect.*) freely exposed, the small yolk-sac (*ys.*) and the large exocœlom (*exc.*). The tropho-placental mass (*tr.m.*) is established and is surrounded by enlarged uterine glands (*gl.*), some of them solid (*gl.*[1]). × 97.

FIG. 32.—Tarsius 617. H.C. Attached pole of blastocyst and upper portion of the tropho-placental mass (*tr.m.*), showing trophoblastic processes (*tr.sp.*) from the lower polar trophoblast penetrating between degenerating masses of uterine epithelium (*ep.*[1]) to become continuous with the tropho-placental mass (*tr.m.*), *ch.m.* thickened chorionic mesoderm. × 245.

FIG. 33.—Tarsius 235. H.C. Section including margin of attached pole of blastocyst and adjoining portion of the tropho-placental mass (*tr.m.*). Note the continuity of the unattached trophoblast of the blastocyst wall (*tr.*) with the latter and the absence over the attached area of any layer of trophoblast distinct from the tropho-placental mass. *mes.* thin mesoderm of the free chorion. *ch.mes.* thickened mesoderm of the attached area, artificially detached from the surface of the tropho-placental mass. *m.bl.* maternal blood extravasation. For the general structure of the blastocyst, *cf.* text-fig. 8, p. 76. Tropho-placental mass 0·6 × 0·44 mm. in diameter. × 290.

PLATE 5.

FIG. 34.—Tarsius 622. H.C. Section of uterine cornu with blastocyst *in situ*. (Blastocyst, 0·83 × 0·76 mm. in diameter, shield-ectoderm about 0·3 mm. in diameter, tropho-placental mass, 0·67 × 0·51 mm. in diameter). Note the latter mass, surrounded by the solid degenerating glands (*gl.*[1])

peripherally to these are much enlarged glands and more laterally still, normal glands in club-shaped groups. In the upper part of the tropho-placental mass are large lacunæ, containing maternal blood (*m.bl.*), here present exceptionally early. × 32.

FIG. 35.—Tarsius 622. H.C. The tropho-placental mass of the preceding figure under higher magnification, to show its characteristic parenchyma-like appearance and the lacunæ in its upper part containing maternal blood. Note the characters of the solid degenerating glands (*gl.*[1]) and the commencing enlargement of the interglandular connective tissue cells, well seen on the right side of the figure. × 121.

FIG. 36.—Tarsius 622. H.C. Sectional view of small area of the tropho-placental mass as seen under the stereo-binocular microscope. Note the characteristic frame-work in the compartments or "cells" of which the nucleated units of the mass are situated.

FIG. 37.—Tarsius 175*a*. H.C. Section of the tropho-placental mass and its surroundings at a stage considerably later than that of Tarsius 622. The mass has increased in bulk, now measuring 1·24 × 0·86 mm. in diameter and possesses a stalk-like prolongation (*sta.*) (0·4 mm. in length × 0·27 mm. in thickness), regarded by HUBRECHT as maternal (trophospongial) in origin. The mass is now beginning to lose its original uniform character, owing to the enlargement of certain of its units and the formation of multinucleate syncytial masses (*mn.*). Note the irregular network of decidual strands (*dec.*) surrounding the mass and enclosing the degenerate remains of the uterine glands (*gl.d.*) in its meshes. *cl.* cleft formed by the artificial separation of the superficial layer of the mass (together with the chorionic mesoderm (*ch.m.*) adherent to it) from the remainder.

For details of the blastocyst *v.* text-fig. 9, p. 78. *Cf.* also for the tropho-placental mass, HUBRECHT ('99), Pl. 9, fig. 62. × 80·5.

FIG. 38.—Tarsius 175*a*. H.C. Portion of the tropho-placental mass under higher magnification, showing the commencing enlargement of its nucleated units, the increase in number of their nuclei and the formation of multinucleate syncytial masses. × 241.

PLATE 6.

FIG. 39.—Tarsius 262*b*. H.C. Later stage than 175*a*. Blastocyst ± 2 mm. in diameter, tropho-placenta mass 1·39 × 1·0 mm. in diameter. The figure shows a portion of the latter mass, distinctly more advanced in differentiation than that depicted in the preceding figure. A large multinucleate mass (*mn.*) is visible near the centre of the figure, containing numerous large darkly stained nuclei, extremely rich in chromatin granules and around it other masses in process of formation by the fusion of the enlarged units. Note especially the large composite mass towards the lower left corner of the figure, the multinucleate constituents of which are still marked off from each other by portions of the "adenoid" frame-work. Lacunar spaces (*l.*) are present between the masses as in fig. 38, but now maternal blood in small amount is present in them both in the central and peripheral regions. × 203.

FIGS. 40 & 41.—Tarsius 261*a*. H.C. Low and high power views of the tropho-placental mass from a stage distinctly later than 262. Blastocyst ± 4·5 mm. in diameter (DE LANGE, 21, p. 58). Tropho-placental mass 2·14 × 1·3 mm. in diameter. In the latter, enlarged uni- and multinucleate masses are now abundant especially in the upper half of the primordium, their nuclei, variable in form and size, are mostly large and intensely staining and show evidence of amitotic division. Between them, occur lacunæ (*l.*) containing maternal blood as yet in small amount. The chorionic mesoderm (*ch.m.*) is beginning to thicken and possesses a wavy under surface (first indication of the mesodermal villi). Round the base of the primordium is a tract of what appears to be degenerating trophoblast (*sytr.d.*). The decidual strands (*dec.*) of the basalis are reduced and the gland-remains have largely disappeared. *sta.*, stalk of the primordium, here eccentric. Fig. 40, × 40. Fig. 41, × 98.

FIG. 42.—Tarsius 22*a*. H.C. *v.* text-fig. 11, p. 80. Portion of the upper region of the tropho-placental primordium (2·4 × 1·9 mm. in diameter), showing the thickened chorionic mesoderm (*ch.m.*) produced into localised down-bulgings, the primordia of the mesodermal villi (*mes.v.*). The tropho-placental primordium is assuming the character of an irregular syncytium enclosing lacunæ (*l.*) containing maternal blood, though many of its constituent multinucleate elements still appear individualised and separated by remains of the "cuticular" frame-work. × 157.

FIG. 43.—Tarsius 164*c*. H.C. Entire view of placenta and uterine wall. Placental mass 3·28 × 1·9 mm. in diameter. As the result partly of its own growth in thickness, partly of the progressive reduction in the thickness of the decidual tissue underlying it, the placenta now projects so that its base lies practically on a level with the surface of the surrounding endometrium. The chorionic mesodermal villi (*mes.v.*) are now beginning to grow into the tropho-placental primordium as thick finger-like processes. *cbs.* central blood-sinus in the placental stalk. *sytr.d.* degenerating trophoblast. *dec.* strands and masses of decidual cells, the gland-remains originally enclosed by them having largely disappeared. Embryonal area of blastocyst ± 1·8 mm. (DE LANGE, '21, p. 56). × 25.

FIG. 44.—Tarsius 164*c*. H.C. Portion of the placenta under higher magnification showing the chorionic mesodermal villi penetrating into what is now the definitive syncytium (*sytr.*) of the tropho-placental primordium, a thin layer of syncytium enveloping each villous outgrowth. As yet there are no umbilical capillaries in the mesodermal villi, though maternal blood is present in the lacunæ of the syncytium. × 116.

PLATE 7.

FIG. 45.—Tarsius 595*c*. H.C. Blastocyst + 8 mm. in diameter (DE LANGE, '21, p. 63). Placenta 4·6 × 2·6 mm. in diameter. The figure shows a sectional view of the entire placenta. It now forms a knob-like projection with a broad base of attachment to the underlying decidual tissue (*d.b.*) which is much reduced. Between the latter and the syncytio-trophoblast (*sytr.*) is a deeply staining zone (*sytr.d.*) of what appears to be degenerate trophoblast. *u.vl.*, umbilical vessel in the chorionic mesoderm. × 16·5.

FIG. 46.—Tarsius 595*c*. H.C. Superficial zone of the same placenta, showing the mesodermal villous outgrowths (*mes.v.*) now much increased in length and beginning to branch. Umbilical vessels (*u.vl.*) are present in the chorionic mesoderm (*ch.m.*) and are penetrating into its villous outgrowths. *sytr.*, syncytiotrophoblast. × 79·5.

FIG. 47.—Tarsius Cl. 1. Later stage (placenta 6 mm. in diameter). The mesodermal villi (*mes.v.*) have increased in length and are more branched as compared with those of 595. The syncytiotrophoblast (*sytr.*) into which they are growing forms a very distinct network. It provides the syncytial investment of the villous outgrowths and is also present between them. *sytr.d.* degenerate trophoblast. × 66.

FIGS. 48–50.—Tarsius Cl. 1. Portions of the syncytiotrophoblast of the same placenta. Note its lacunæ bounded by what appears to be a "brush" border comparable with that on the surface of the syncytiotrophoblast of the human chorionic villi and especially the remarkable branching forms assumed by its nuclei, evidently preparatory to direct division. Fig. 49, × 545. Fig. 50, × 534.

PLATE 8.

FIGS. 51 & 52.—Tarsius 76. H.C. Placenta, conical, 10 × 11 mm. in diameter. Embryo G.L. 29 mm. The placenta is now well established and essentially consists of villous branches or trabeculæ (*v.br.*), connected up by syncytial junctions so as to form a coarse network, the meshes of which constitute the intervillous lacunar blood-spaces (*ivs.*) occupied by the maternal blood. Each villous branch consists of an axis of chorionic mesenchyme, carrying the umbilical capillaries and a thin investing layer of nucleated syncytium. *ch.m.* chorionic mesoderm. *mes.v.* a main villous stem arising from the chorion. *u.vl.* umbilical vessel. Fig. 51, × 56. Fig. 52, × 260.

FIG. 53.—Tarsius 812. H.C. Placenta 13·5 × 9 mm. in diameter × 4 mm. in thickness. Portion of the villous (trabecular) network, the villous branches being still relatively thick. × 188.

FIG. 54.—Tarsius 405. H.C. The fœtal surface of the intact placenta is shown in fig. 28, Pl. 3. Placenta 15 × 12 mm. in diameter × 7·5 mm. in thickness. Portion of the villous network, the villous (trabecular) branches being now much finer than those of 812. × 192.

FIG. 57.—Hapale 2. Section through marginal region of the attachment of the blastocyst. *ch.l.* free wall of blastocyst (chorion læve). *ep.* greatly thickened uterine epithelium. *ep.n.* pycnotic nuclei of the latter, in process of degeneration. *tr.pl.* attaching (ectoplacental) trophoblast. × 266.

FIG. 58.—Hapale 2. Isolated portion of the attaching (ectoplacental) trophoblast. × 275.

PLATE 9.

FIG. 55.—Hapale 2. Wax-plate model of embryo B (prepared by Dr. C. J. HILL), seen in median longitudinal section. *aev.* amnio-embryonal vesicle. *c.st.* connecting stalk primordium. *ys.* yolk-sac vesicle. *ys.p.* yolk-sac process.

FIG. 56.—Hapale 2. Median longitudinal section through embryo A. Lettering as in fig. 55. *gl.e.* gland epithelium. *str.* stroma of uterine mucosa. *mes.* mesothelium. *mes.r.* median portion of an incomplete horseshoe-shaped band of mesoderm which is prolonged forwards from the mesoderm of the connecting stalk (*c.st.*). *ys.end.* yolk-sac endoderm, the marked thickening of the embryonal endoderm may possibly represent the prochordal plate. *tr.pl.* ectoplacental (attaching) trophoblast, note that the uterine epithelium has disappeared except for groups of darkly stained pycnotic nuclei. × 266.

FIGS. 59 & 60.—*Nasalis larvatus* (Keim S., SELENKA). H.C. Low and higher power views of blastocyst and the related endometrium, showing the attached blastocyst, the position of the embryo (*emb.*) at the base of the central villus (*v.c.*) and the thickened endometrial cushion (*ecu.*). Fig. 59, × 28. Fig. 60. × 77.

FIG. 61.—*Nasalis larvatus* (Keim S., SELENKA). H.C. Longitudinal section through the embryo, *cf.* text-fig. 16, p. 106. *aev.* amnio-embryonal vesicle, note postero-dorsal prolongation of amnion. *ch.* chorion. *cytr.* cytotrophoblast, in part cut tangentially. *exc.* exocœlom. *ivs.* intervillous blood-space. *mes.* mesothelium. *ys.end.* yolk-sac endoderm. *v.c.* central villus. × 323.

PLATE 10.

FIG. 62.—*Nasalis larvatus* (Keim S., SELENKA). H.C. Section of the blastocyst and the related endometrium, to show the details of the structure of the blastocyst and its villi (*v.c.*, *v.*) and the changes in the endometrium. For description, see text, pp. 136–140. Note especially the cell-columns (*c.c.*) of the villi, the intervillous blood-space (*ivs.*) which is filled by maternal blood, the irregular peripheral (basal) syncytium (*p.sytr.*). In the endometrium, note the stroma (*str.*), dense in its deeper zone, much looser and œdematous-looking in its superficial zone. *cp.* greatly enlarged capillary. *cp.*[1] capillary, the endothelium of which has proliferated. *cp.''* lumen of capillary into which projects a prolongation of the peripheral syncytium. *cn.* cell-nest or epithelial ingrowth of endometrial cushion (*ecu.*). *gl.* enlarged uterine gland. × 120.

FIGS. 63 & 64.—*Chrysothrix sciureus* 467. B.C. Longitudinal sections through the caudal extremity of the embryo (0·978 mm. in length, blastocyst 6 mm. diameter), *cf.* fig. 18*a*, Pl. 21. *c.st.*[1] and *c.st.*[2] the two parts of the connecting stalk (*v.* text, pp. 113, 114). *all.d.* (?) allantoic canal (?). *amn.cd.* caudal prolongation of amniotic cavity. *cp.*[1] developing capillary in mesoderm of connecting stalk. × 120.

FIG. 65.—*Galago maholi.* Fœtus 1, G.L. 24 mm., H.L. 11·5 mm.

FIG. 66.—*Tarsius spectrum.* Fœtus, G.L. 25·5 mm., H.L. 13·5 mm.

FIG. 67.—*Hapale jacchus*, H.C. 1. Fœtus B, G.L. 34 mm., H.L. 13·75 mm.

FIG. 68.—Homo H.H. 12. Fœtus, G.L. 25 mm., H.L. 12 mm.

Plate 11.

Fig. 69.—*Chrysothrix sciureus* 505. B.C. Showing portion of the attached (ectoplacental) area of the chorion and the related endometrium (*v.* text, pp. 119, 120). *ch.m.* chorionic mesoderm. *cytr.*, *sytr.* cyto- and syncytio-trophoblast. *gl.d.* cell-nests formed by the degenerating epithelium of the neck portions of the uterine glands. *z.r.* zone of the endometrium destined to be resorbed. *z.c.* compact zone. *z.sp.* deep or spongy zone, containing the irregularly enlarged and tortuous portions of the uterine glands. × 98.

Fig. 70.—*Chrysothrix sciureus* 505. B.C. Another portion of the attached area and the related endometrium to show the details under higher magnification. *cp.* capillary. *str.* stroma. × 320.

Figs. 71 & 72.—*Chrysothrix sciureus* 467. B.C. Caudal region of the placenta. Note the folds occupied by chorionic mesoderm, the increase in the thickness of the syncytiotrophoblast (*sytr.*), and the presence in the latter of lacunæ (*l.*) and intraplacental maternal capillaries (*cp.*). *bl.ex.* blood extravasation. *gl.cn.* gland cell-nest. *gl.d.* degenerate remains of the same. Fig. 71, × 55. Fig. 72, × 119.

Plate 12.

Fig. 73.—*Chrysothrix sciureus* 467. B.C. Portion of the anterior region of the placenta well in front of attachment of connecting stalk. Note the absence of the large "folds" or outgrowths met with in the posterior region, the reticular area of syncytiotrophoblast, and the irregular prolongations of the latter into the compact zone (*z.c.*), one such prolongation enclosing degenerate masses of gland-epithelium (*gl.d.*). × 119.

Fig. 74.—*Chrysothrix sciureus* 467. B.C. Another portion of the placenta from its anterior region. The syncytiotrophoblast is here less massive, but is seen to be produced into a well-marked prolongation enclosing degenerate remains of the uterine glands (*gl.d.*). In the lower part of the section note the numerous gland cell-nests (*gl.cn.*). × 198

Fig. 75.—*Chrysothrix sciureus* 467. B.C. Margin of placenta. Note the abrupt junction of the cytotrophoblast of the placental area with that of the unattached chorion (chorion læve) (*ch.l.*), the greatly enlarged glands outside the placental area (*gl.*) and the gland cell-nests (*gl.cn.*). × 147·5

Fig. 76.—*Cebus macrocephalus* 509. B.C. Portion of marginal region of placenta, showing the invasion of a maternal capillary by a hollow sprout (*syn.sp.*) of the reticular syncytiotrophoblast (*sytr.*). × 153.

Plate 13.

Fig. 77.—*Cebus macrocephalus* 509. B.C. Superficial zone of the ectoplacental trophoblast showing the cytotrophoblast (*cytr.*) and the syncytiotrophoblast which is coarsely reticular in character, its lacunæ (*l.*) containing maternal blood. *icp.* intraplacental capillary. × 123.

Fig. 78.—*Cebus gracilis* 475. B.C. Transverse section of embryo and adjoining portion of the placenta fœtalis, showing its lobulation and the massive character of the syncytiotrophoblast (*sytr.*). *all.d.* allantoic canal. *c.st.* connecting stalk. *icp.* intraplacental capillary. *mes.v.* mesodermal axis of chorionic villus. ×32·5.

Figs. 79 & 80.—*Cebus gracilis* 475. B.C. Low and high power views of portion of secondary placenta. Note its lobulated character, the pars compacta (*p.c.*) containing large numbers of degenerate cells and the greatly enlarged glands (*gl.*) of the pars spongiosa. *st.* syncytial tract in proximity to which intraplacental capillaries (*icp.*) and small masses of decidual cells are situated (see text, p. 125). Fig. 79, × 41. Fig. 80, × 99.

Fig. 81.—*Cebus gracilis* 475. B.C. Portion of the primary placenta illustrating the branching character of the chorionic villi (*mes.v.*). *ivs.* lacunar (later intervillous) blood-space. *u.cp.* umbilical capillary. × 78·5.

FIG. 82.—*Cebus gracilis* 475. B.C. Section of a commencing villous branch, showing its mesodermal axis (*mes.v.*) and its investing layer of cytotrophoblast (*cytr.*). *sytr.* syncytiotrophoblast. *l.* lacuna. × 356.

PLATE 14.

FIG. 83.—*Chrysothrix nigrivittatus* 600. B.C. Section through the primary (ventral) placenta, showing the branching chorionic villi (*mes.v.*), the intervillous syncytium (*iv.syn.*), the pars compacta (*p.c.*), with degenerating cells (*dg.c.*) specially abundant on its deep surface and the pars spongiosa (*p.sp.*). *u.vl.* umbilical vessel in the chorionic mesoderm (*ch.m.*). × 38·5.

FIG. 84.—*Chrysothrix nigrivittatus* 600. B.C. Section of a villous branch, specially to show its relations to the intervillous syncytium (*iv.syn.*). *fb.* fibrinoid. *ivs.* intervillous blood-space. *vbl.* vesicular blood corpuscle. × 220.

FIG. 85.—*Cebus macrocephalus* 528. B.C. Section through the secondary (dorsal) placenta. The intervillous syncytium (*iv.syn.*) is still strongly marked. *th.* thrombus in a large blood-space. × 51.

FIG. 86.—*Cebus macrocephalus* 528. B.C. Pregnant uterus opened, displaying the primary (ventral) placenta (*pr.pl.*) on the left and the secondary (dorsal) placenta (*sec.pl.*). The cut stems of the umbilical vessels supplying the primary placenta are seen just above the centre of the latter. Note the radiating arrangement of the vessels on the surface of the primary placenta and the interplacental vessels passing over its right margin to supply the secondary placenta.

FIG. 87.—*Chrysothrix nigrivittatus* 648. B.C. Section through the primary (ventral) placenta. Note the reduction of the intervillous syncytium (*iv.syn.*) and the increase of the villous stems (*mes.v.*) and their branches. *icp.* intraplacental capillary. *p.c.* pars compacta. *p.sytr.* peripheral (basal) syncytium. × 28.

PLATE 15.

FIG. 88.—*Chrysothrix nigrivittatus* 648. B.C. Villous branches of the primary placenta seen in section. They are invested by a thin layer of villous syncytium (*v.syn.*) and are connected up into an irregular network partly by direct anastomosis but mainly by strands of intervillous syncytium (*iv.syn.*). *er.* erythropoiesis in an enlarged umbilical capillary. × 230.

FIG. 89.—*Cebus gracilis* 474. B.C. Placenta as seen in section under low magnification. Note the compactly arranged villous branches and the large intraplacental capillaries (*icp.*). ×17·5.

FIG. 90.—*Cebus gracilis* 474. B.C. Superficial portion of the placenta, showing the amnion (*amn.*), chorion (*ch.*), a villous stem, occupied by a large umbilical vessel (*u.vl.*) and the villous branches, many of them containing enlarged capillaries (*er.*) in which erythropoiesis is in active progress. *iv.syn.* intervillous syncytium, frequently transformed into fibrinoid (*fb.*). × 98.

FIG. 91.—*Cebus gracilis* 474. B.C. Deep zone of the placenta. *p.sytr.* peripheral syncytium, here quite thick. *p.c.* pars compacta. × 98.

PLATE 16.

FIG. 92.—*Cebus gracilis* 474. B.C. Portion of a villous branch showing an enlarged capillary, in which erythropoiesis is in progress. *hbl.* hemocytoblast. *ebl.* erythroblast. *nbl.* normoblast. *eryc.* erythrocyte. *mkc.* megakaryocyte.

FIG. 93.—*Chrysothrix nigrivittatus* 31*a*. B.C. Low power view of section of the primary (ventral) placenta. *ch. m.* chorion. *fb.* fibrinoid largely replacing the peripheral syncytium. *6l.* uterine gland. *m.v.* maternal vessel. *msc.* muscularis. *p.c.* pars compacta. × 17·5.

FIGS. 94 & 95.—*Chrysothrix nigrivittatus* 816. B.C. Portions of the villous system from the single dorsal placenta. In fig. 94, the villous branches (trabeculæ) are connected by intervillous syncytium to form a network, whilst in fig. 95 they mostly lie free in the intervillous blood-space. × 140.

FIG. 96.—*Chrysothrix nigrivittatus* 31*b*. B.C. Portion of the villous system from the primary (dorsal) placenta. The villous branches are again seen to be connected up by intervillous syncytial anastomoses to form a network. × 140.

PLATE 17.

FIG. 97.—*Cebus macrocephalus* (?) 33*a*. B.C. Portion of the villous system of the placenta. The villous branches, simple and irregularly branched, are largely free of each other and lie in a continuous intervillous blood-space. × 128.

FIG. 98.—*Cebus apella* 624. The uterus opened to show the primary (dorsal) placenta (4·9 × 4·3 cm. in diameter) and the secondary (ventral) placenta (5·6 × 4·1 cm. in diameter) and the interplacental vessels (*i.pl.v.*) connecting the primary with the secondary placenta. *u.c.* umbilical cord. The caudal extremity of the uterus is directed upwards.

FIG. 99.—*Cebus apella* 624. Fœtus, C.R.L. 10·3 cm., D.C.L. 22·5 cm., H.L. 5·5 cm.

FIG. 100.—*Macacus nemestrinus* (DUCKWORTH). Low power view of the knob-shaped placental primordium. *ch.l.* unattached chorion of blastocyst wall. *ch.m.* chorionic mesoderm. *v.* villus. *ivs.* intervillous blood-space. *gl.* uterine gland. *art.* arteriole. *ven.* venule. × 36·5.

FIG. 101.—*Macacus nemestrinus* (DUCKWORTH). Section of the placenta, showing the chorion (*ch.m.* chorionic mesoderm), its villi (*v*) with their cell-columns (*c.c.*), the intervillous blood-space (*ivs.*) and the superficial zone of the endometrium. *art.* arteriole. *art.*[1] capillary (? arteriole), the endothelium of which is represented by detached oval cells. *cg.* serous coagulum. *cp.* enlarged capillary. *p.sytr.* peripheral syncytium. *str.* stroma. × 150.

PLATE 18.

FIG. 102.—*Macacus nemestrinus* (DUCKWORTH). Section of placenta, showing on the right a branched villus. *gl.cn.* gland cell-nest. × 135.

FIG. 103.—*Macacus nemestrinus* (DUCKWORTH). Section through the margin of the placenta. *ch.l.* free chorion of blastocyst wall. *ep.* uterine epithelium. *gl.* uterine gland. *gl.*[2] uterine gland containing maternal blood. *gl.cn.* gland cell-nest. *sy.sp.* syncytial sprout. × 130.

FIG. 104.—Human chorionic vesicle (Bi I, FLORIAN). Section of the placenta, by kind permission of Dr. FLORIAN, *v.* his photomicrograph of this same section (FLORIAN, 1928 (*a*), Tafelabb. 1), for comparison with fig. 101 of the Macacus placenta (D). *b.sp.* blood-space in trophoblast-shell, prolonged from the intervillous blood-space (*ivs.*). *c.c.* cell-columns of cytotrophoblast. *ch.m.* chorionic mesoderm. *cytr.* cytotrophoblast. *cytr.*[1] *cytr.*[2] cytotrophoblast of "shell." *m.v.* maternal vessel. *p.syn.* syncytial sprouts which form a network penetrating into the decidual tissue (*str.*), (Proliferationsplasmodium. FLORIAN), *sytr.*[1] syncytiotrophoblast of cell-column. *sytr.*[2] vacuolated mass of syncytium (degenerierendes (?) Plasmodium, FLORIAN). *v.syn.* villous syncytium (Resorptionsplasmodium, FLORIAN). × 99.

FIG. 105.—*Semnopithecus femoralis*. Low power view of section of placenta. Fœtus G.L. 35 mm. H.L. 15 mm. *amn.* amnion. *ch.m.* chorionic mesoderm. *ivs.* intervillous blood-space. *p.sp.* pars spongiosa. uterine glands (*gl.*) greatly reduced. *p.sytr.* peripheral syncytium, vacuolated. *v.* villus. *v.a.* attachment of villus to basalis. *v.st.* villous stem. *z.j.* junctional zone (chorio-basalis), here very degenerate. × 28.

PLATE 19.

FIG. 106.—Homo. Section of placenta. Fœtus G.L. 29 mm. *c.c.* cell-column, greatly reduced. *fb.* fibrinoid. *msc.* muscularis. *p.c.* pars compacta. *p.sp.* pars spongiosa. *sytr.i.* isolated mass of degenerate syncytium ("cell-island"). *v.* villus. *v.a.* attaching villus. *v.st.* stem of villus. × 11·5,

FIG. 107.—*Semnopithecus hosei* 749. R.C.S. Section of placenta. *p.sytr.* peripheral syncytium. *v.a.* base of attaching villus penetrating deeply into the junctional zone (*z.j.*). Note the sharp line of separation between the latter zone and the deep zone of the pars compacta, composed of decidual cells. × 16.

FIG. 108.—*Macacus cynomolgus* (*Macaca irus*) 737. R.C.S. Portion of the villous field of the placenta, showing the presence of irregular sprout-like outgrowths from the syncytiotrophoblast of the villi, which may end freely or may anastomose with other outgrowths or may fuse with the syncytial covering of other villi and so in the latter two events serving to connect up adjoining villi. × 154.

FIG. 109.—*Semnopithecus* sp. (R.A.). Portion of the villous field, showing the villi connected by syncytial junctions so as to form an irregular network. × 132.

FIG. 110.—Human chorionic vesicle H232 of about 15 mm. diameter. (From the collection of Professor J. T. WILSON, to whom I am indebted for the photograph of the specimen).

FIG. 111.—Orang utan 2 (after STRAHL, '03, figs. 10 and 12). *a.* uterus opened to display the decidua capsularis *d.c.* (diameter about 4·2 cm.). *b.* the chorionic vesicle of the same, isolated.

PLATE 20.

FIG. 112.—Human chorionic vesicle (Bi I, FLORIAN, '28*b*, fig. 1). Sectional view of the vesicle *in situ* (by kind permission of Dr. FLORIAN). Measurements (FLORIAN): Internal diameter of vesicle, 2·13 × 2·12 × 2·3 mm., embryonal shield, 350μ in length × 343μ in breadth, with primordium of primitive streak and cloacal membrane. Embryo is of about the stage of the embryo Beneke (FLORIAN-BENEKE, '30/31). *aev.* amnio-embryonal vesicle. *ch.* chorion. *ch.m.* chorionic mesoderm. *d.c.* decidua capsularis. *d.b.* decidua basalis. *exc.* extra-embryonal cœlom. *gl.* uterine gland. *ivs.* intervillous blood-space. *m.bl.* maternal blood extravasation. *m.v.* maternal blood-sinus. *op.tr.* operculum deciduæ (TEACHER) marking the point of entrance of the vesicle into the endometrium. *v.* villus. *ys.* yolk-sac. × 25·5.

FIG. 113.—Photomicrograph of section 43 through the Beneke embryo (STRAHL-BENEKE, '10, FLORIAN-BENEKE, '30/'31), by kind permission of Dr. FLORIAN. The figure shows very clearly the amnio-embryonal (*aev.*) and the yolk-sac (*ys.*) vesicles and their investing layer of mesoderm (*mes.*). *tr.* and *ch.m.* trophoblast and mesoderm of chorion. *cg.* coagulum in exocœlom. *v.* villus. Diameter of chorionic vesicle, 2·15 × 1·2 × 2·2 mm. × 96.

FIG. 114.—*Hylobates Rafflesi.* Preparations of the pregnant uterus, embryo Ab (after SELENKA, '00, figs. 19 and 20, p. 183). *a.* uterus opened to show the decidual swelling. *b.* section through the uterine wall and decidual swelling showing the chorionic vesicle (*ch.ves.*) *in situ*. *ar.* artery. *blv.* blood-vessel. *d.b.* decidua basalis. *d.c.* decidua capsularis. *d.b.* decidua basalis. A window has been cut in the chorion through which the embryo is visible.

FIG. 115.—*Hylobates* sp. Advanced fœtus and placenta (from the Raffles Museum, Singapore, through the kind offices of Professor J. L. SHELLSHEAR). The placenta, single and discoidal (somewhat contracted and folded in this specimen) measures 7·5 × 5·4 cm. in diameter, and 2·55 cm. in thickness. Fœtus, G.L. 9·2 cm., H.L. 3·8 cm. The long umbilical cord is attached eccentrically, nearer to one margin. The amnion has been removed except round the attachment of the cord.

FIGS. 116 & 117.—Illustrate the structure of the placental villi as seen in section, in the full-term human placenta and in an advanced placenta of the Gorilla, respectively. Note the agreement in their structure and relations. In both, the villi are invested by a single layer of villous syncytium enclosing a mesodermal axis in which are situated the umbilical vessels and capillaries and in both syncytial connections between the villi are seen to be present (largely converted into darkly stained fibrinoid in the human placenta). The Gorilla placenta (11·7 × 10·5 cm. in diameter) was given to me some years ago by the late Professor L. BOLK. The fœtus to which it relates was described by him in 1926 ('Z. Anat. Entw.,' Bd. 81) and the genital organs in 1922 ('Anat. Anz.,' Bd. 55). × 275.

PLATE. 21.

FIG. 5*a*.—Longitudinal section through the embryonal area and yolk-sac of blastocyst of Tarsius 86 (after HUBRECHT, '02, fig. 47, Pl. VI).

FIG. 6*a*.—Similar section of the blastocyst of Tarsius 235 (after HUBRECHT, '02, fig. 48, Pl. VI). *E*. Shield-ectoderm. *Exc*. Exocœlom. *M*. Mesoderm. *N*. Yolk-sac. *pp*. Prochordal plate. *pw*. " Protochordal wedge " (HUBRECHT), really the primitive streak primordium. *Tr*. Trophoblast.

FIG. 18*a*.—*Chrysothrix sciureus* 467. Median section through the embryo (semidiagrammatic). *all.d*. (?) allantoic diverticulum (?). *amn*., *amn.c*. amnion, amniotic cavity. *bl*. blastoporic depression. *bv*. capillaries forming in the mesoderm of the connecting stalk (*c.st.*[1]). *ch*. chorion. *ch.m*. chorionic mesoderm. *cyt-troph*. cytotrophoblast. *c.st.*[1], *c.st.*[2] the two regions of the connecting stalk. *embr.ect*. embryonal ectoderm. *ex.cœ*. exocœlom. *hp*. head-process. *p.pl*. prochordal plate. *pr.str*. primitive streak. *syn-troph*. syncytiotrophoblast. *y-s.c*. yolk-sac cavity.

FIG. 19*a*.—*Semnopithecus pruinosus*. Blastocyst Lk. (after SELENKA, '03, fig. 7, p. 334). For explanation of lettering see list of common reference letters. *sytr*.[1] syncytiotrophoblast in intervillous space (*ivs*.) *tr.pl*. area of thickened ectoplacental trophoblast of secondary placenta.

FIG. 20*a*.—*Macacus* (*Cercocebus*) *cynomolgus* (*Macaca irus*). Blastocyst Ca (after SELENKA, '00 fig. 28, p. 197), showing the primary placenta on the left and the secondary on the right. For explanation of lettering, see list of common reference letters.

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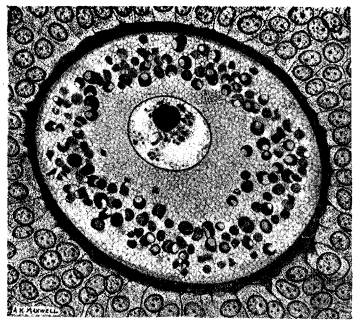
[*Addendum, added in proof, April 22nd*, 1932.—Subsequent to correcting the first proofs of this lecture, I received from my friend, Professor POL GERARD, of Bruxelles, a copy of his preliminary paper on the development of *Galago Demidoffi* (' Bull. Acad. Roy. Med. Belgique, Séance,' 19 déc., 1931). In this paper, which is of outstanding interest and importance, the author shows that, in its development, this species exhibits certain astounding and wholly unexpected features which mark it off from all other Lemurs so far known, including even two other species of the same genus. These features comprise : (1) The temporary presence of a capsularis around the early blastocyst, presumably formed by secondary enclosure and not as the result of true interstitial implantation ; (2) the markedly reticular character temporarily assumed by the extra-embryonal endoderm in the early blastocyst ; (3) the secondary formation of a " closed " amniotic cavity ; (4), and most significant in the present connection, the presence of a specially differentiated, localised area of the diffuse placenta, involving that part of the chorion with which the primary allantoic sac fuses, and termed by Professor GERARD the " zone d'implantation." This area, which eventually occupies about one-quarter of the entire extent of the placenta, is clearly distinguishable by its definitely thickened character and by its histological structure. According to Professor GERARD'S interpretation, the uterine epithelium has completely disappeared over the entire extent of the area, whilst the trophoblast has undergone differentiation into two layers : (*a*) an external layer, formed of a single row of very large, clear cells, and (*b*) a deep layer composed of small palisade cells, arranged in places several deep. The external layer has taken the place of the uterine epithelium, and so lies in direct contact with the connective tissue stroma of the uterine mucosa. Moreover, the maternal capillaries form a very rich plexus which is actually situated between the outer ends of its cells and may even extend as far as their mid-regions. The remainder of the placenta differs in no way from that of other Lemurs, the uterine epithelium persisting intact and the trophoblast remaining one-layered. We must await the publication of Professor GERARD'S full paper before attempting to discuss the significance of his remarkable observations. Meantime, I would only point out that here in the placenta of *Galago Demidoffi*, we have actually presented to us just the kind of intermediate stage we postulated in attempting to show how the localised discoidal placenta of the other Primates might have evolved from the diffuse epithelio-chorial placenta of the typical Lemur (*cf*, pp 65–67.)]



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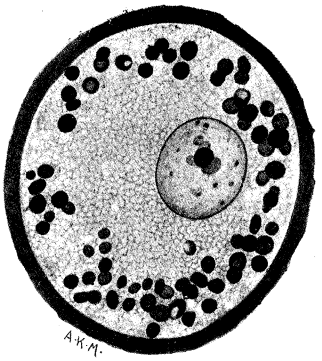

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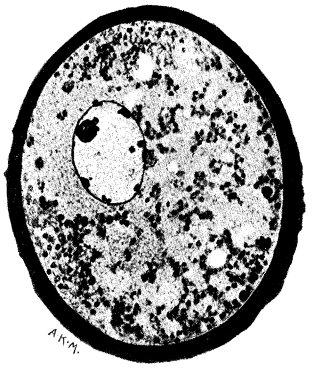

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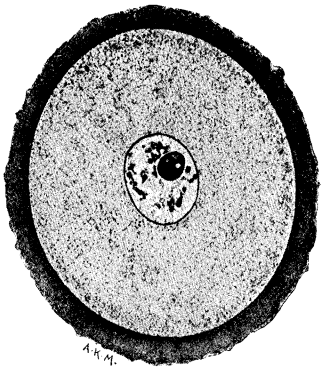

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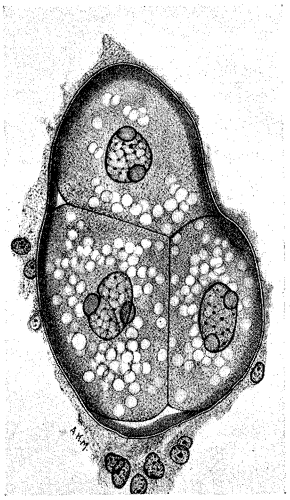

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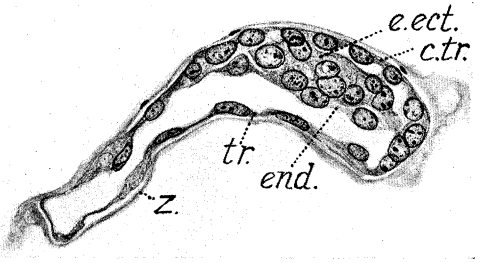

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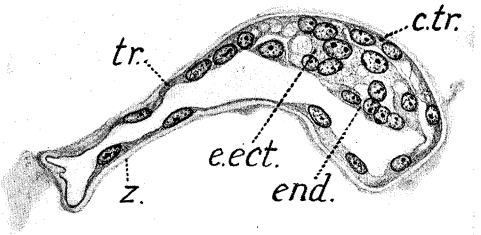

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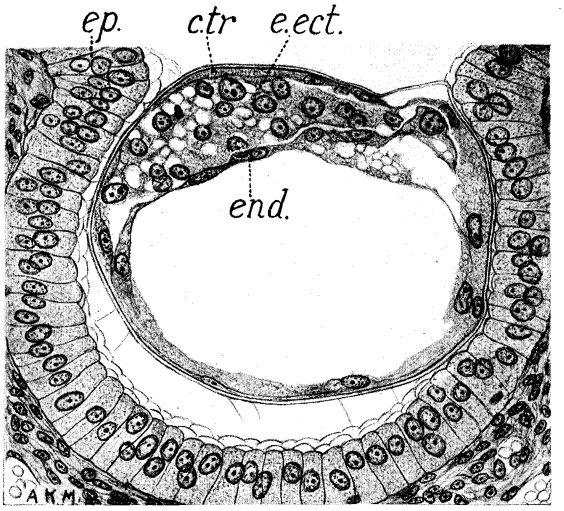

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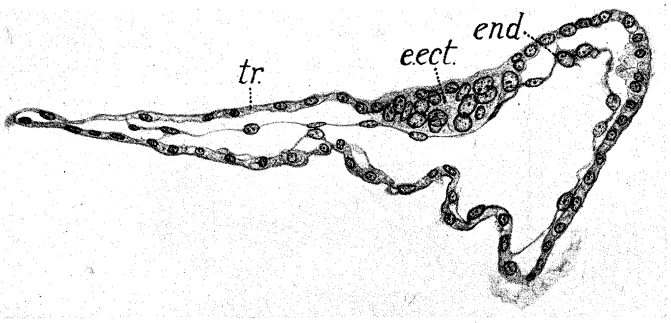

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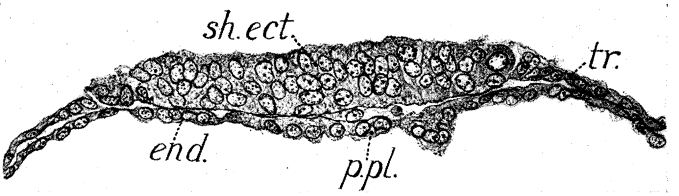

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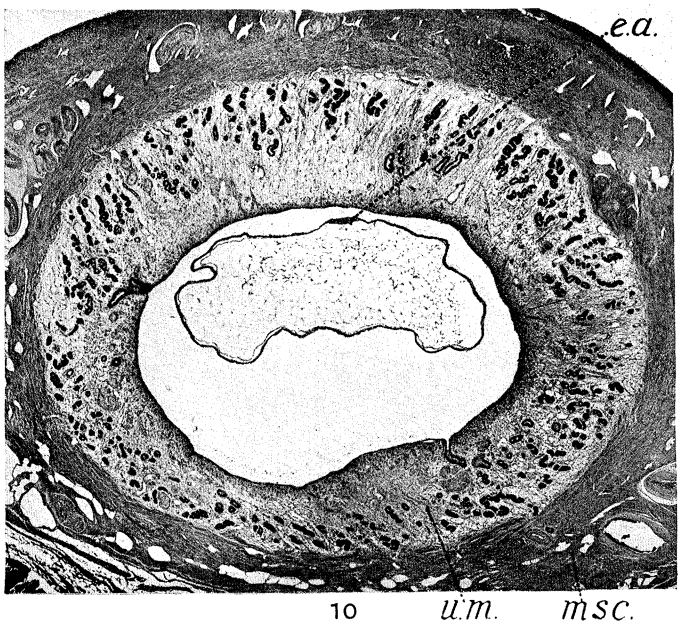

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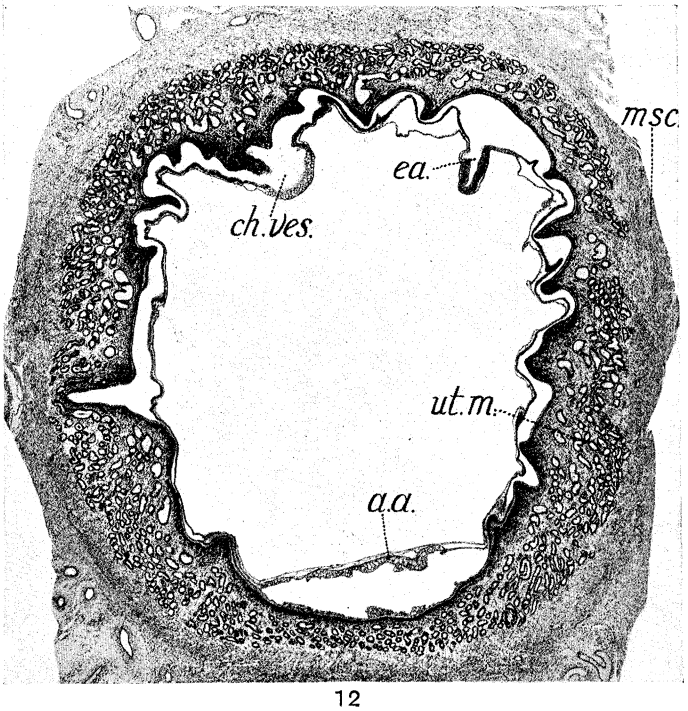

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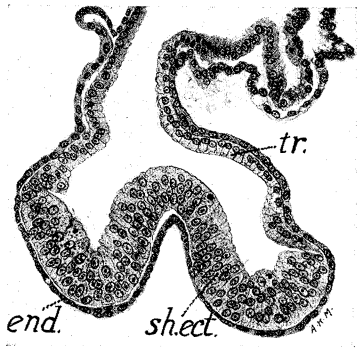

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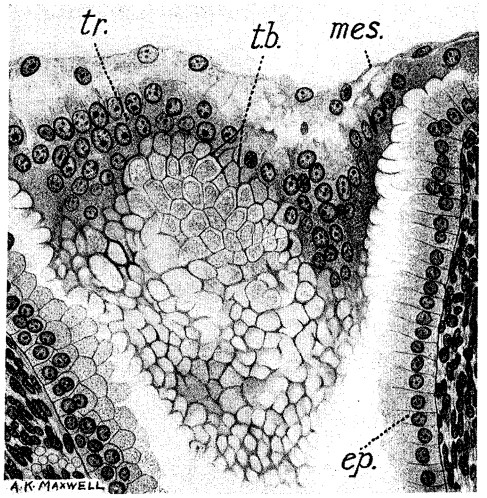

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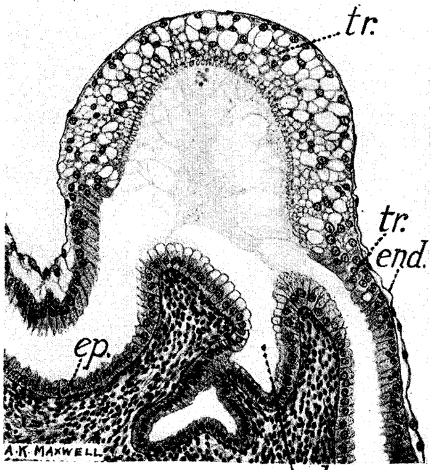

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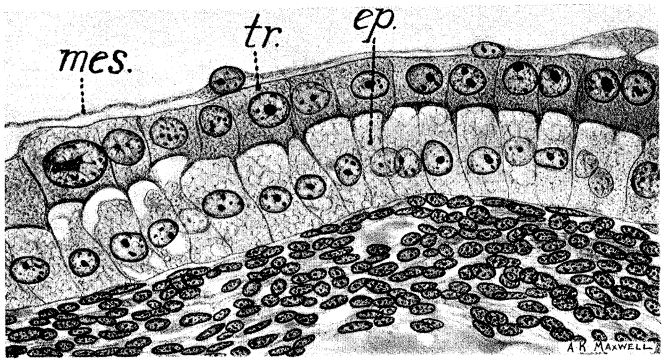

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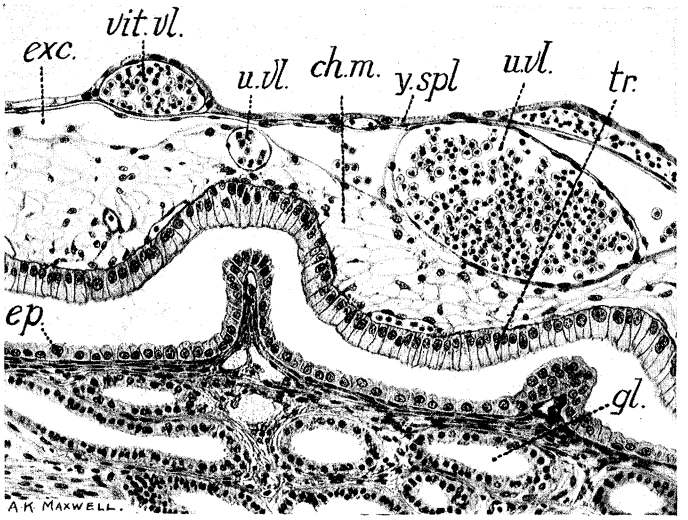

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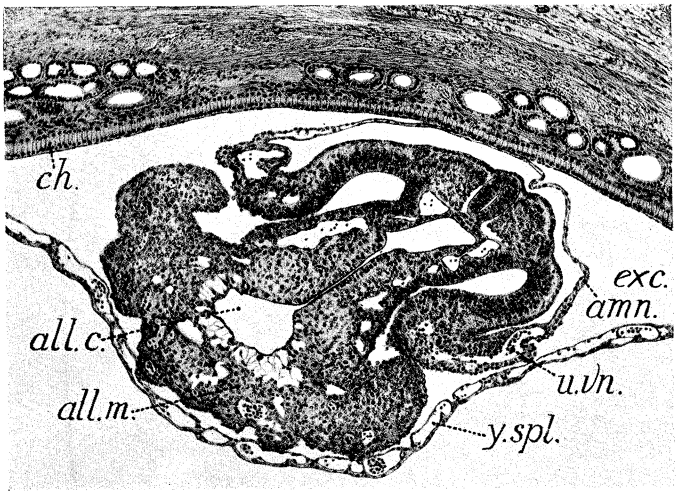

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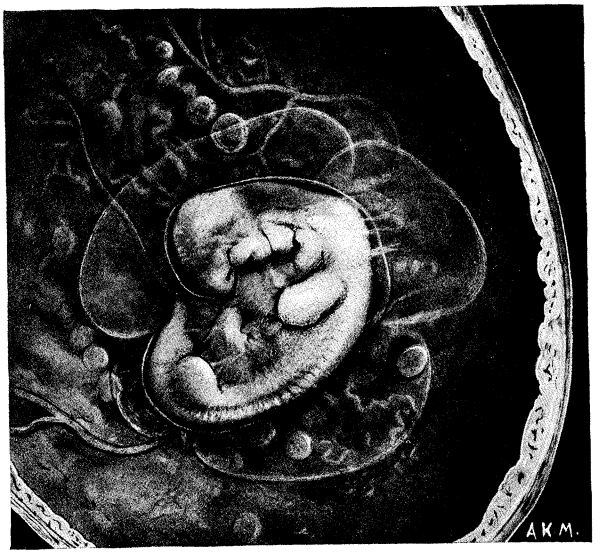

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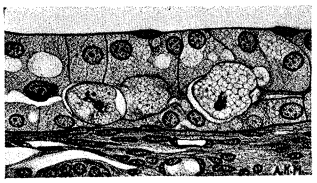
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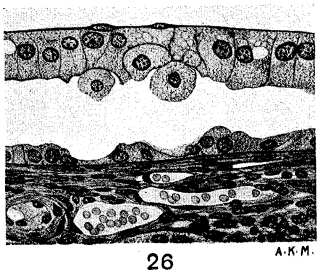

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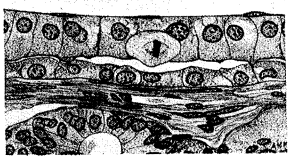
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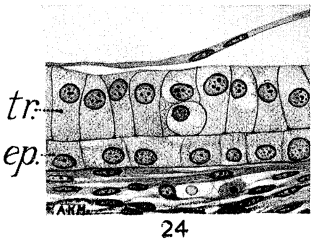

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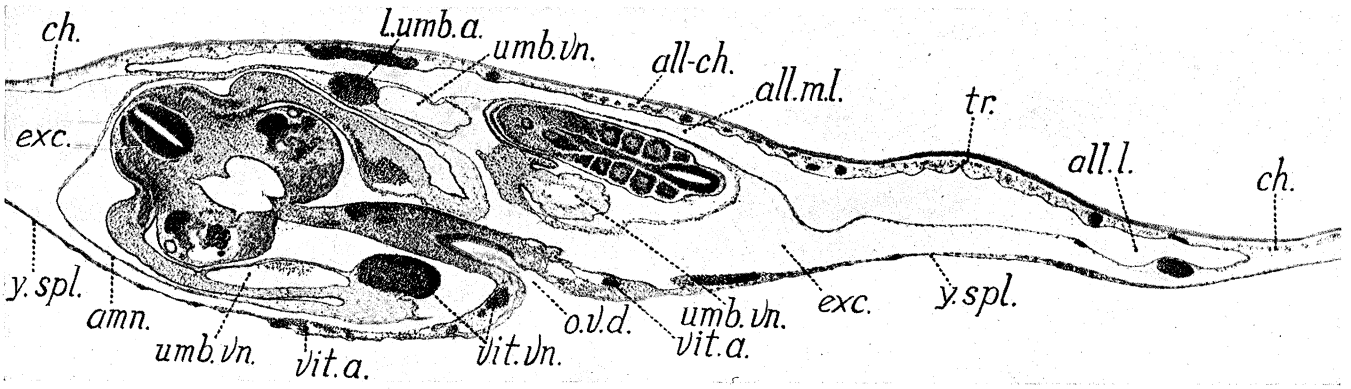

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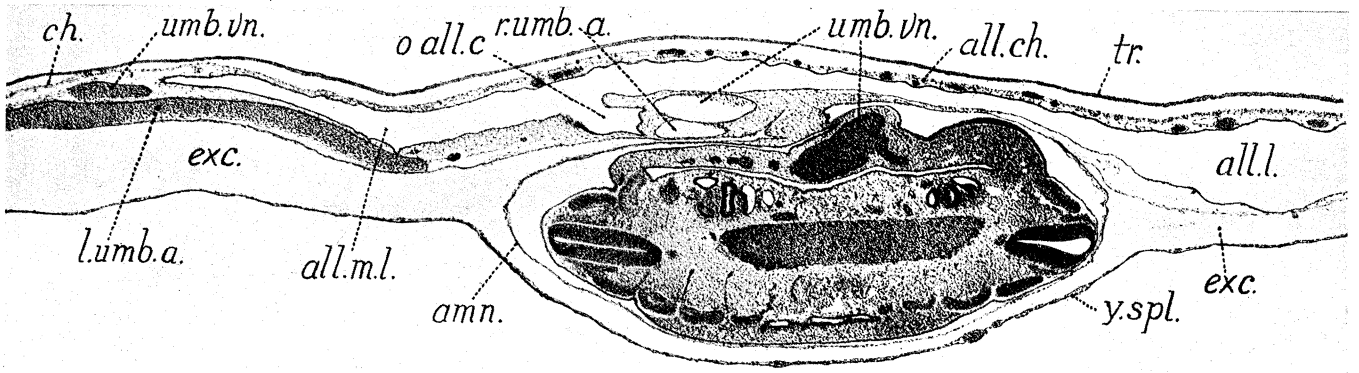

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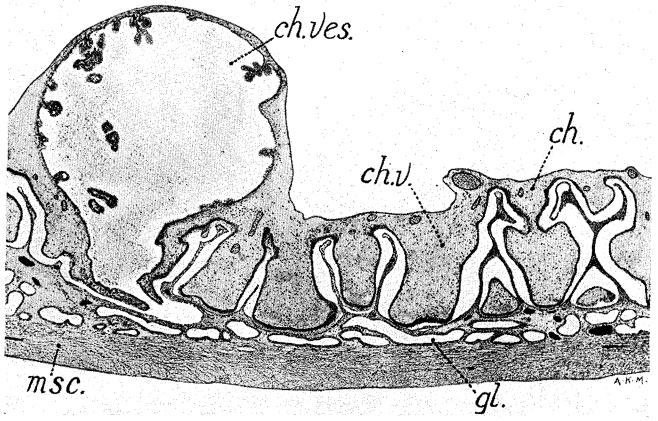

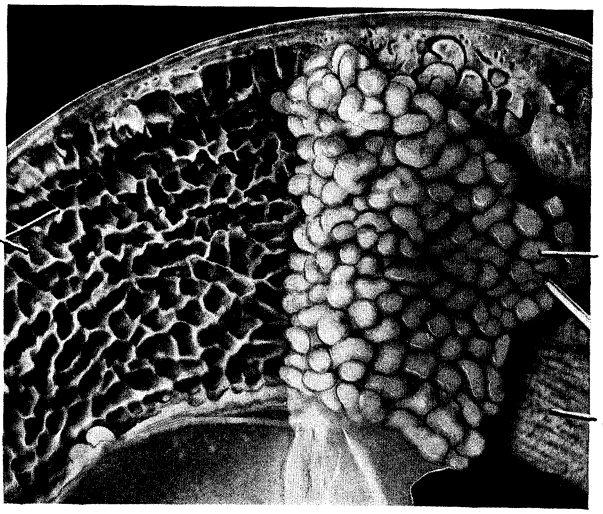

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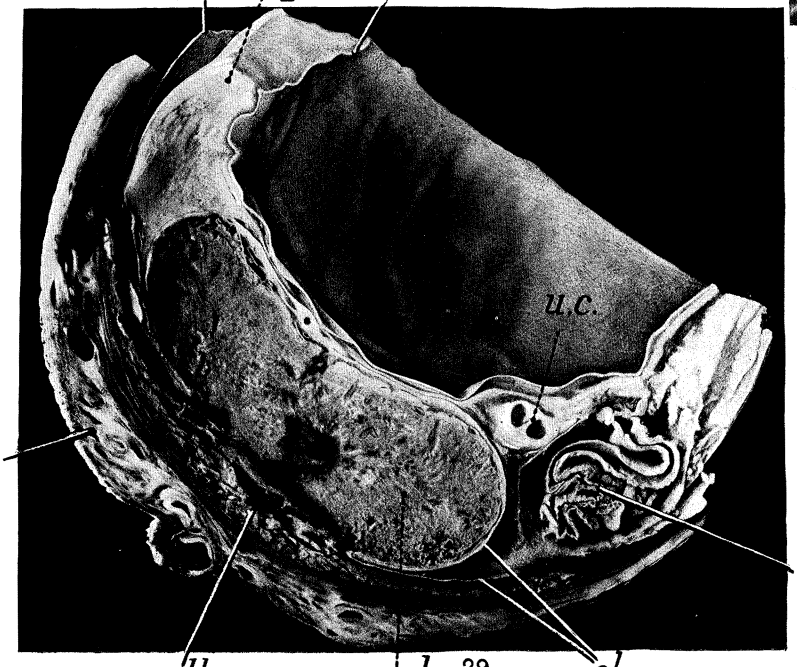

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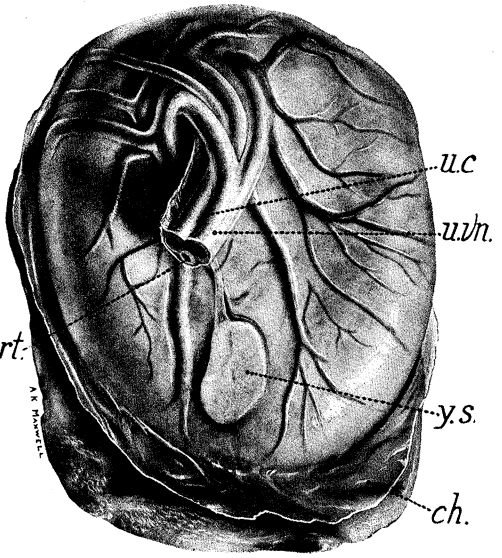

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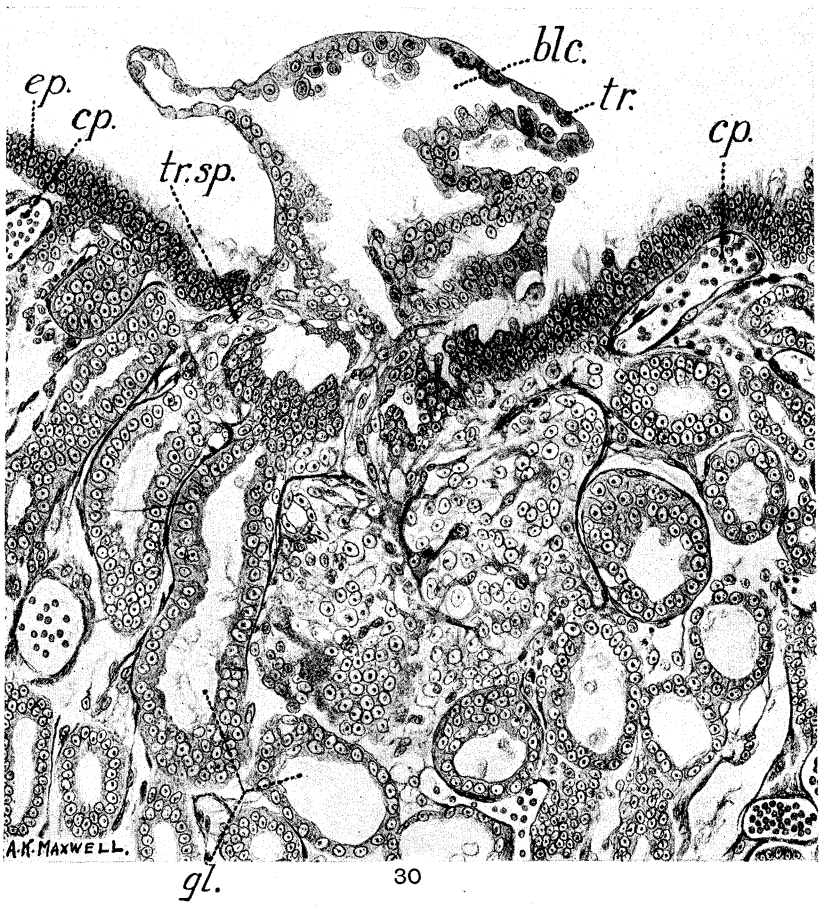
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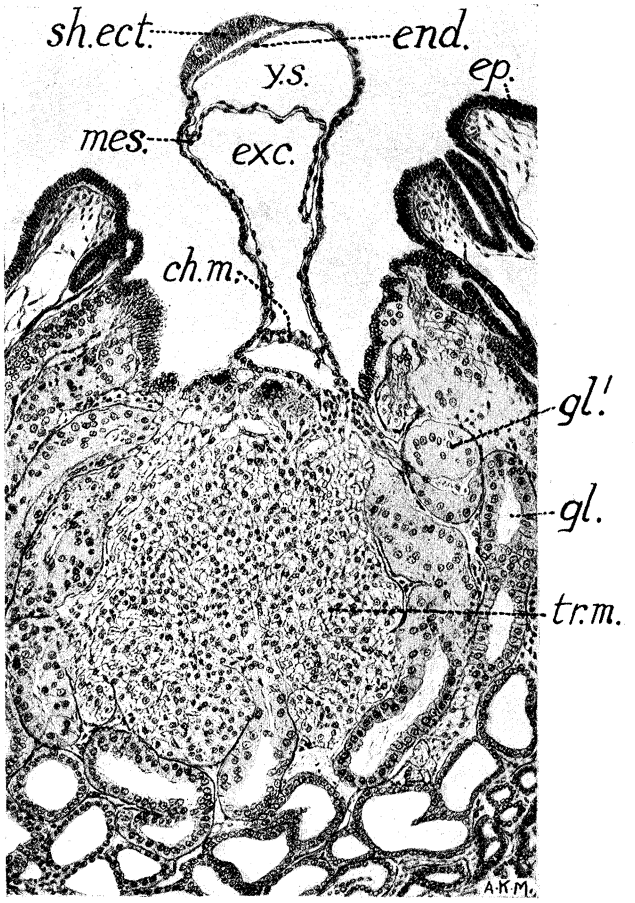
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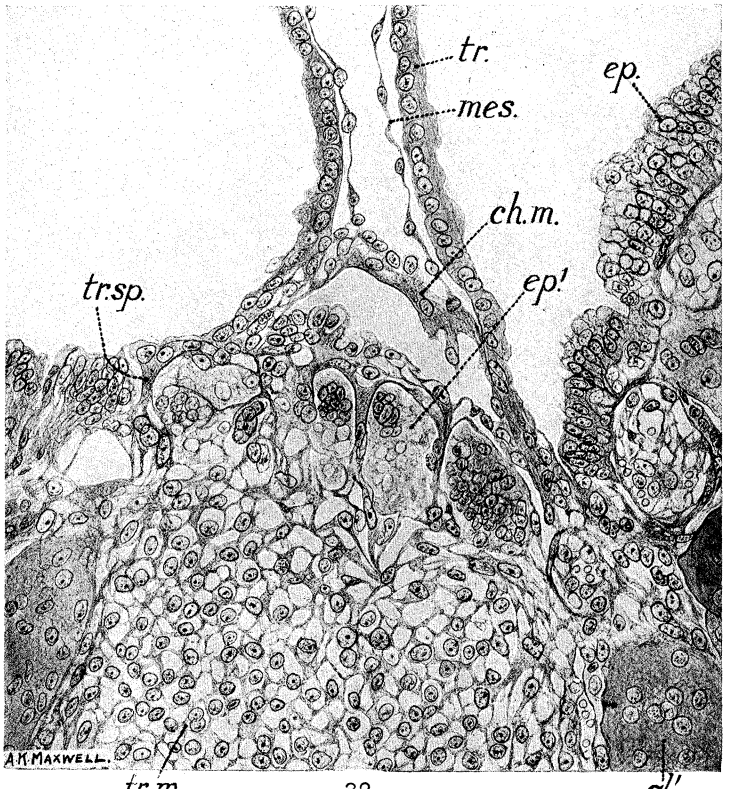
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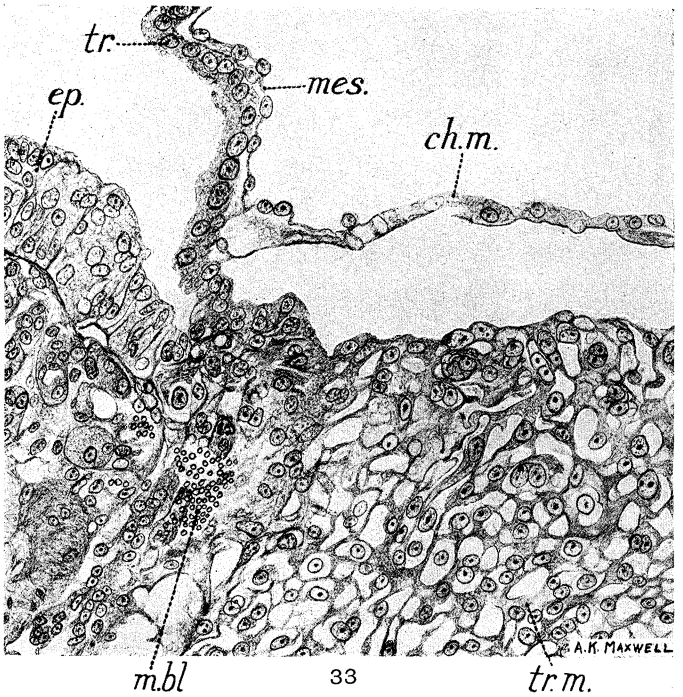
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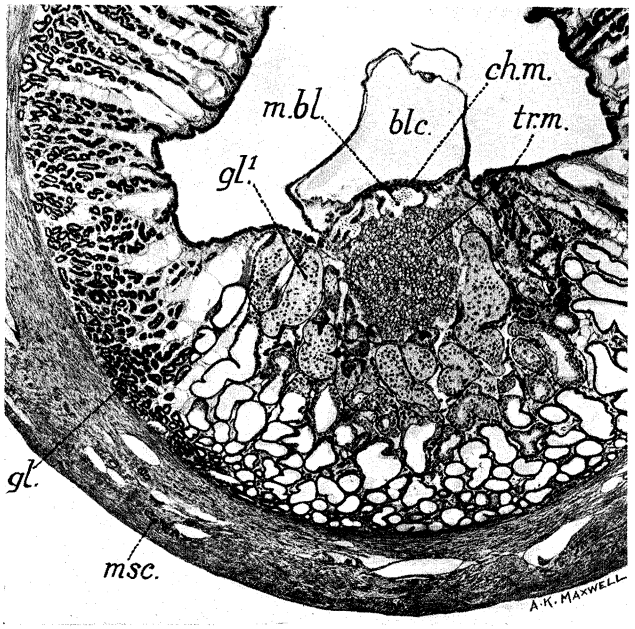
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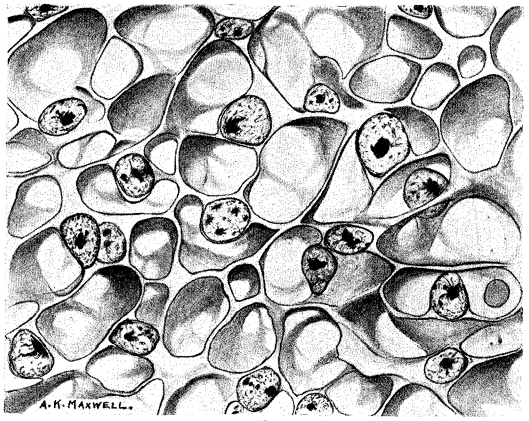
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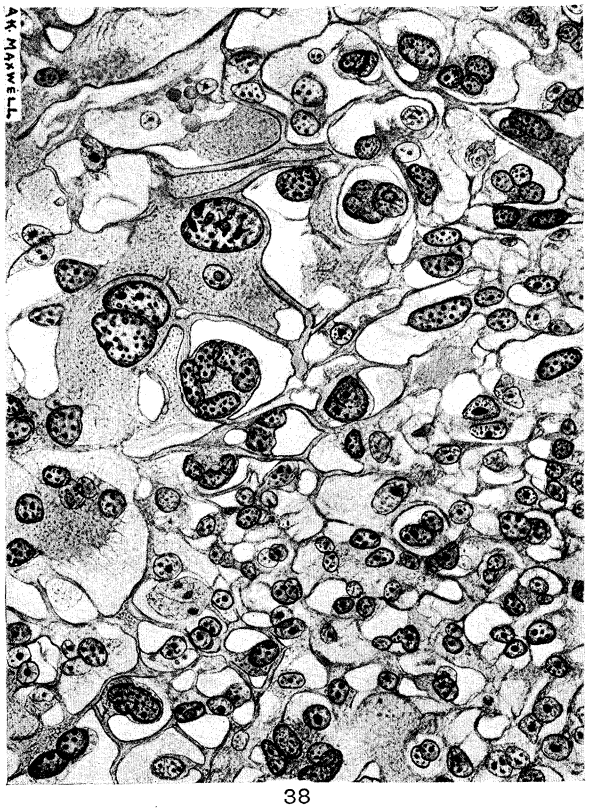
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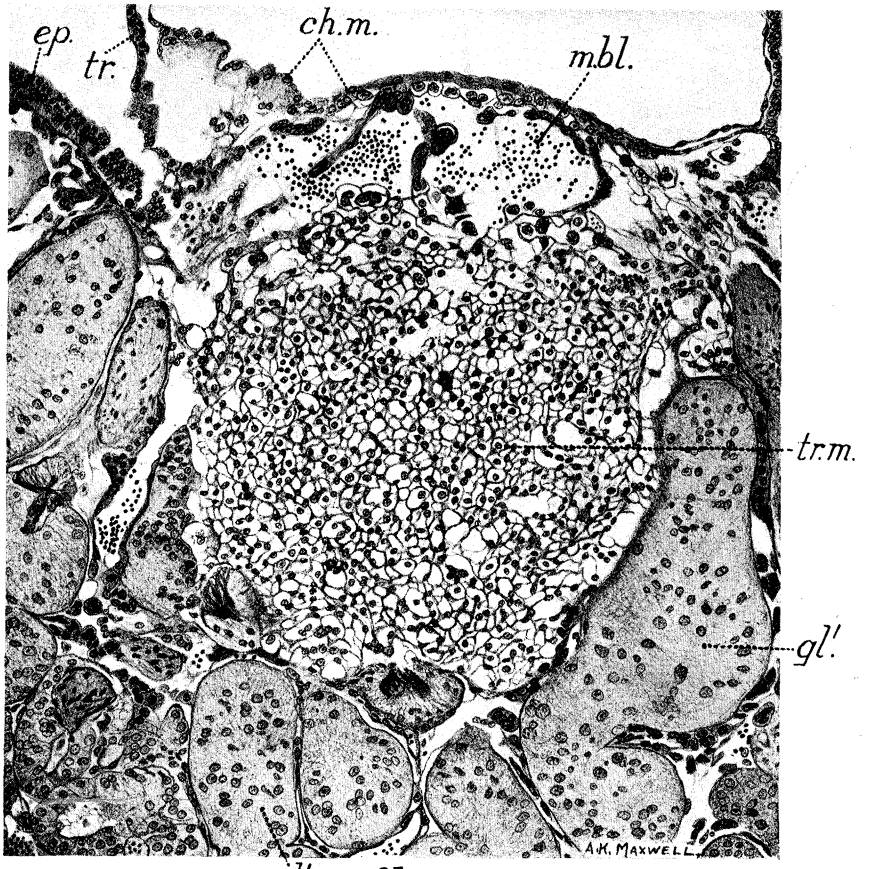
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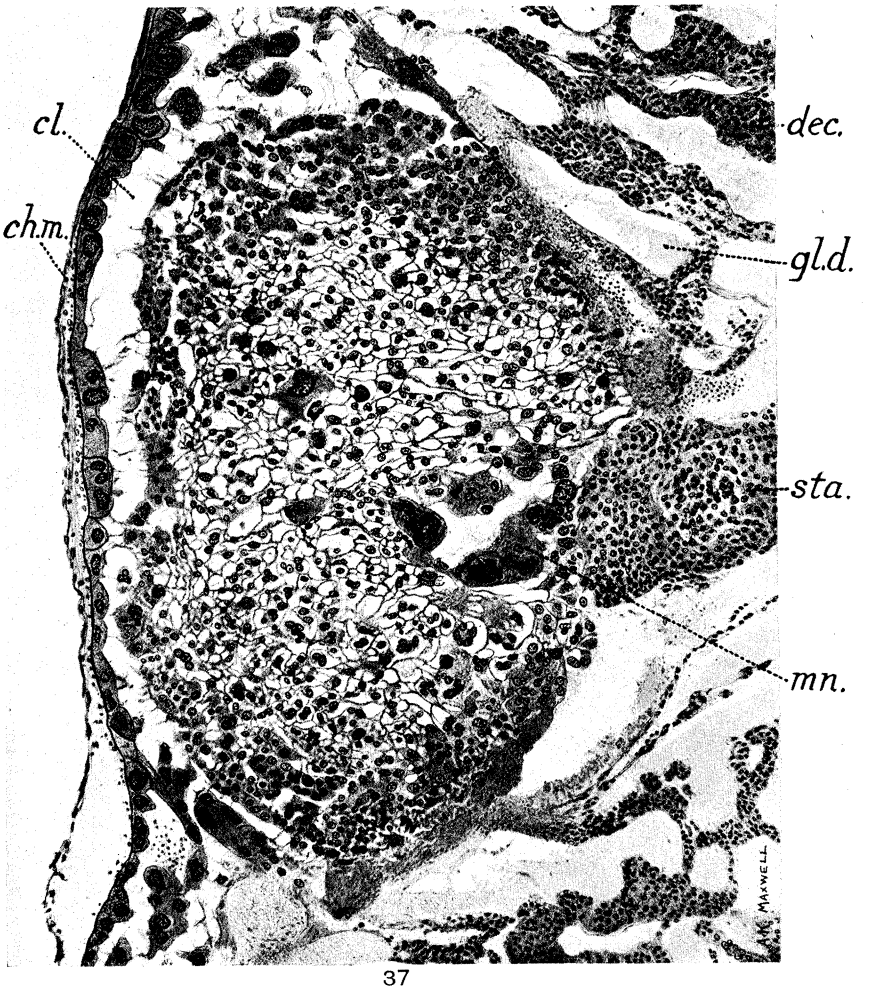
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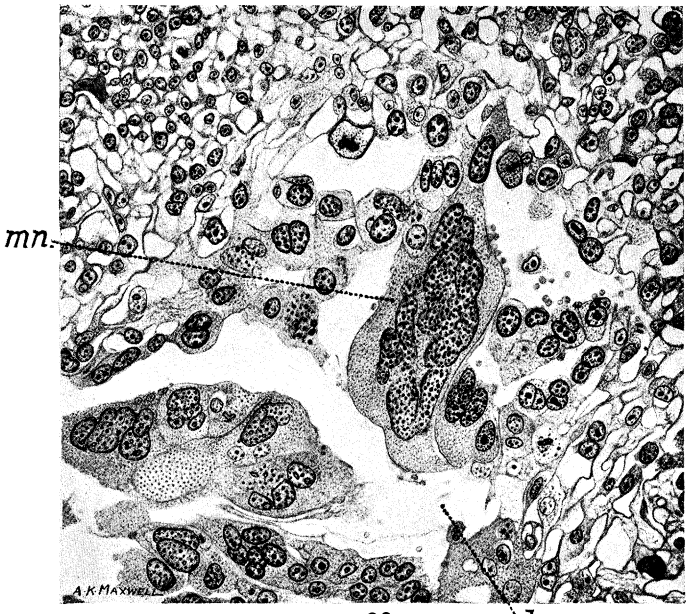

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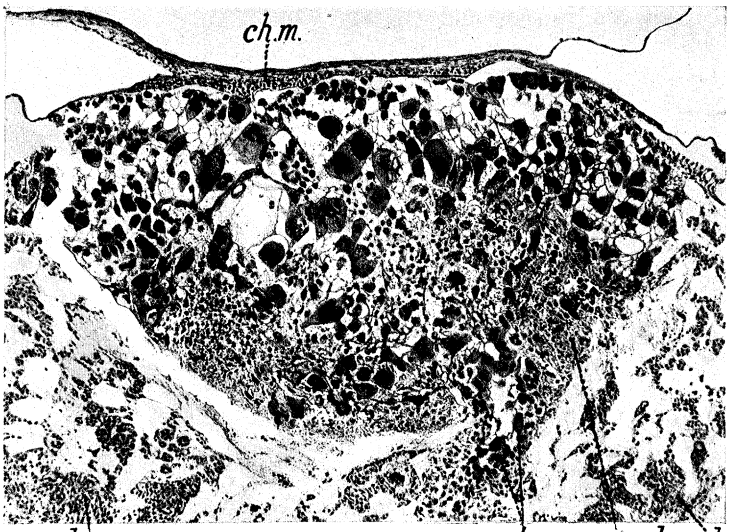

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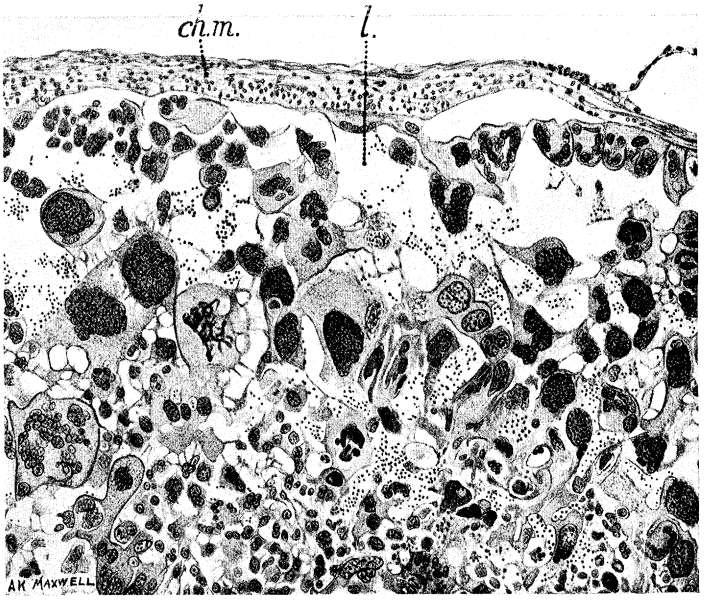

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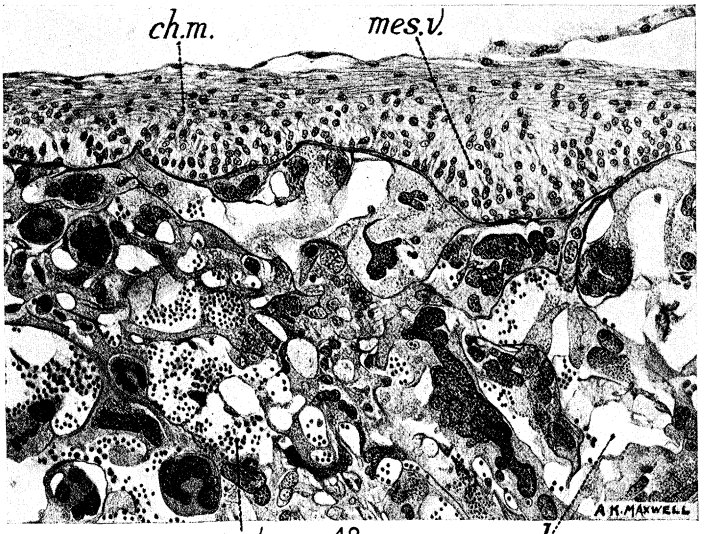

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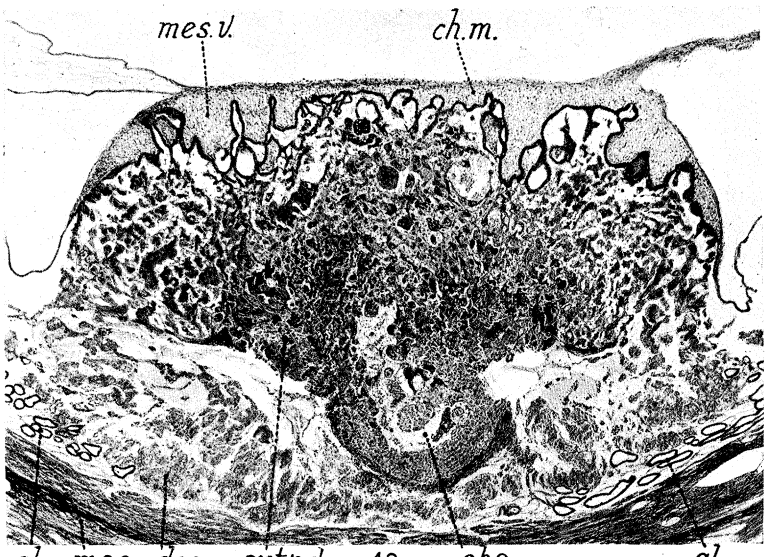

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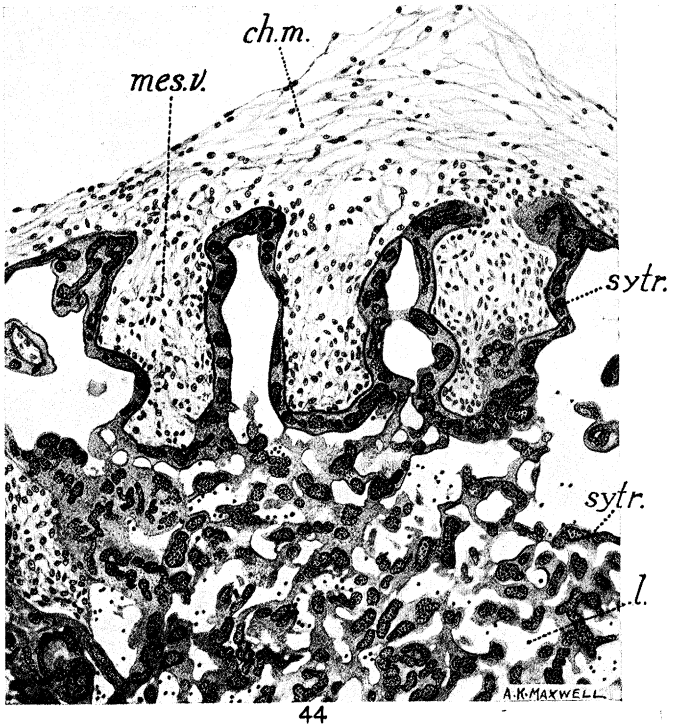

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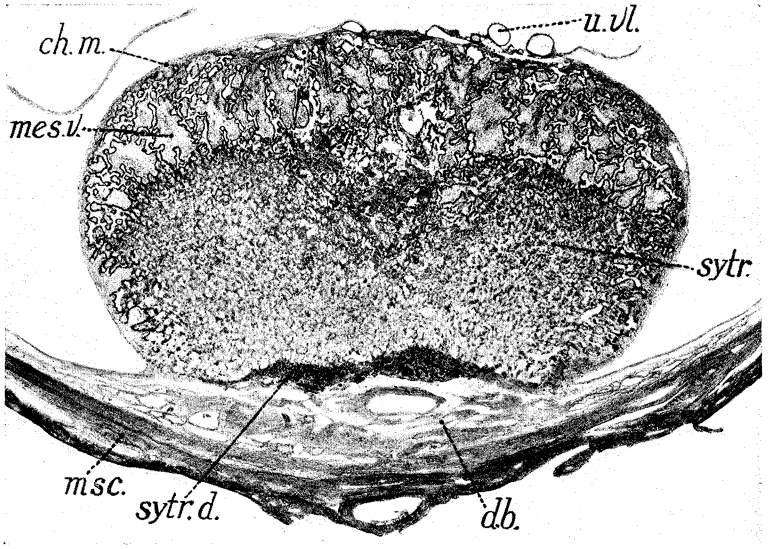

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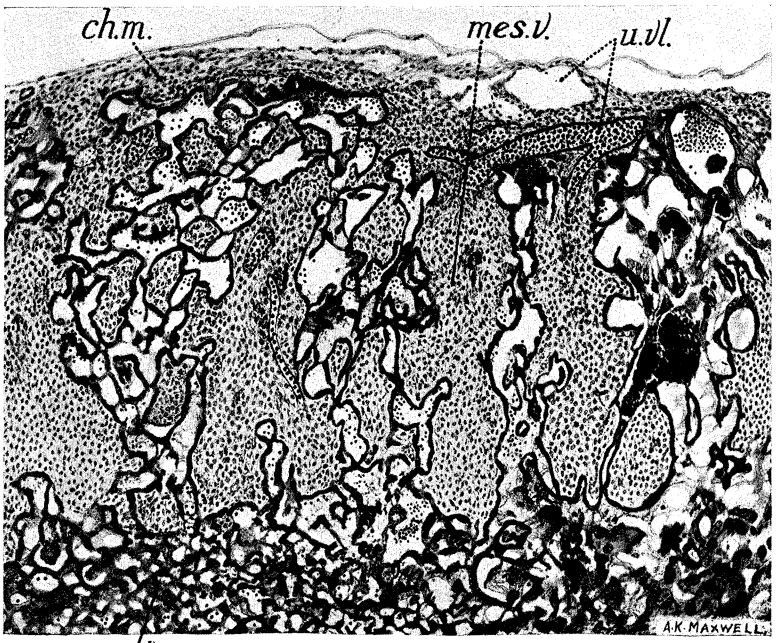

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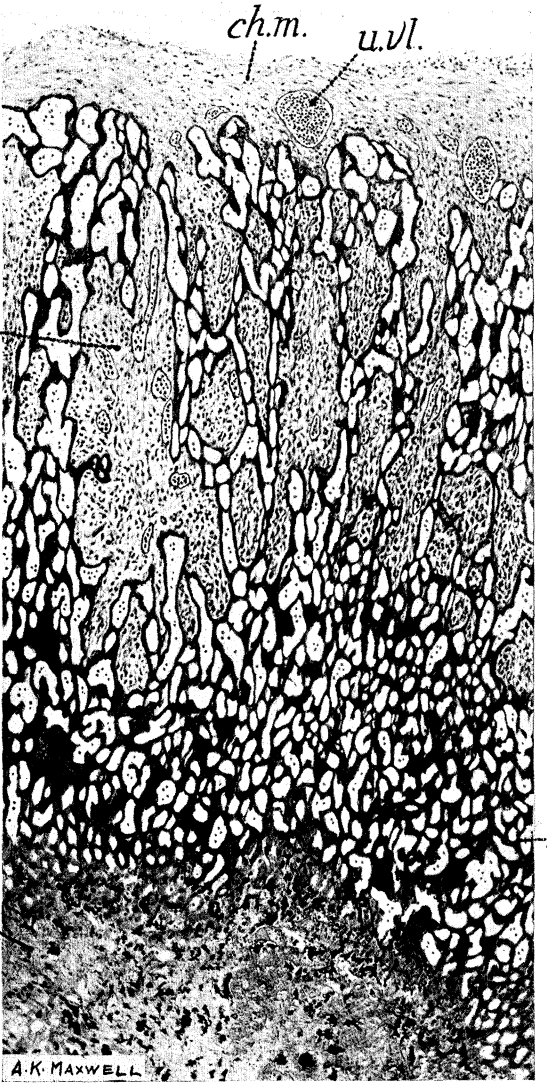

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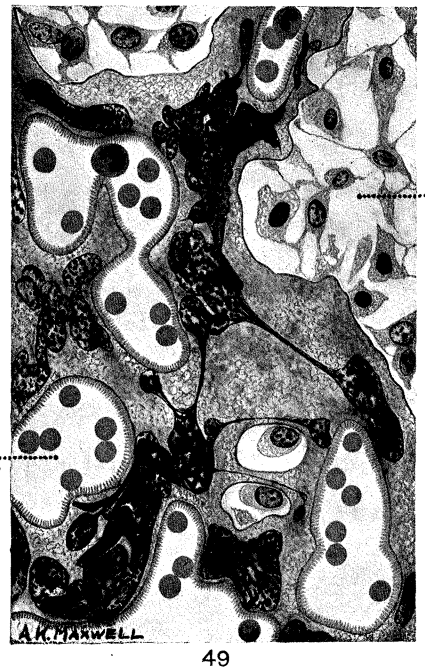

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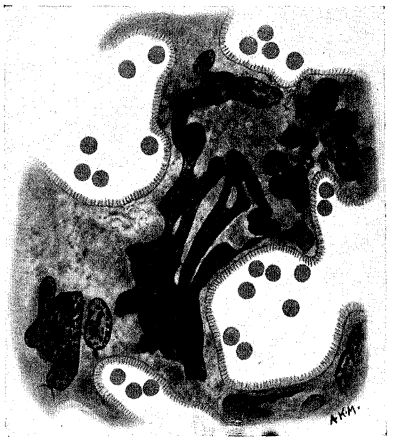

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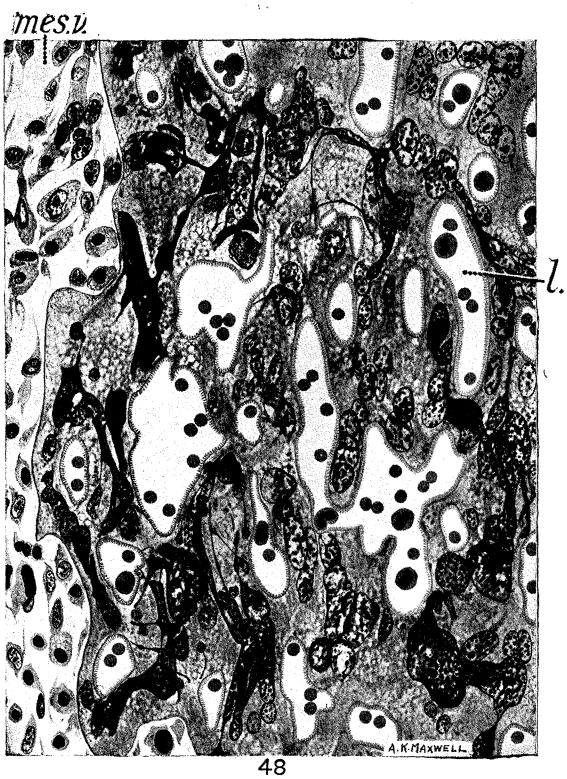

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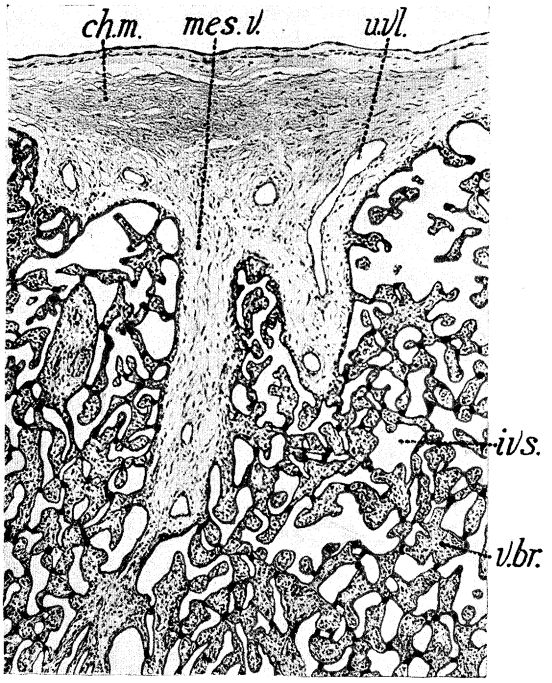

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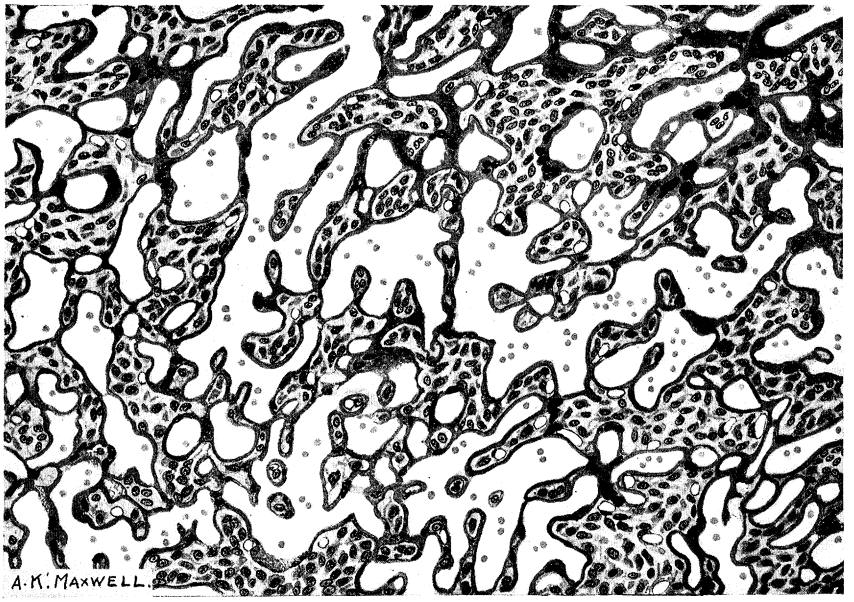

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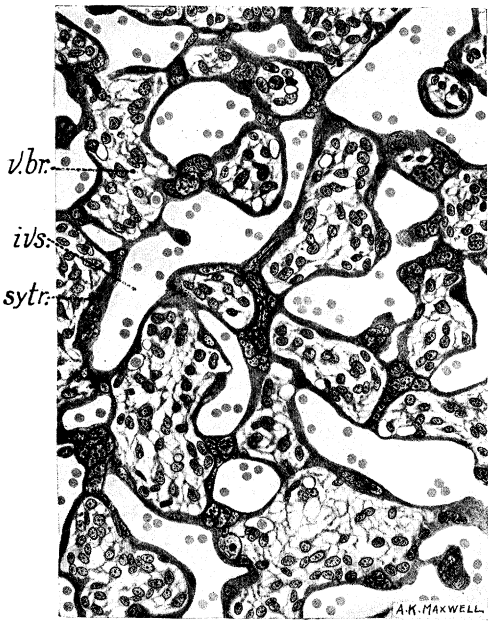

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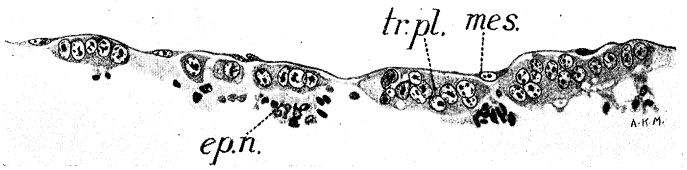

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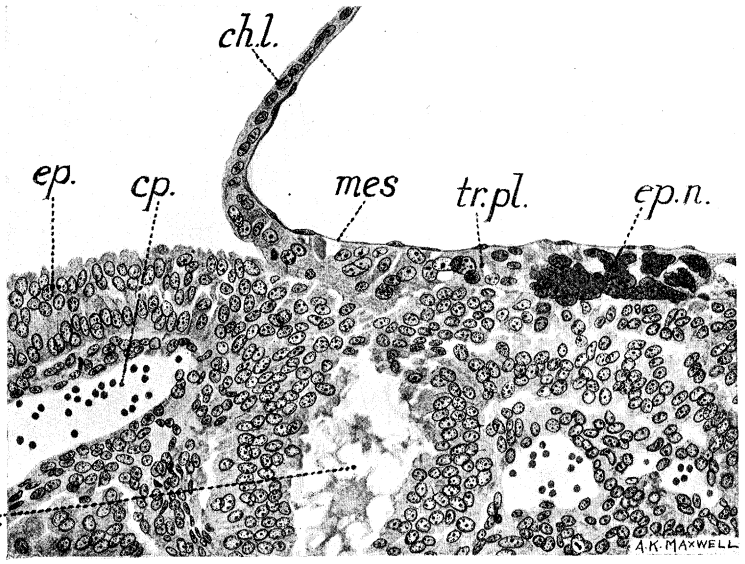

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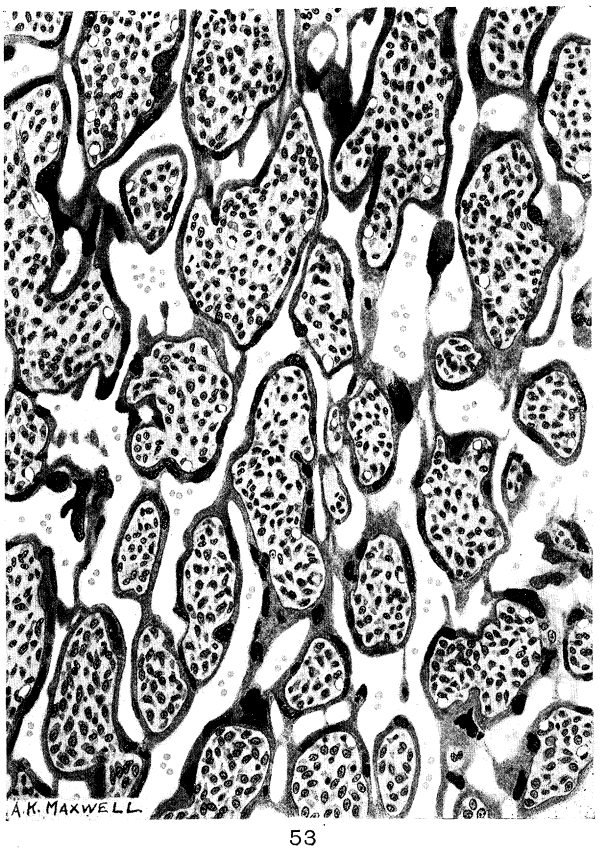

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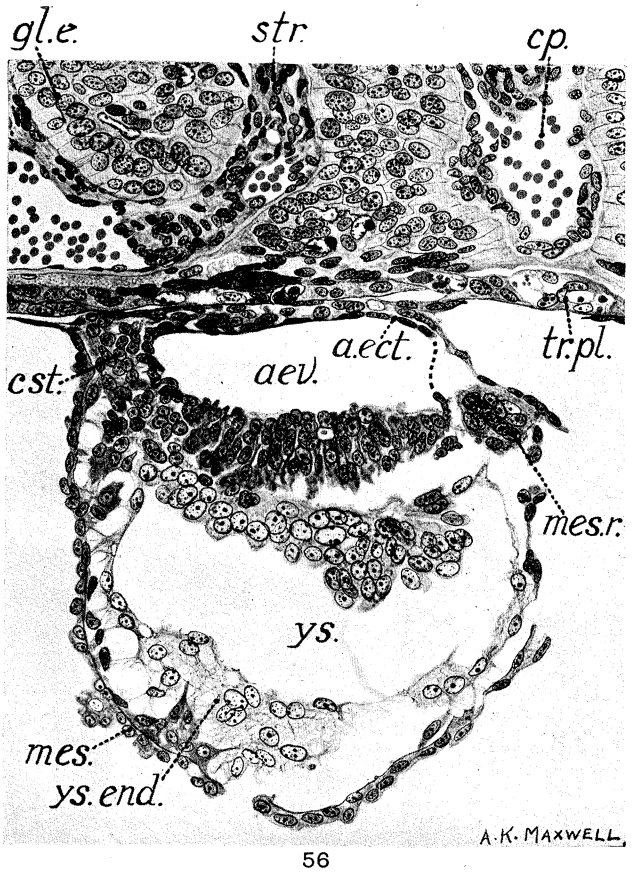
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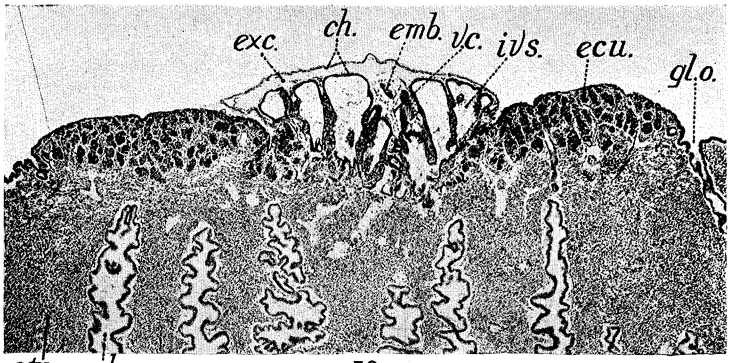
56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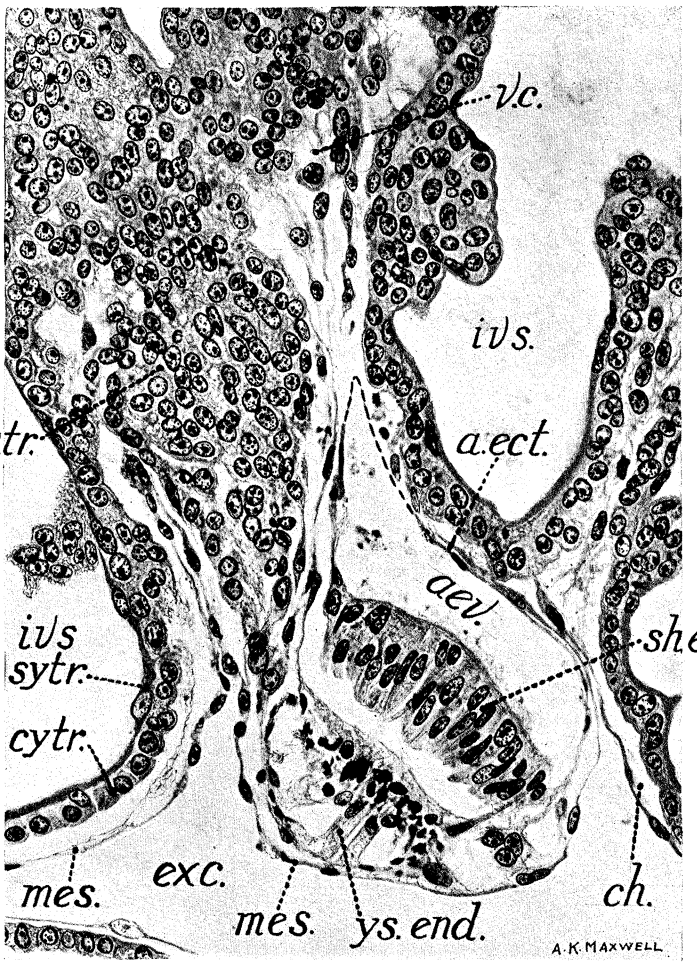
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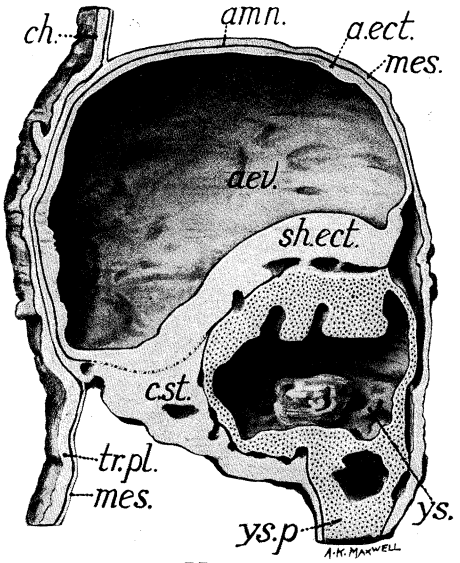
61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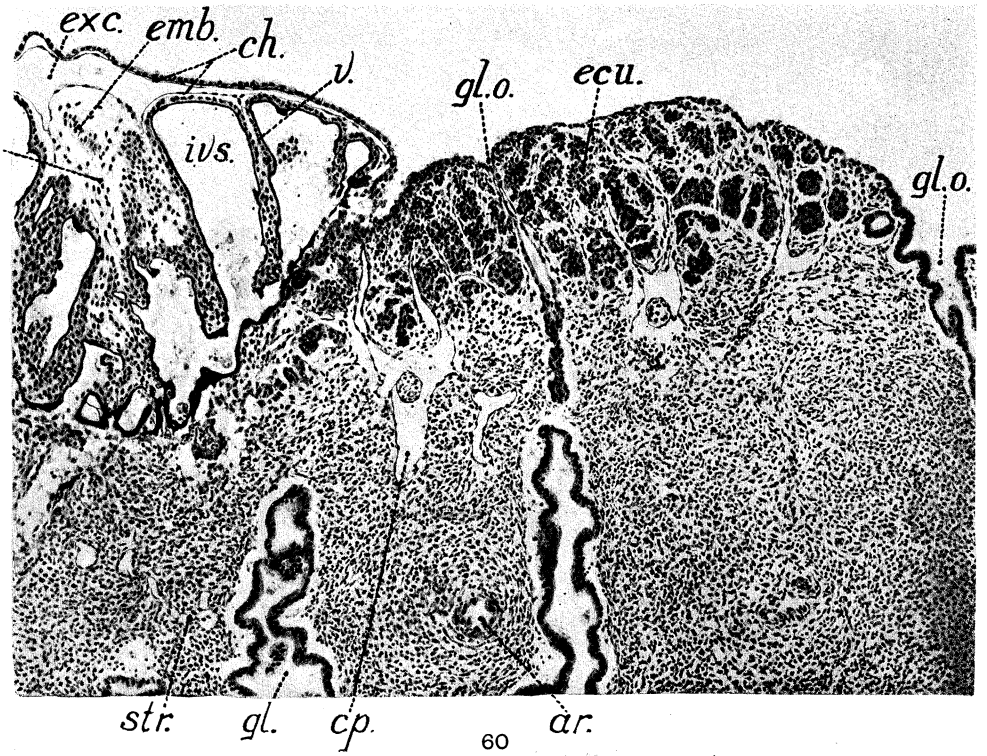
A.K. MAXWELL

55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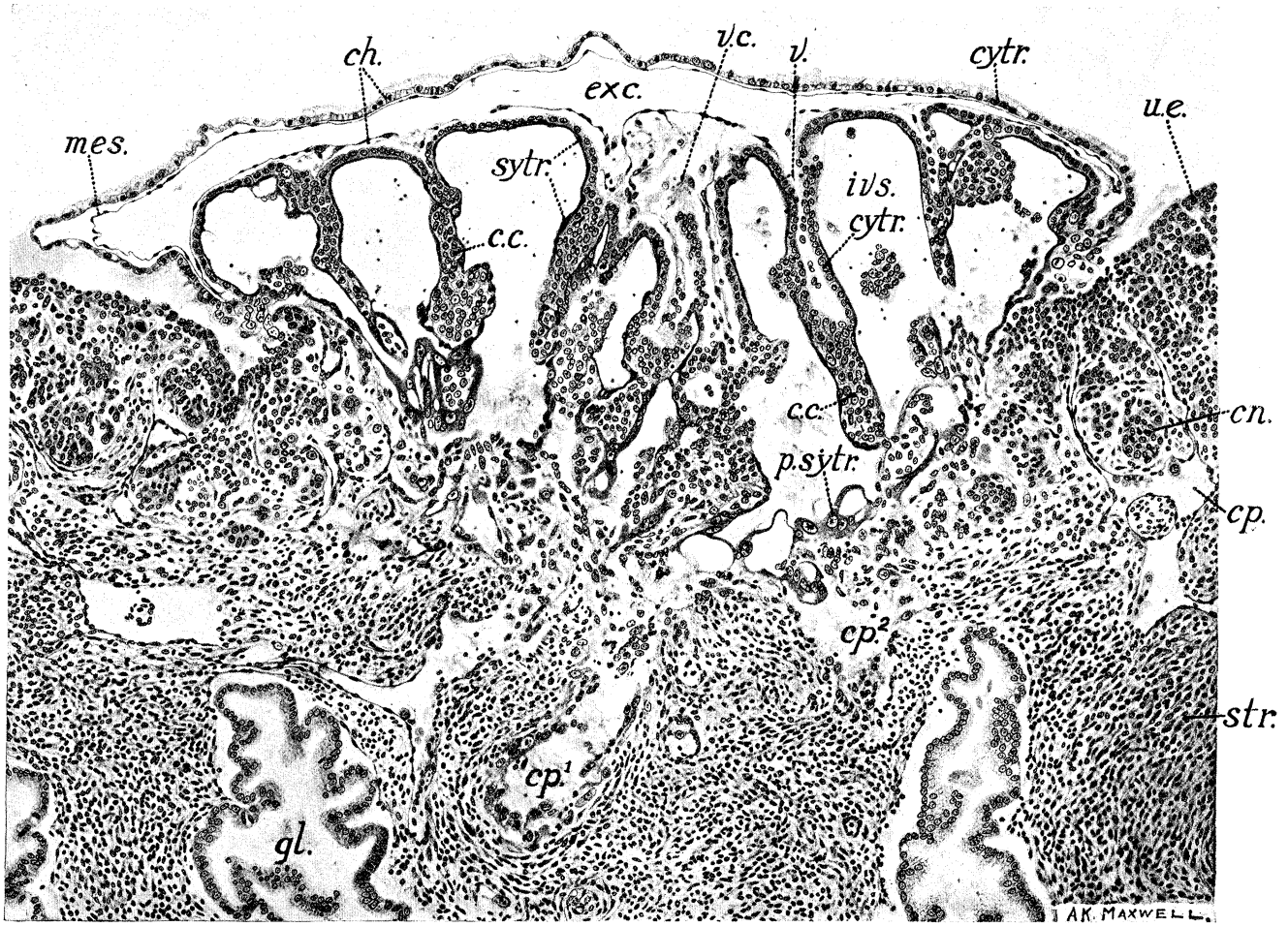
60



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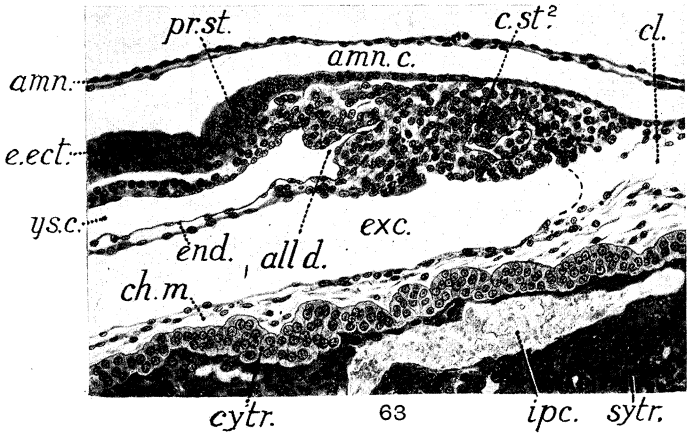

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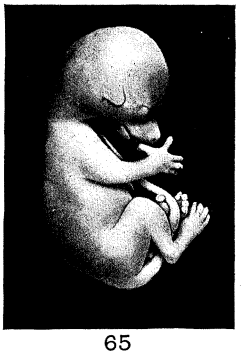

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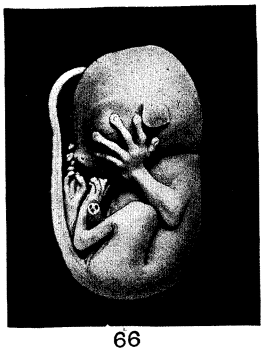

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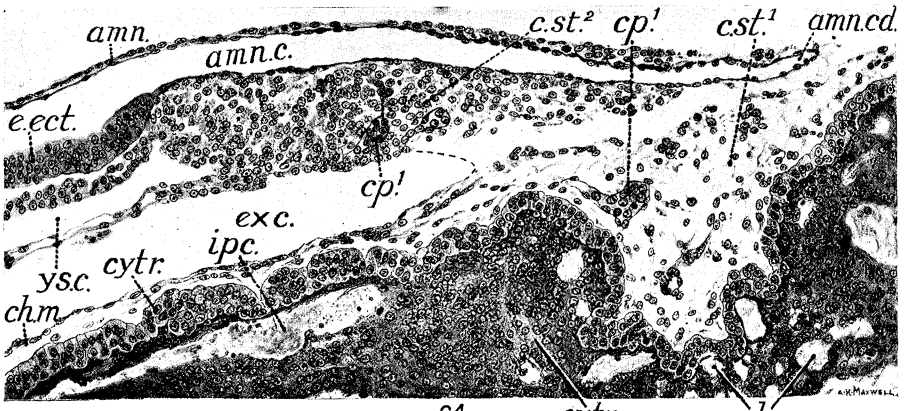

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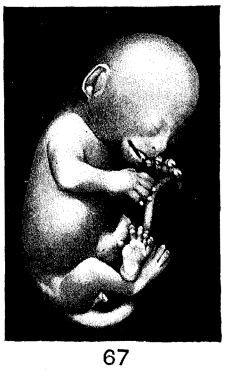

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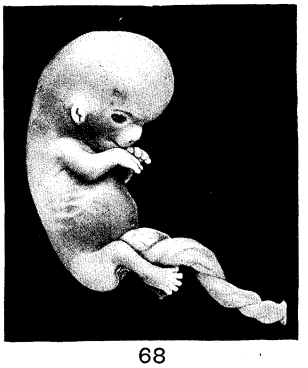

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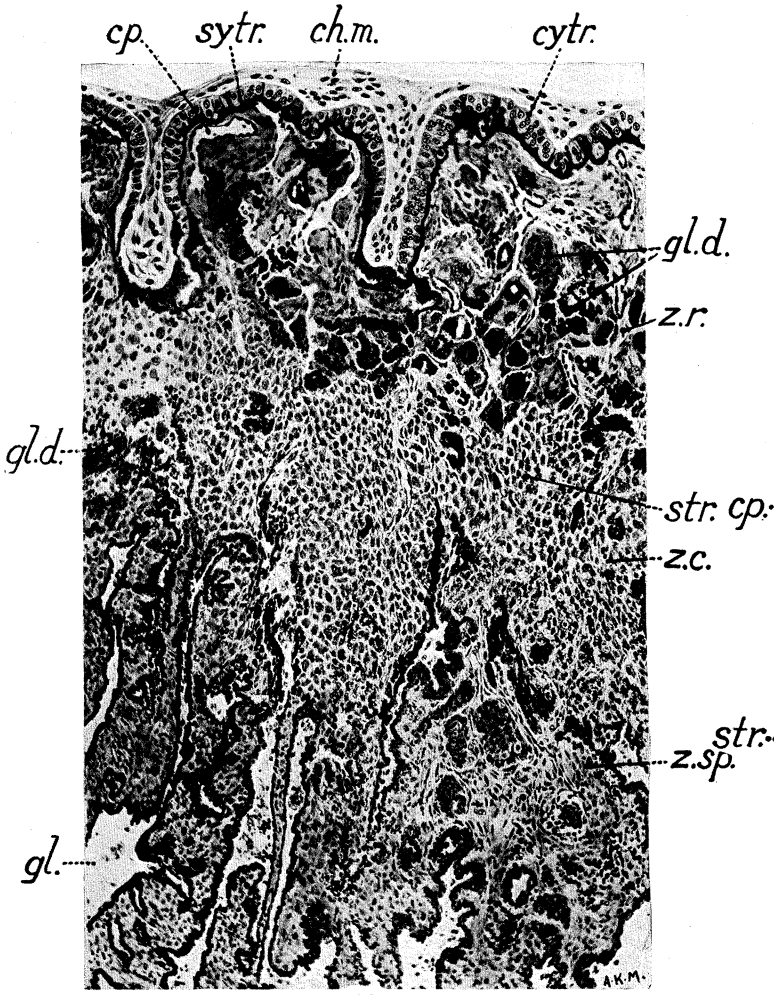
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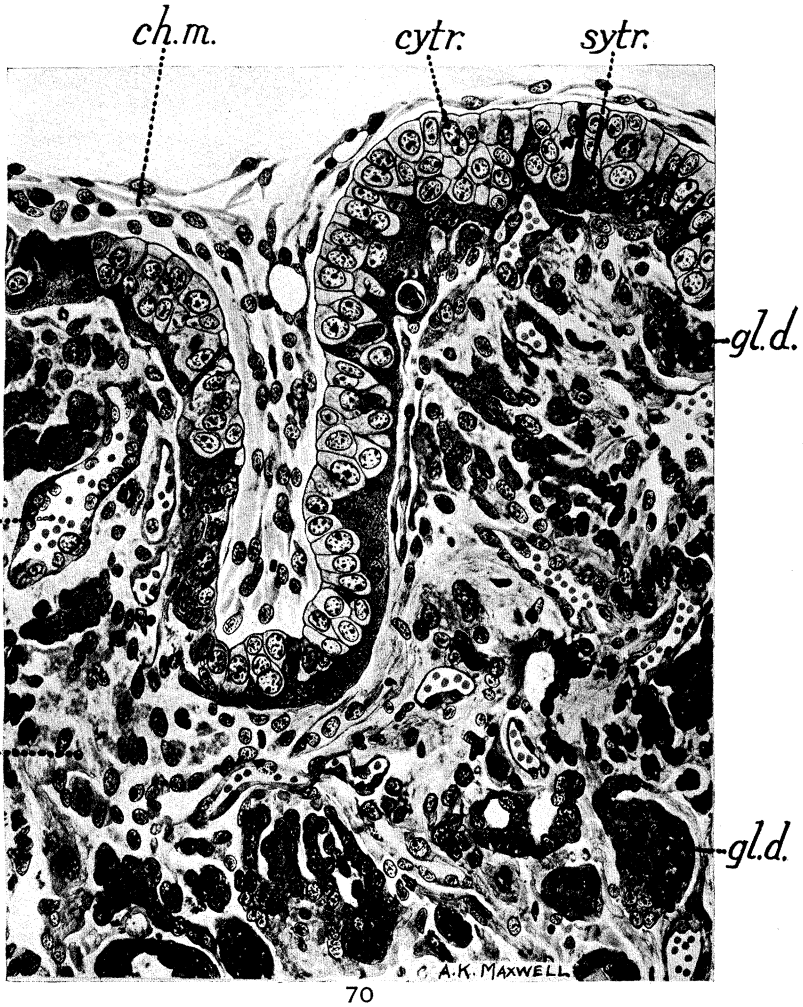
gl.d.
z.r.
gl.d.
str. cp.
z.c.
z.sp.
gl.
A.K.M.

69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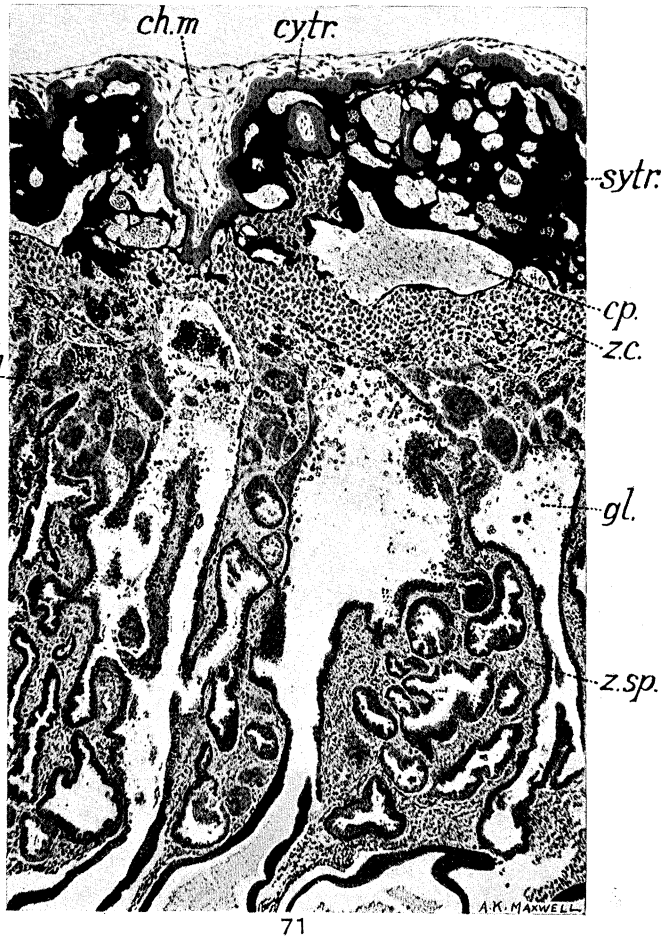
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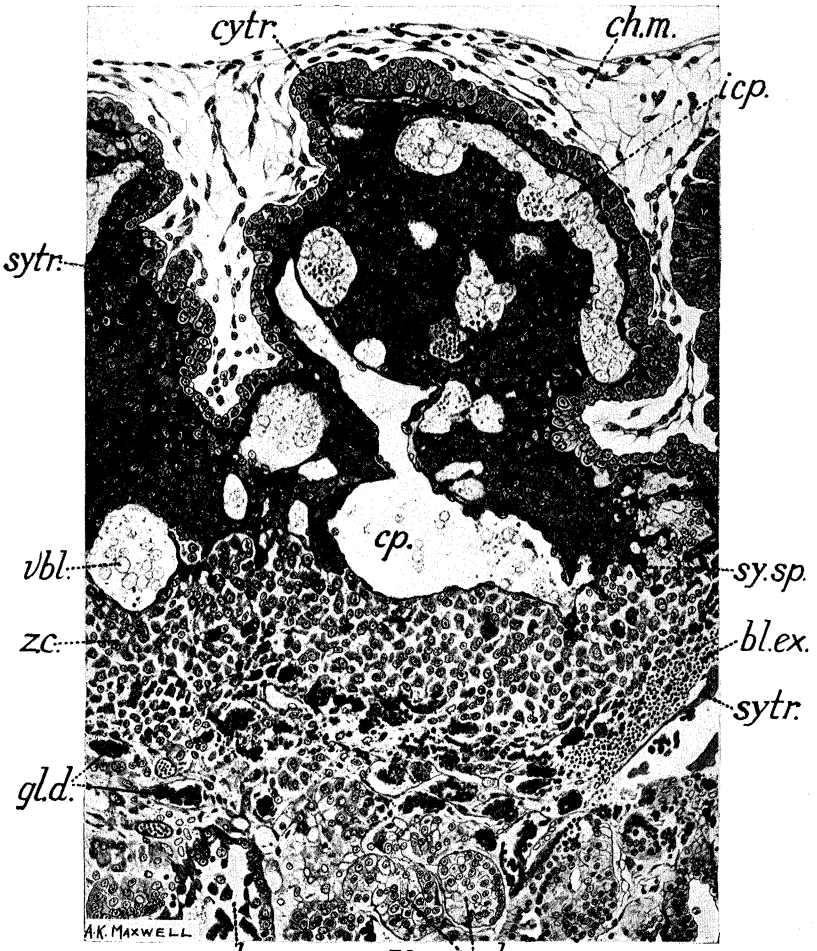
A.K. MAXWELL

71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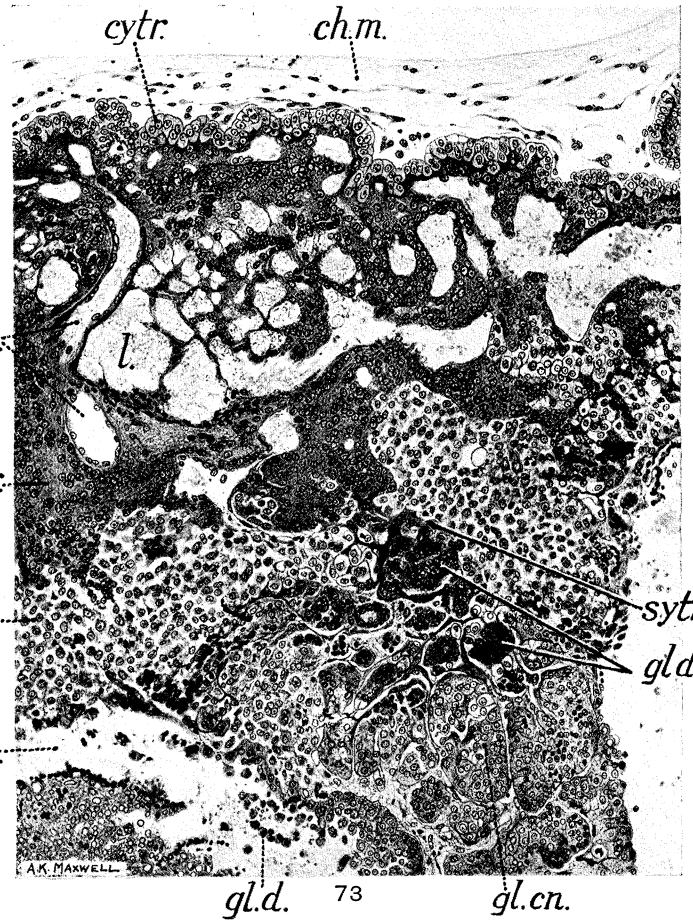
gl.
gl.cn.

72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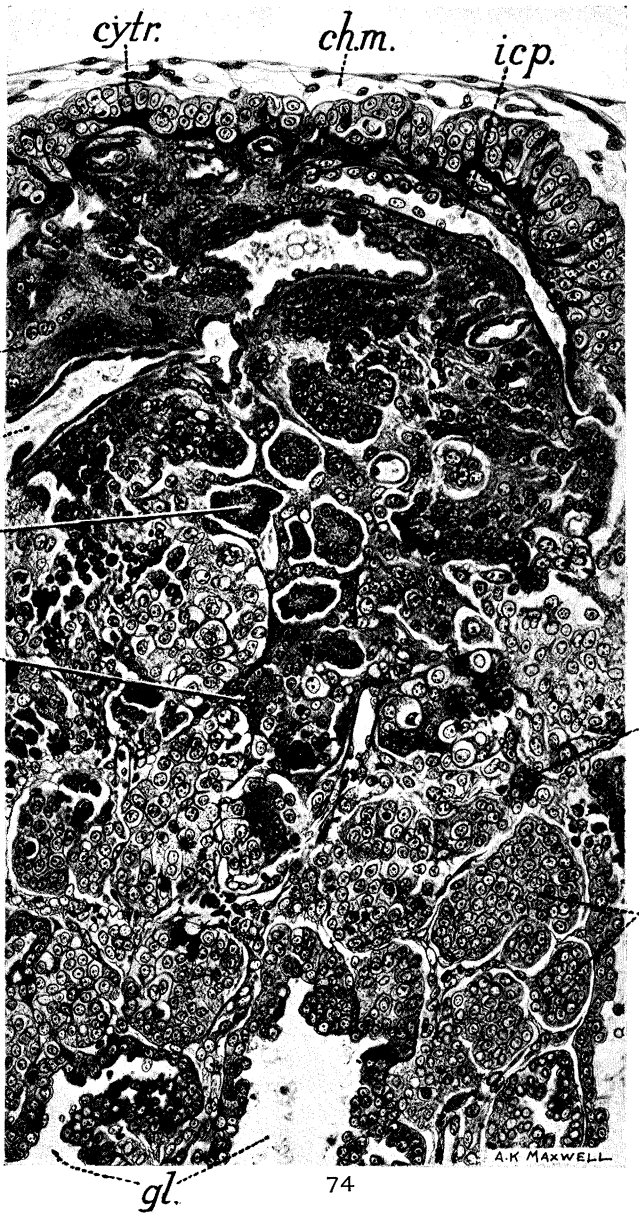
gl.d.
gl.
A.K. MAXWELL
gl.d.
gl.cn.

73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sy.sp.
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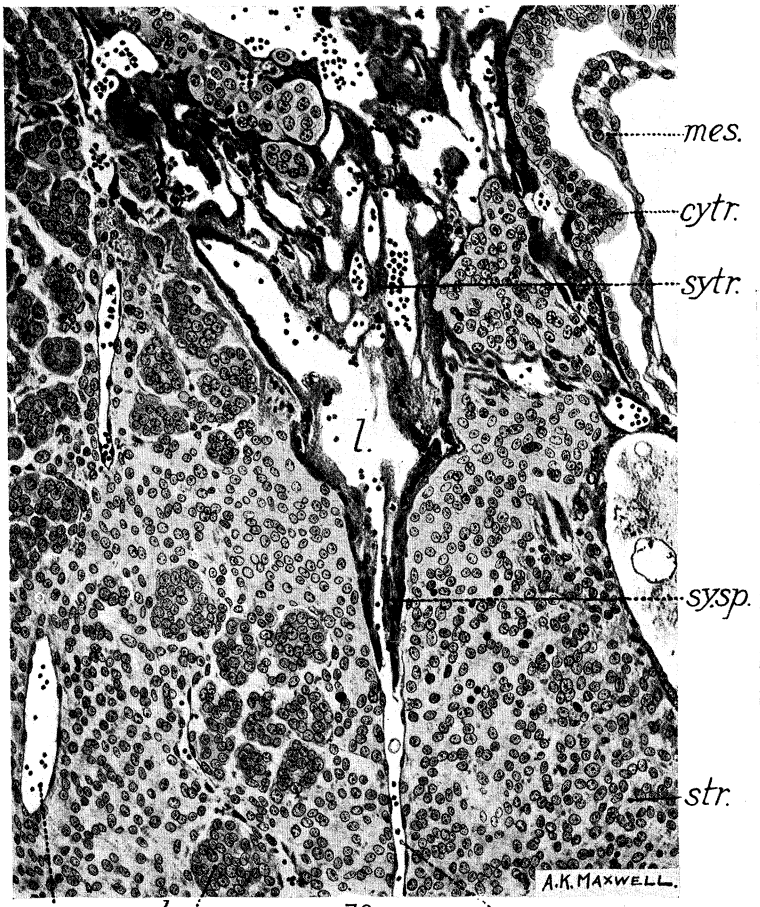
A.K MAXWELL

74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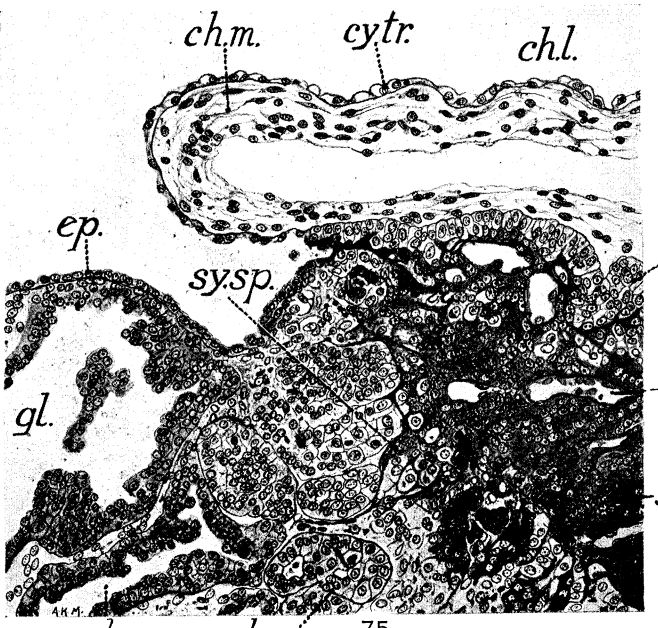
cp.
gl.cn.
cp.

76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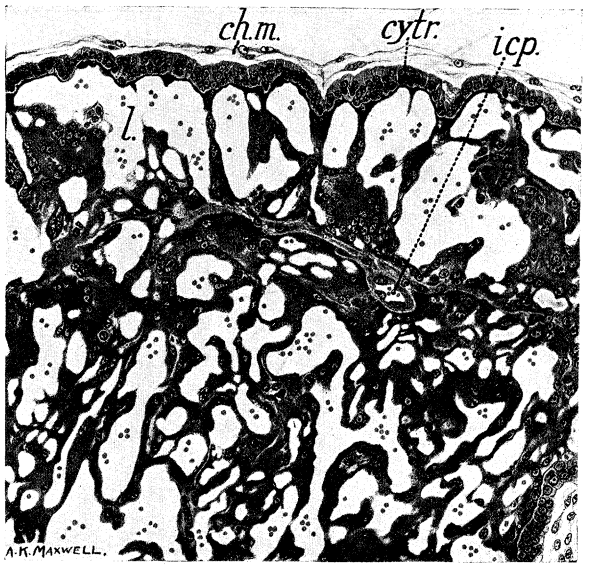
75



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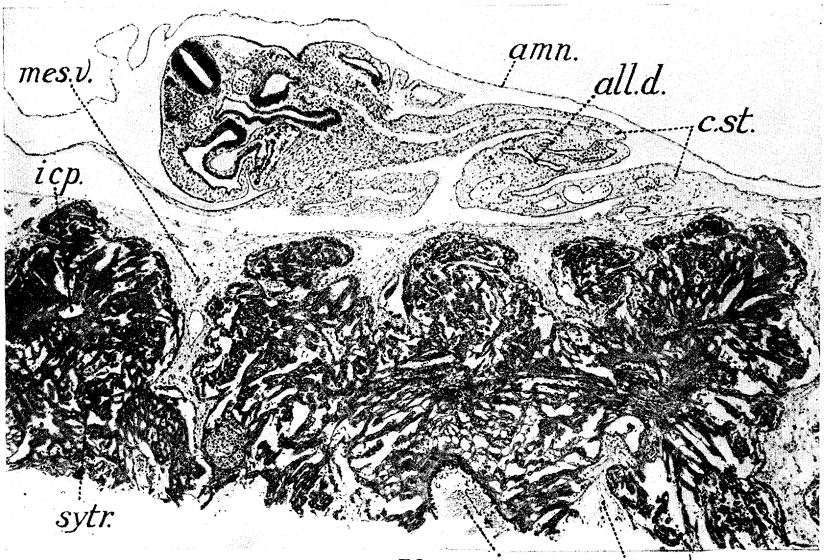

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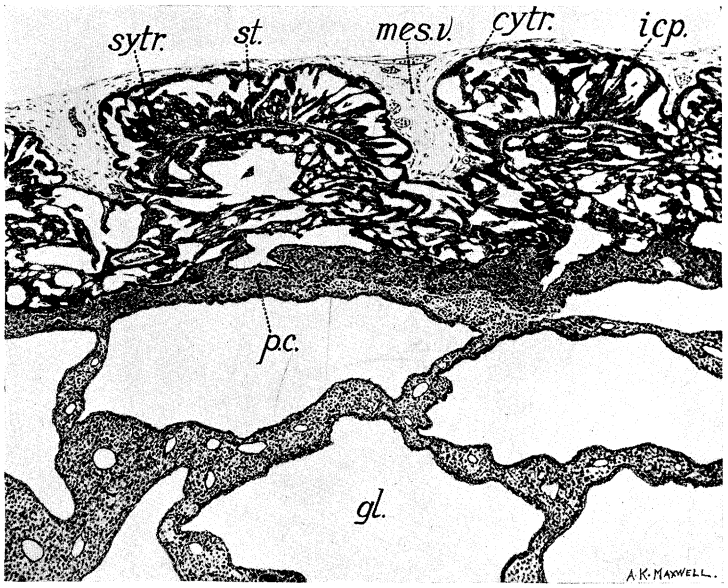

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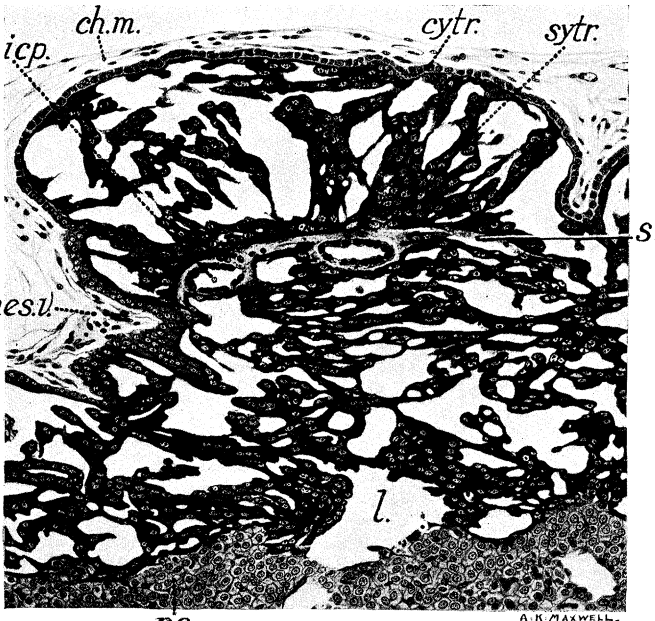

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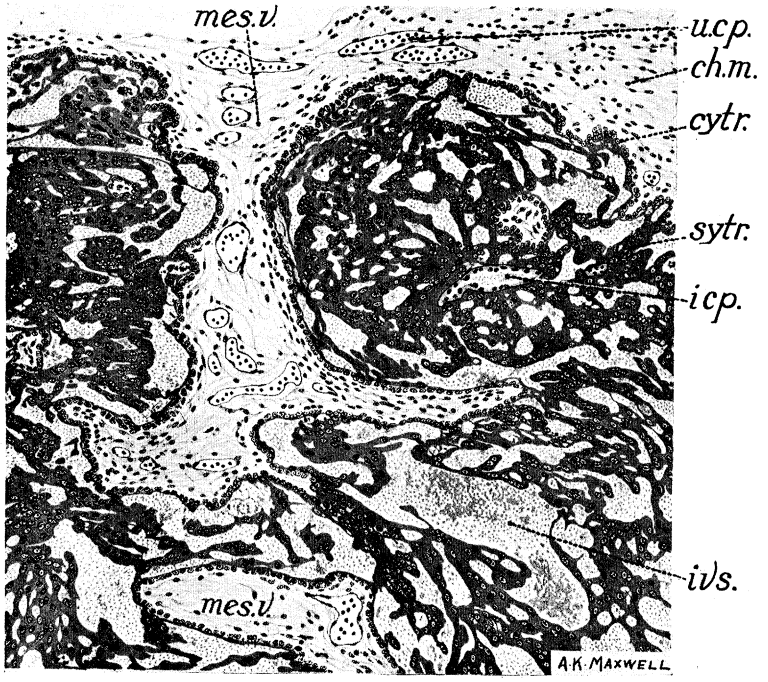

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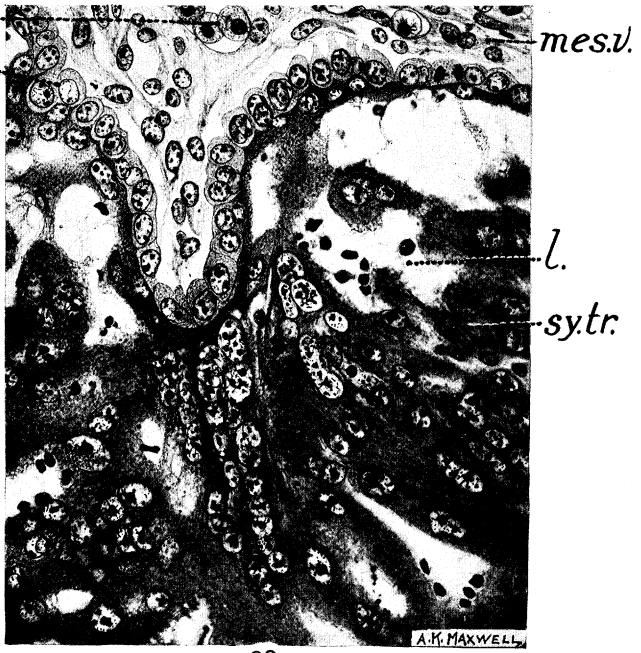

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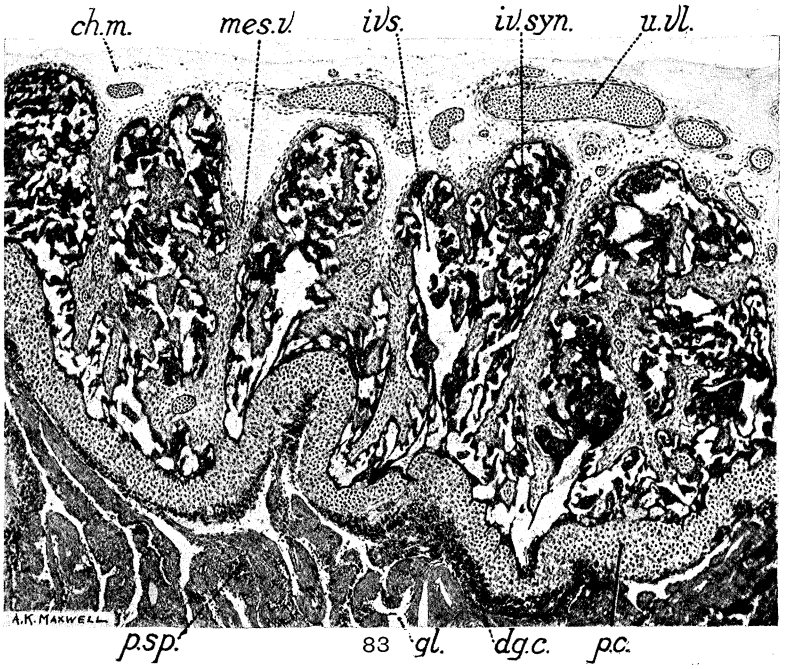
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gl.
dg.c.
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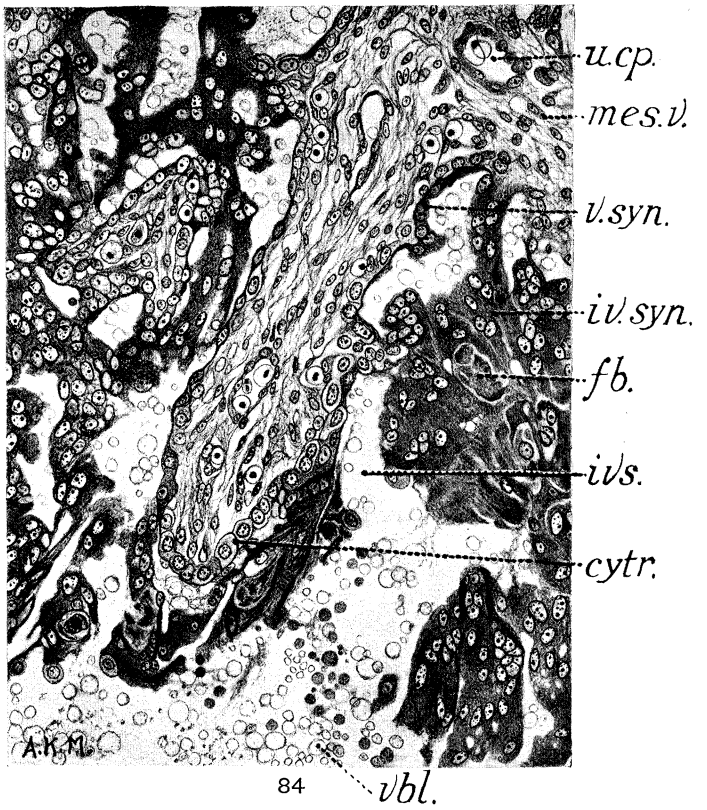
83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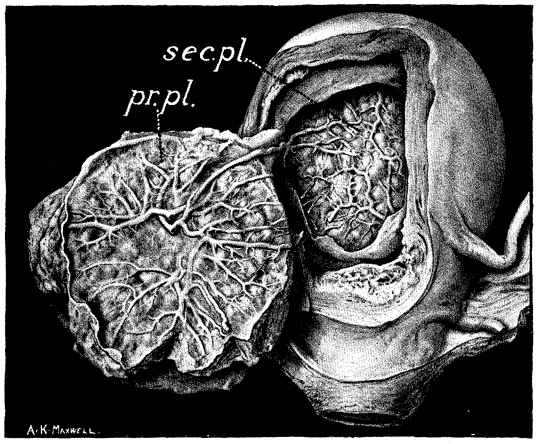
84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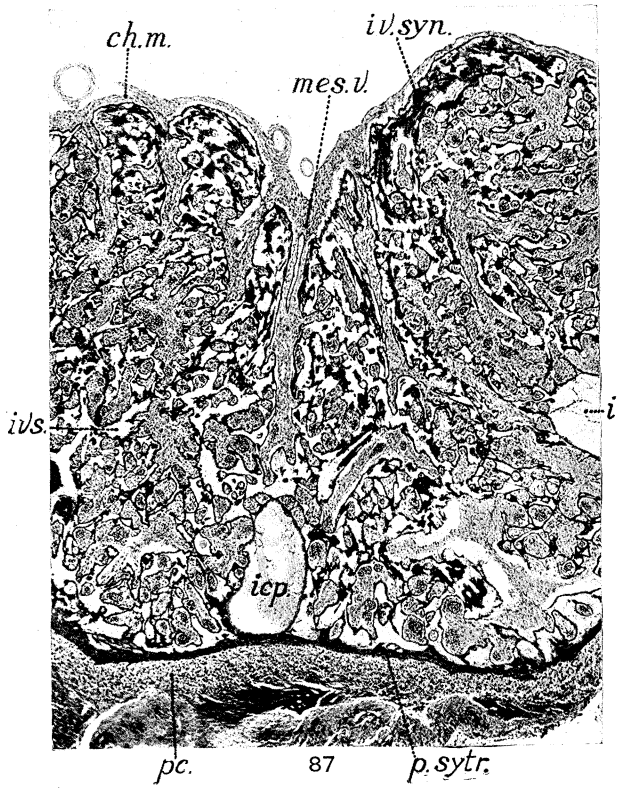
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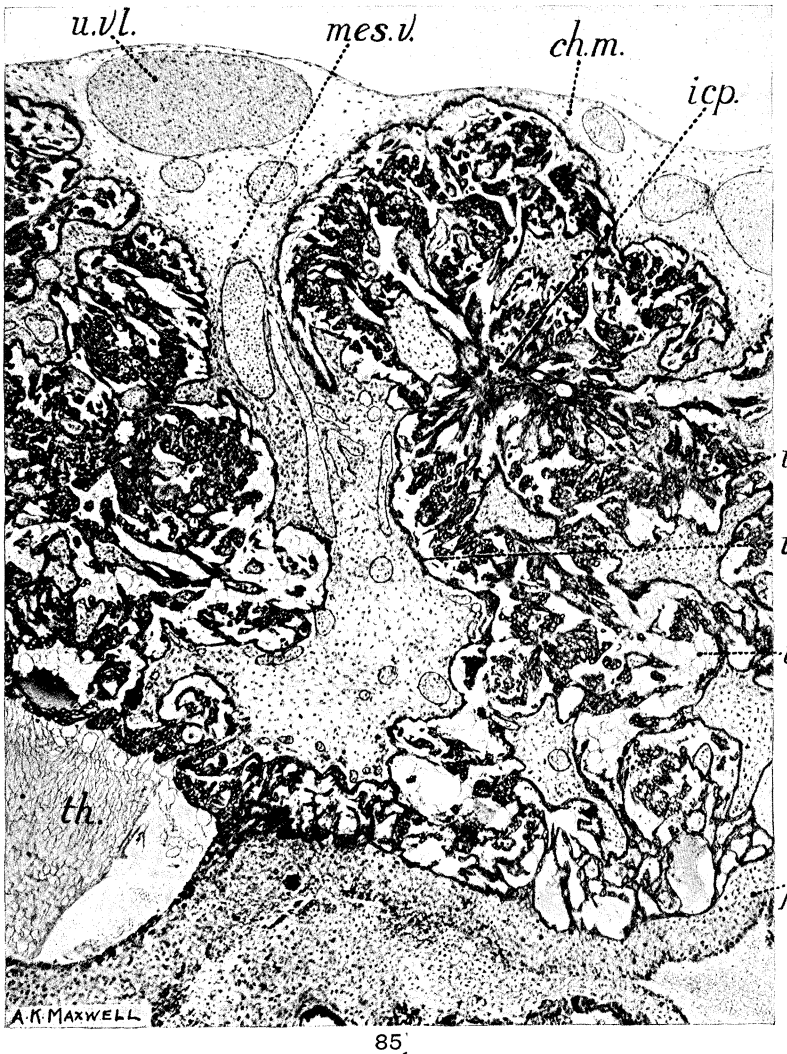
87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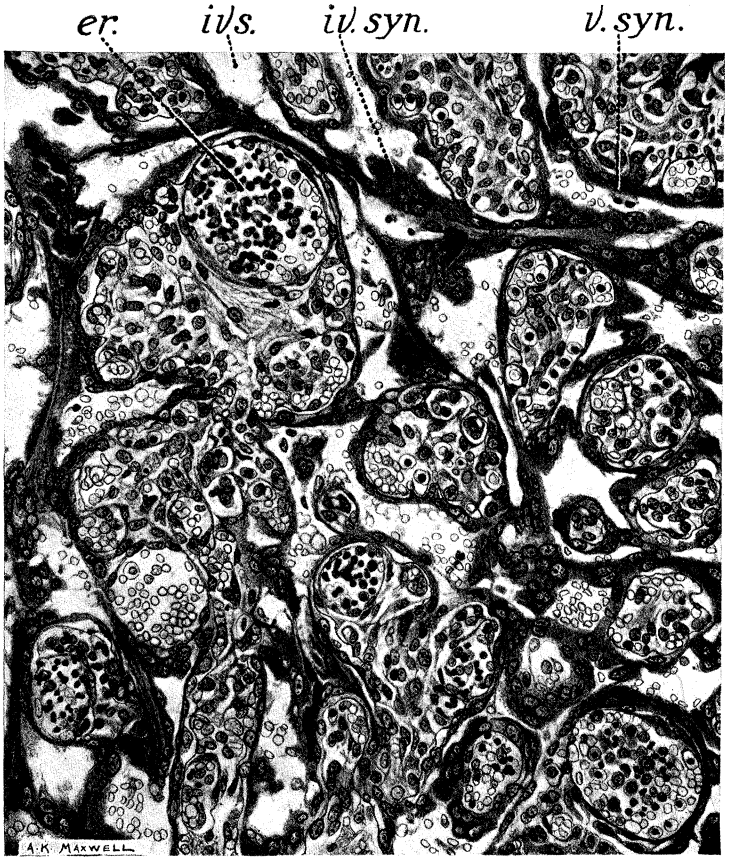
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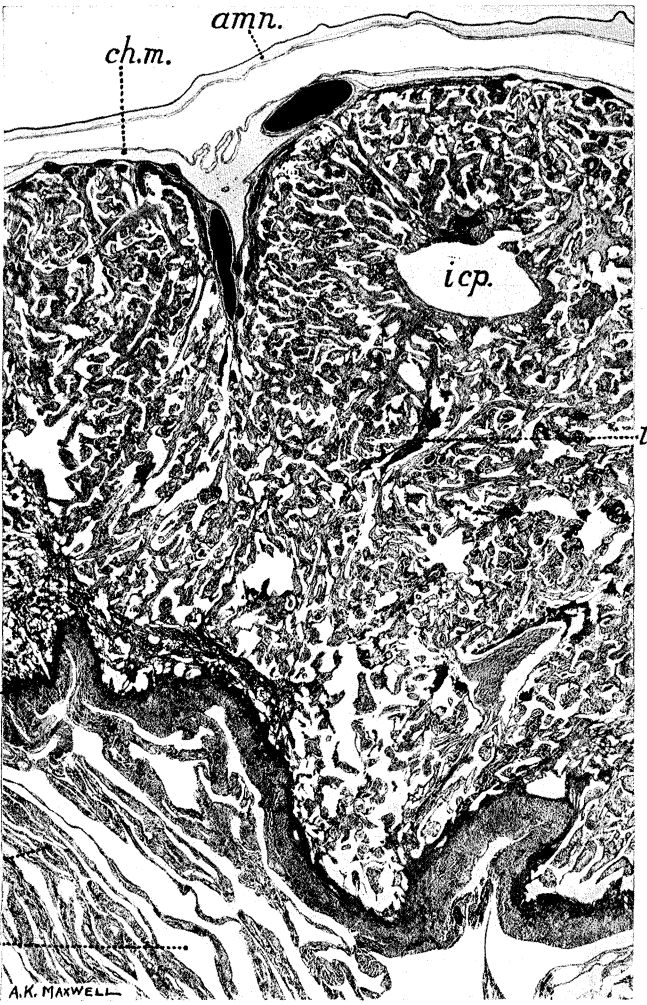
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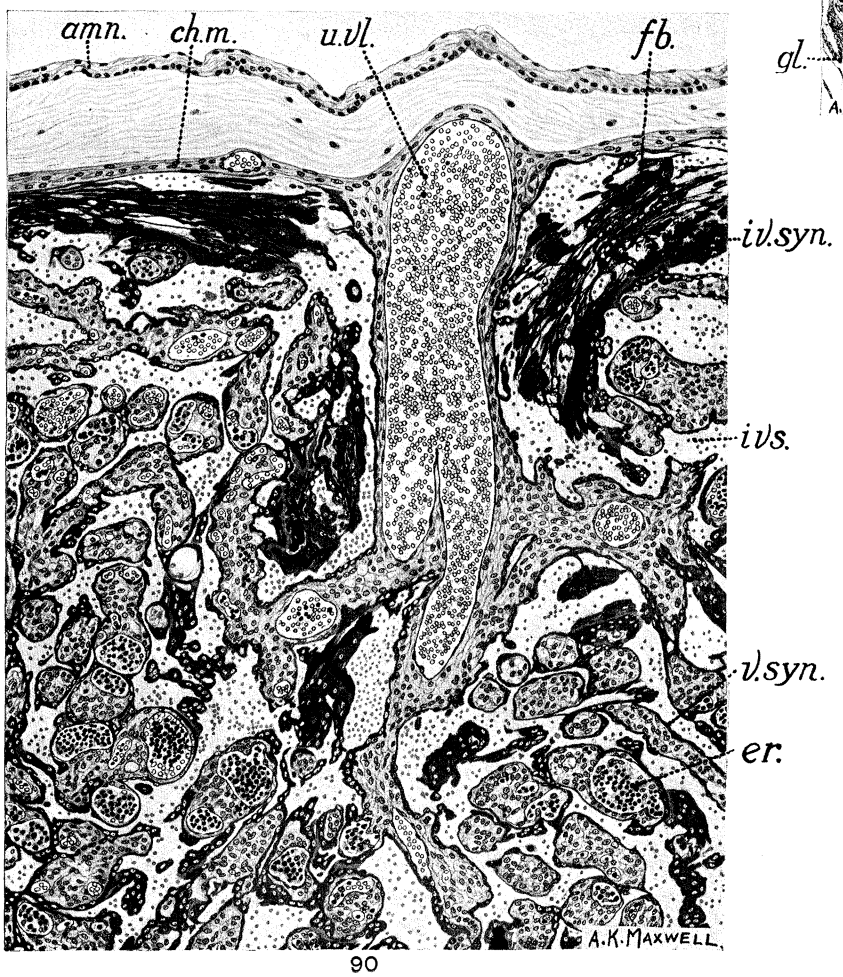
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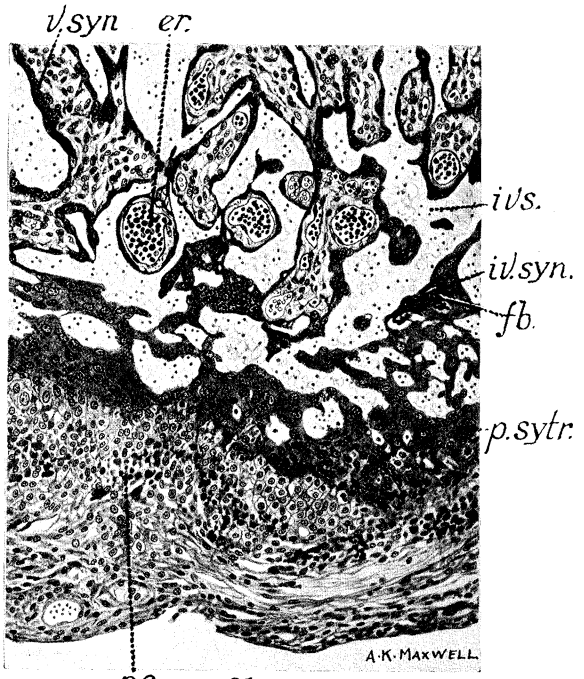
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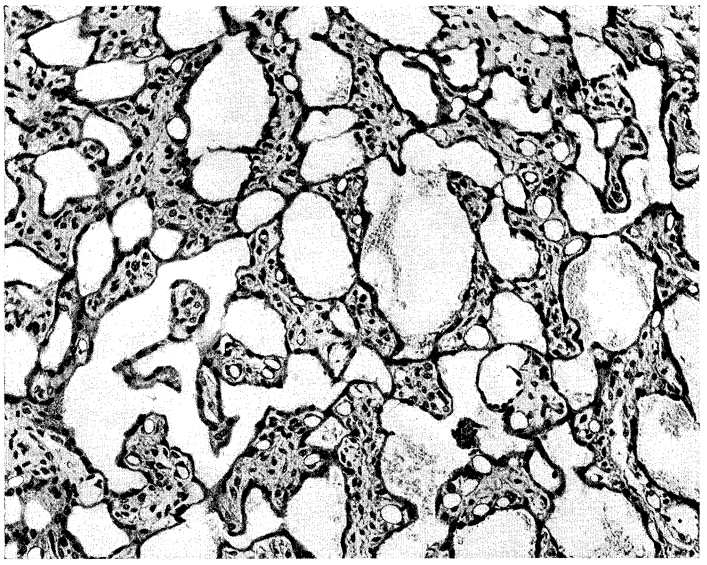

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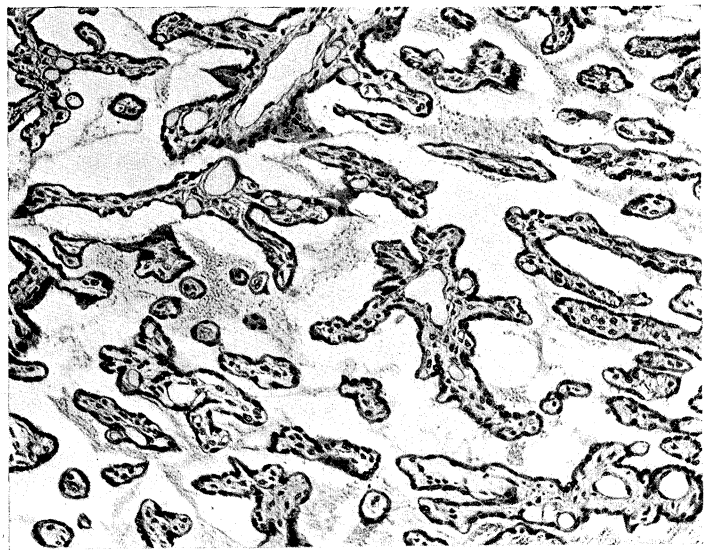

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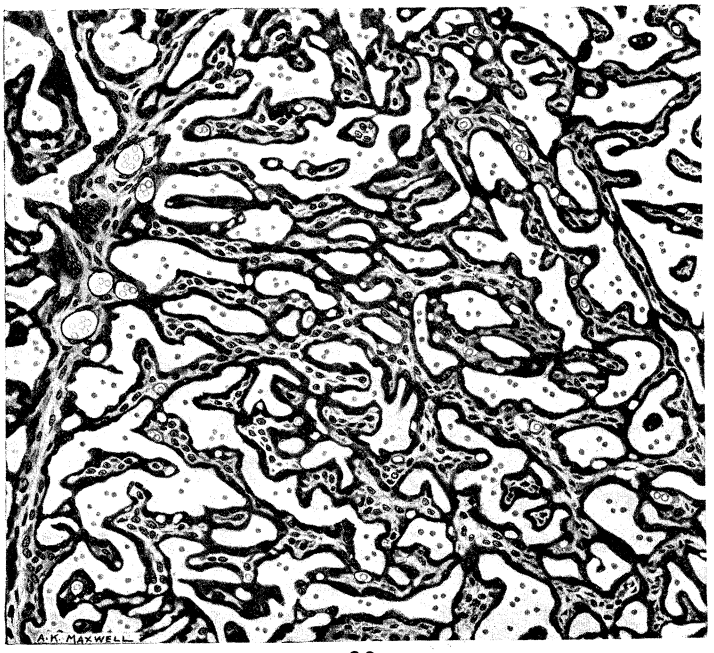
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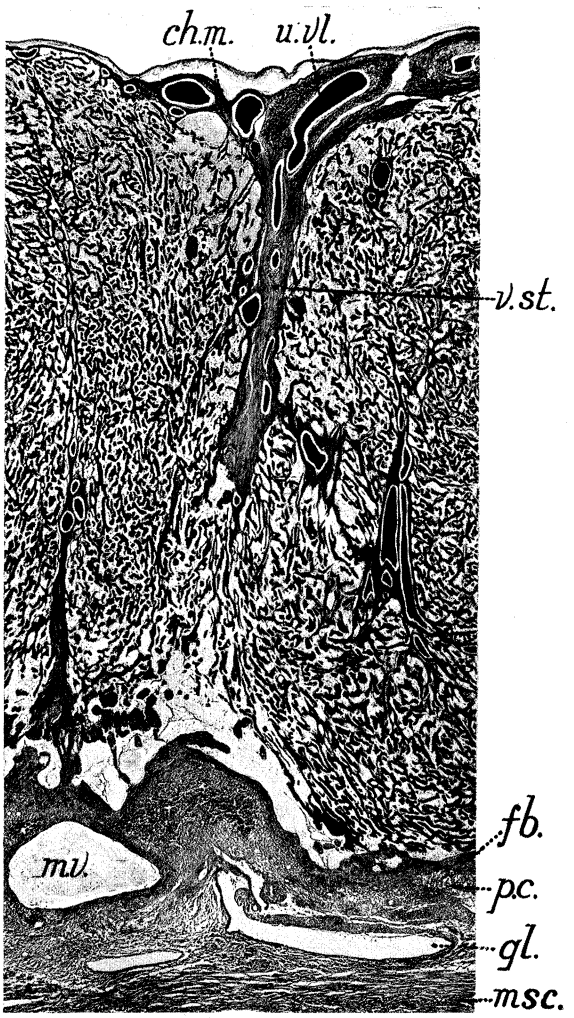
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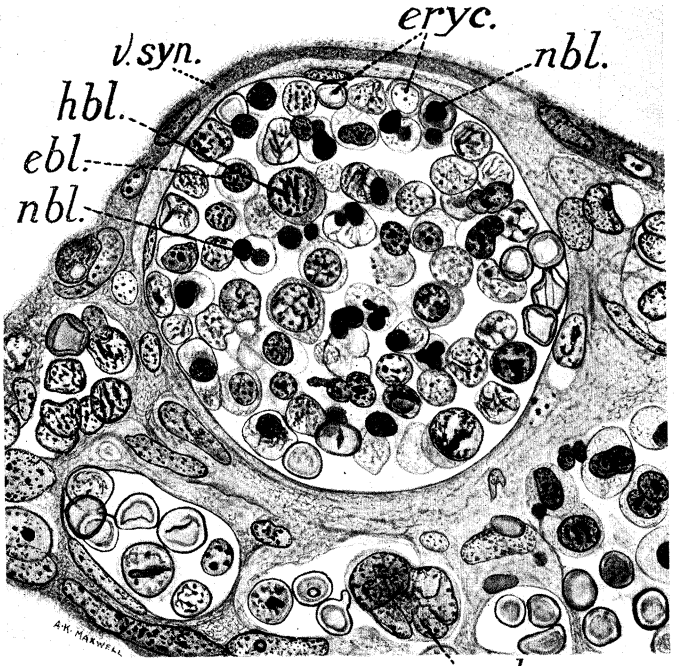
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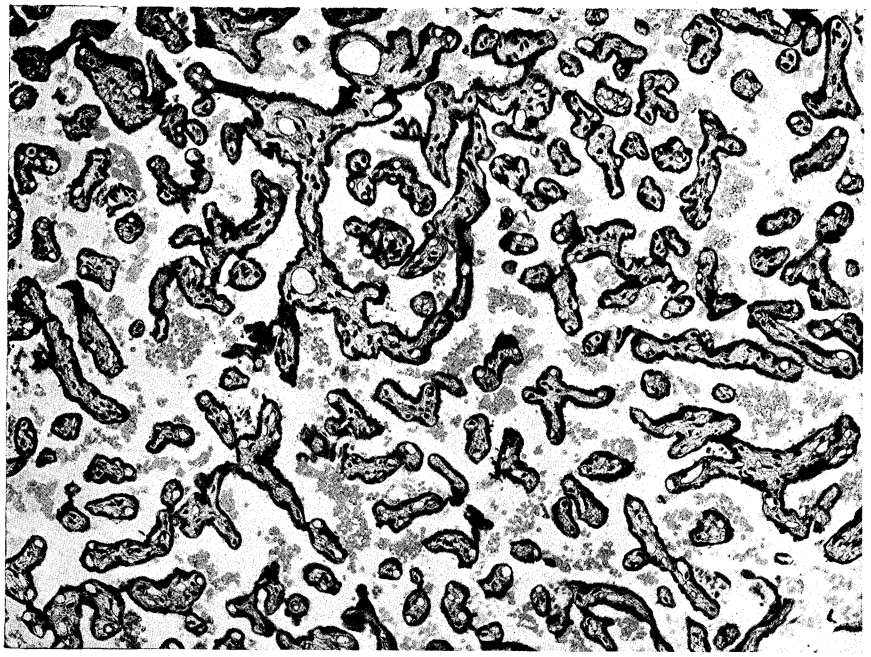

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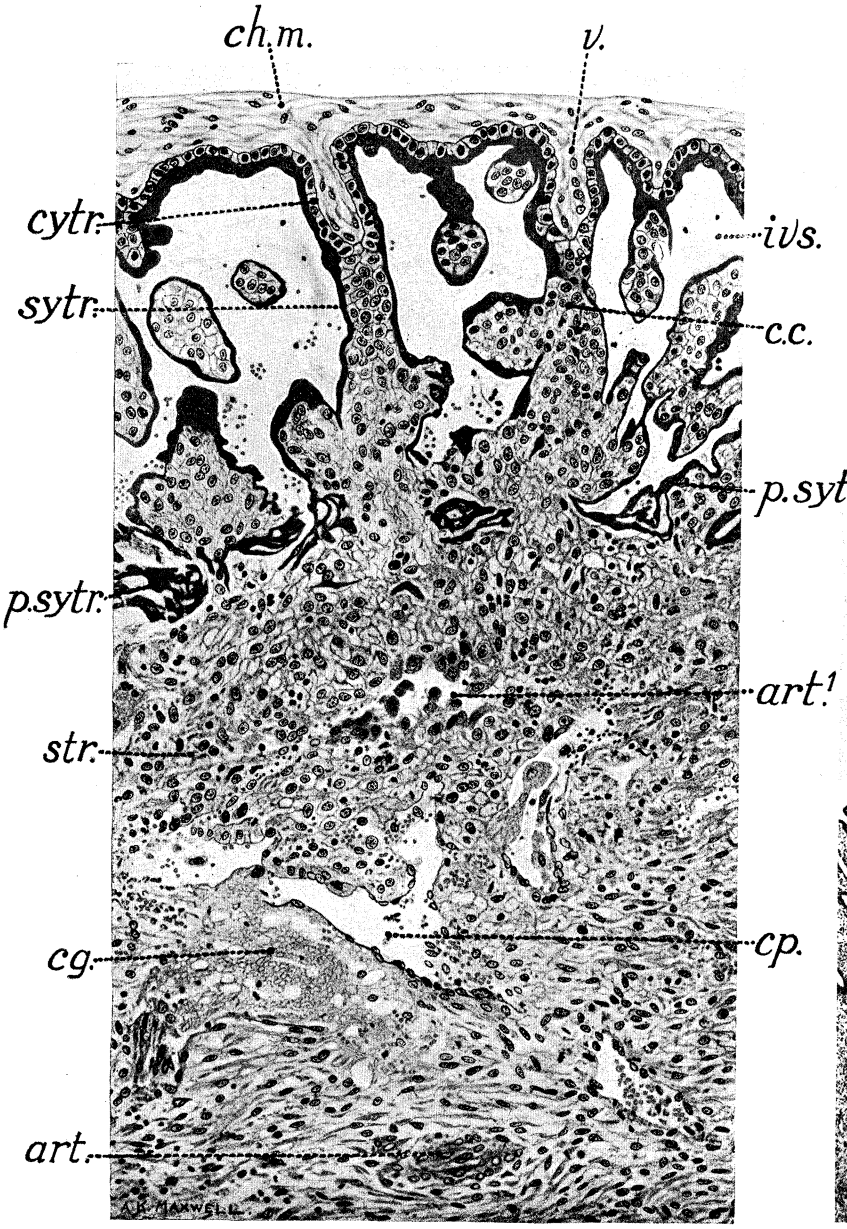

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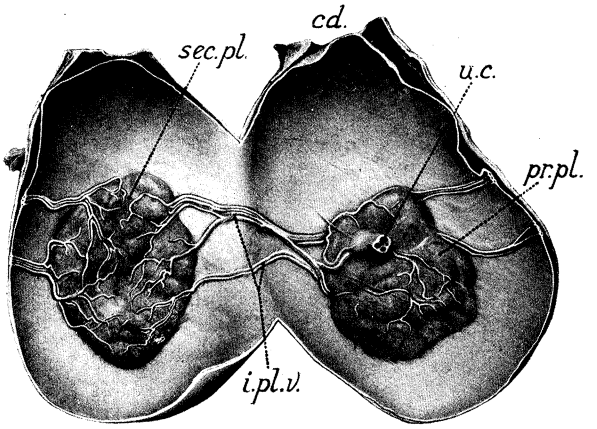

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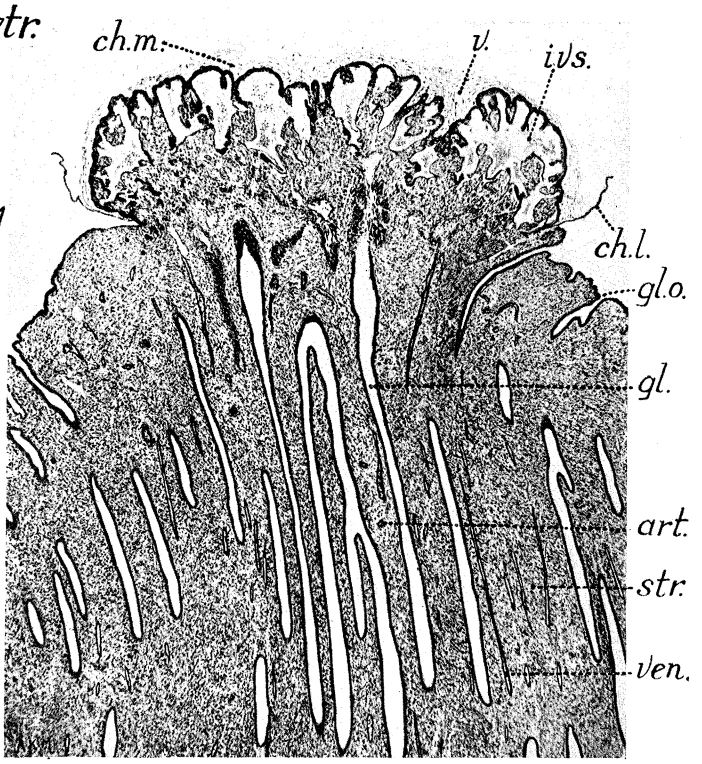

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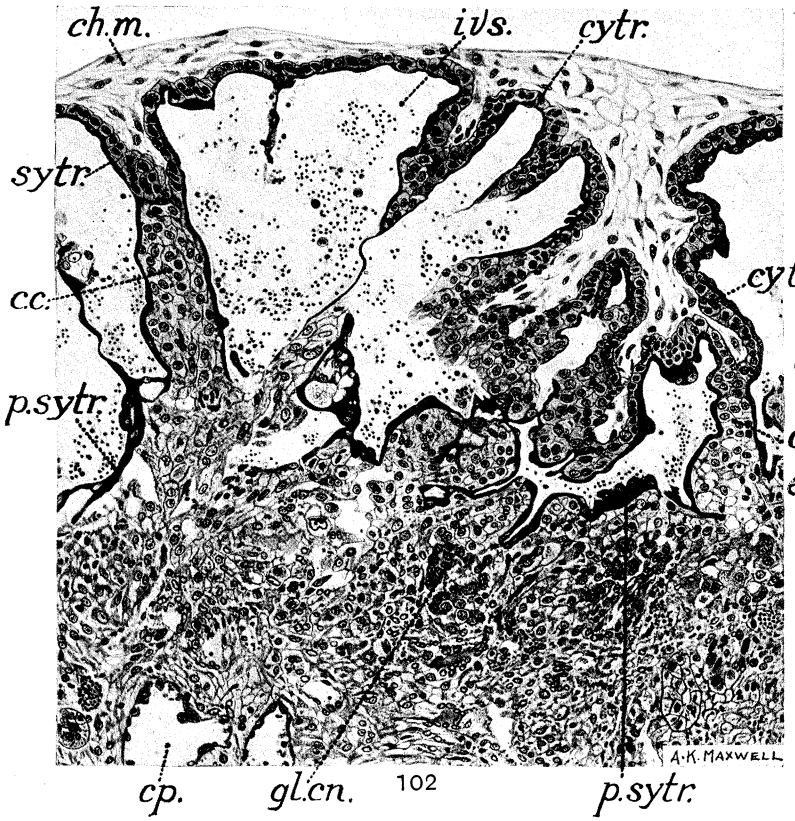

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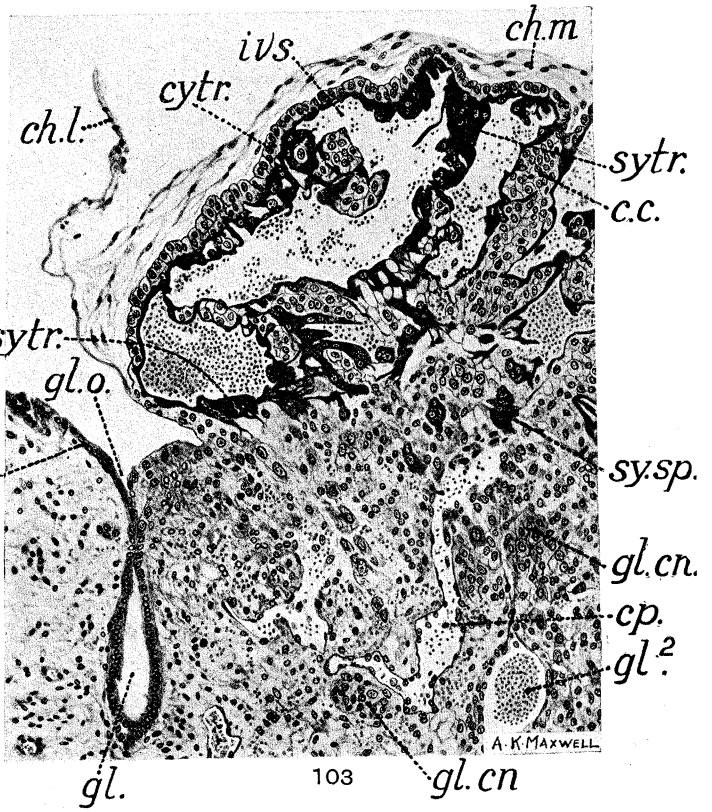

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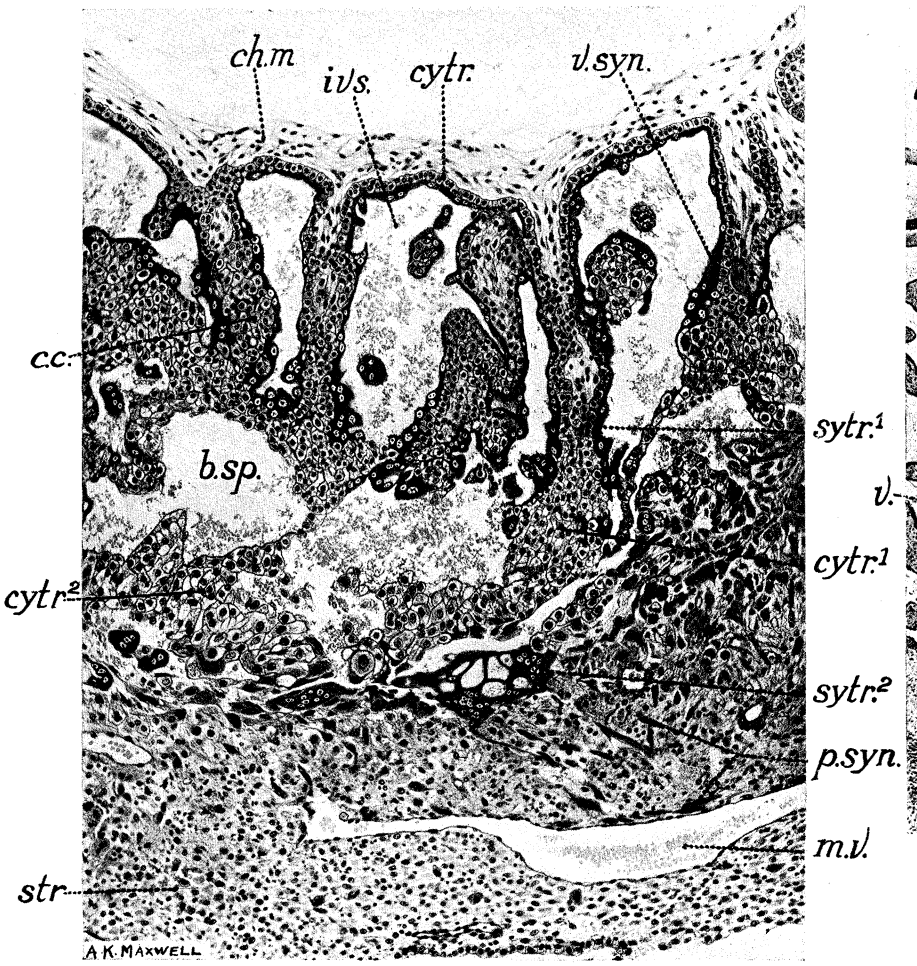

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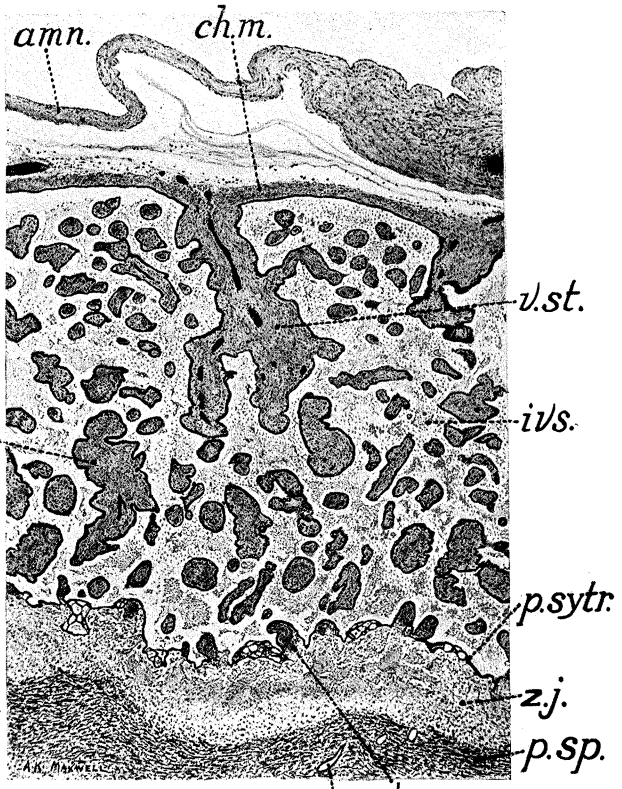

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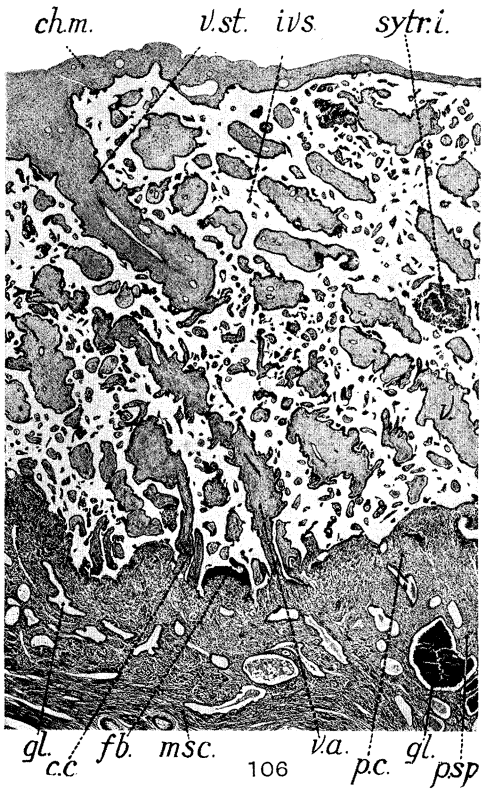

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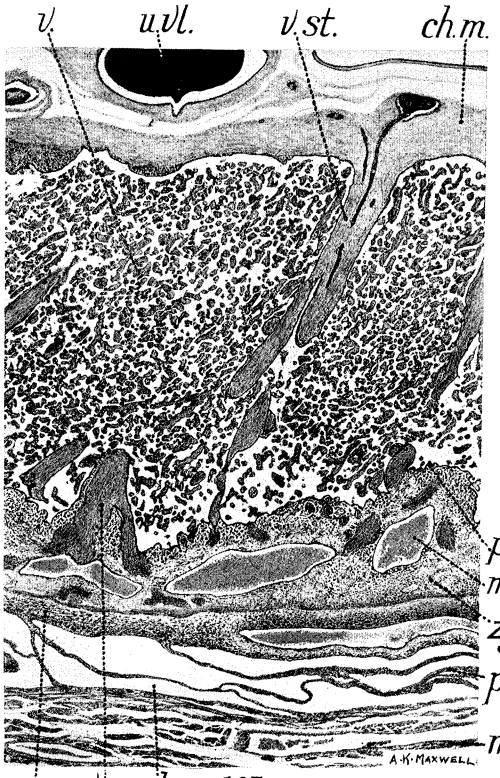

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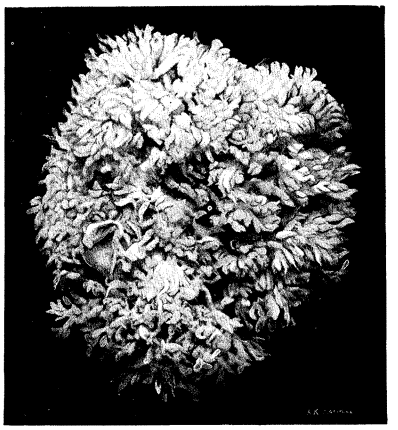

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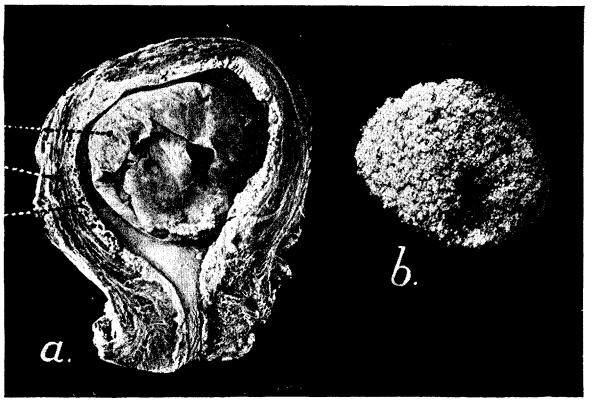

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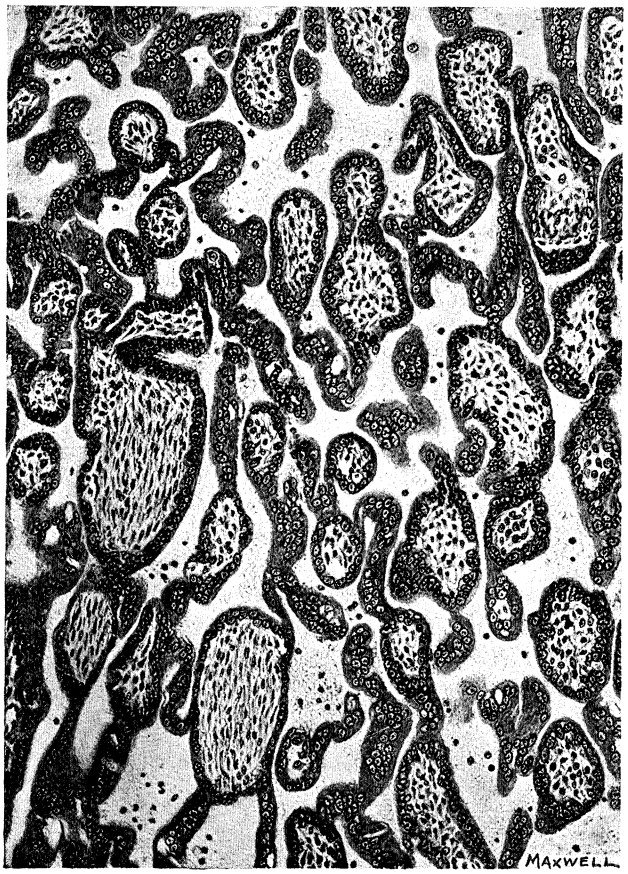

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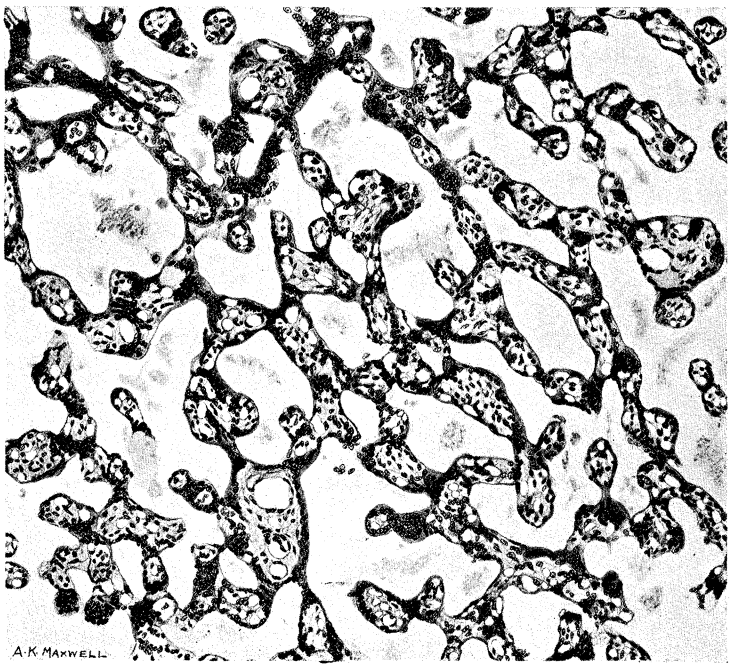

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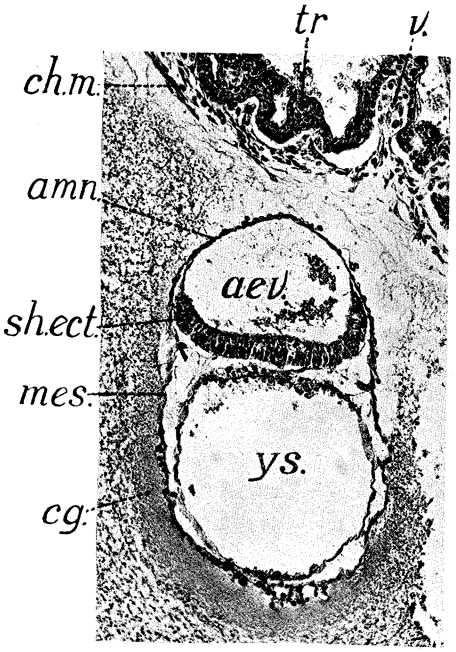

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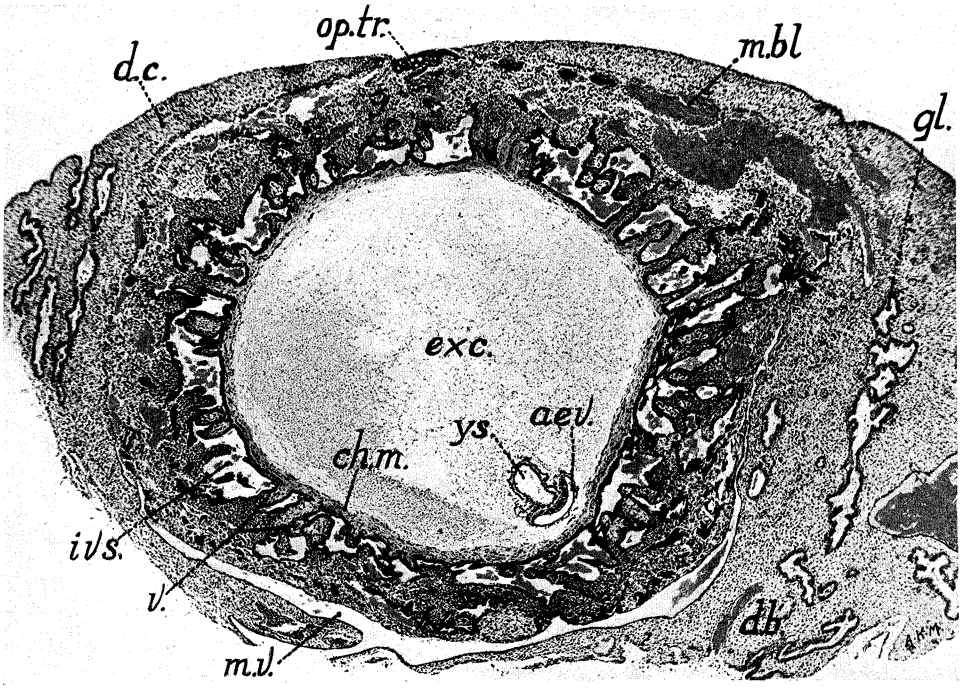

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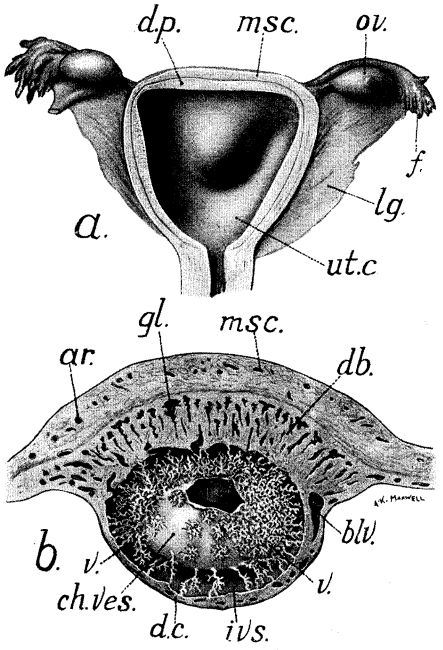

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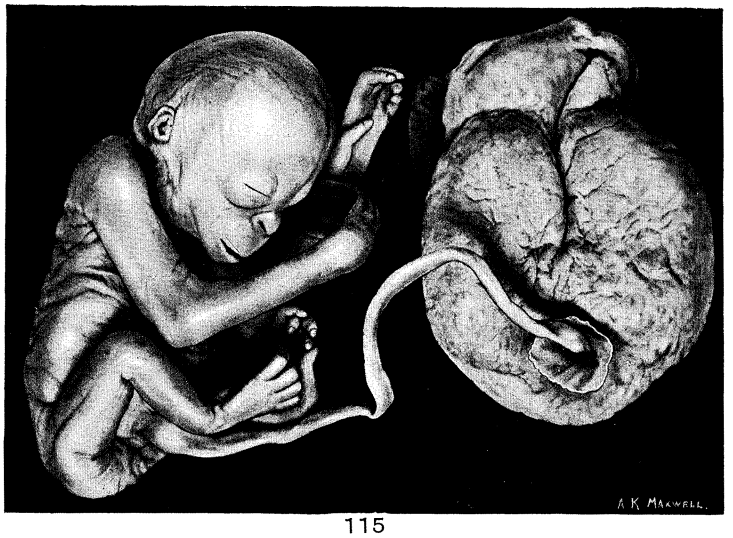

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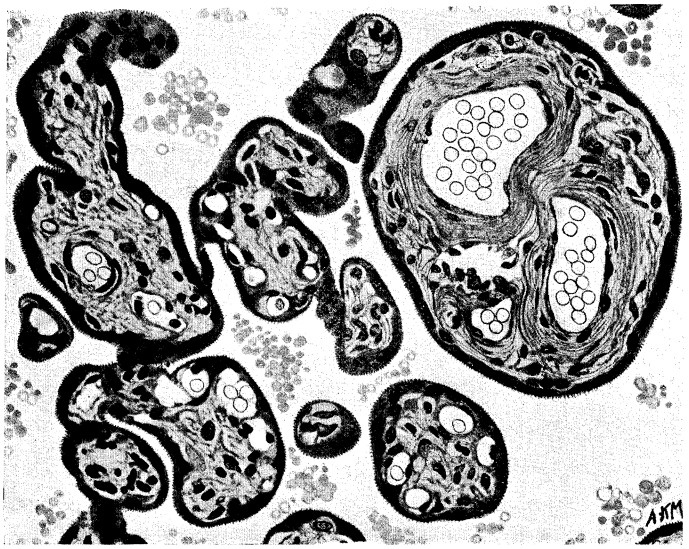

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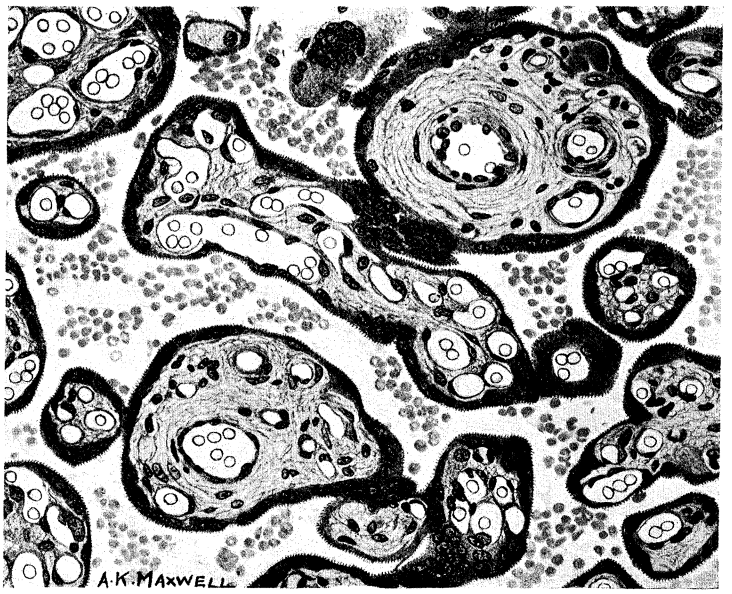

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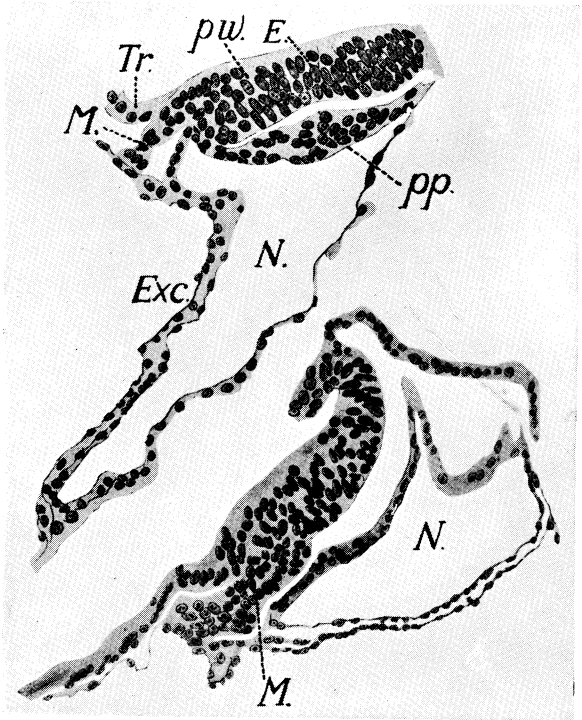

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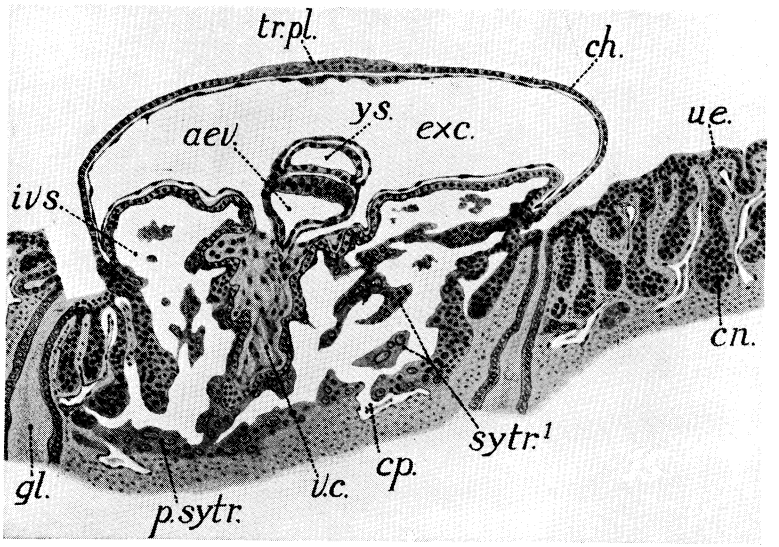

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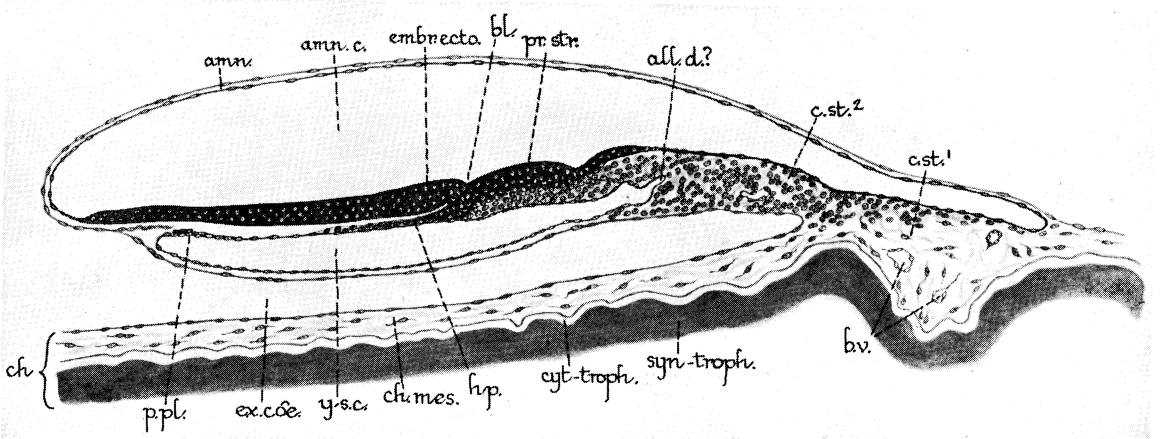

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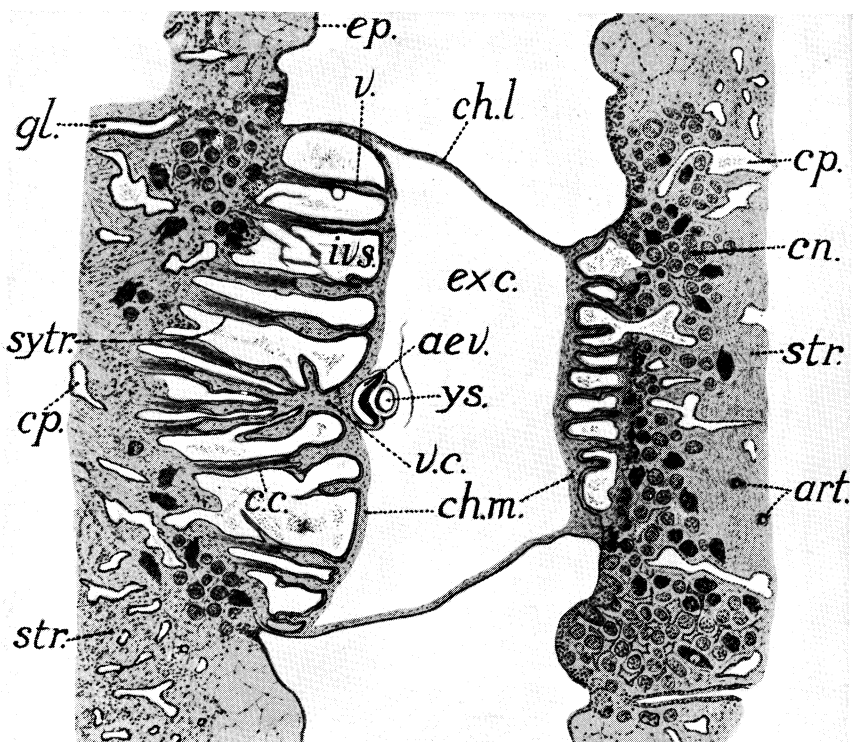

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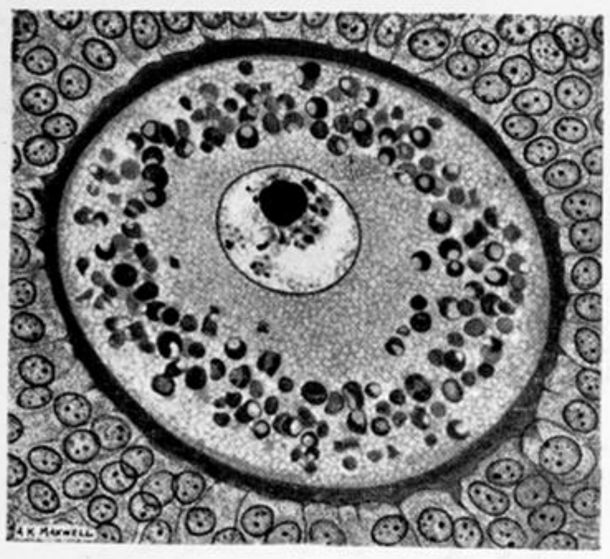

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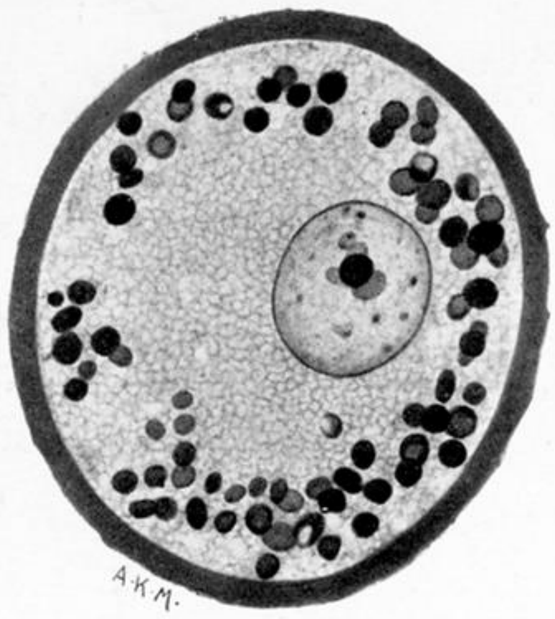

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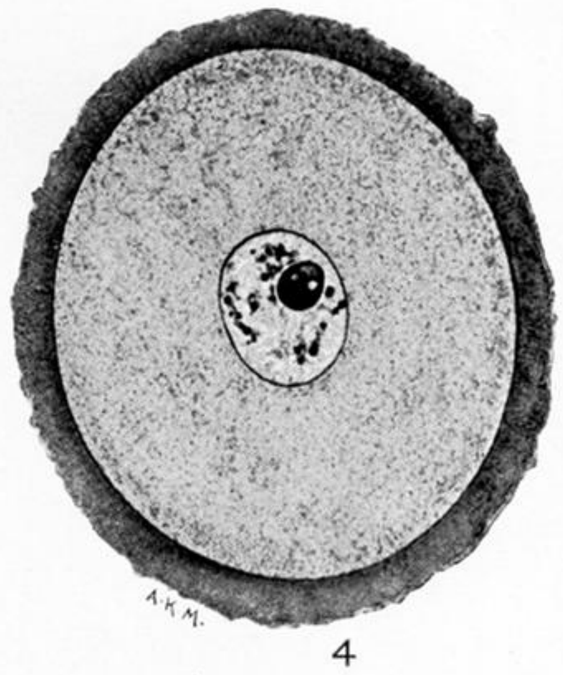

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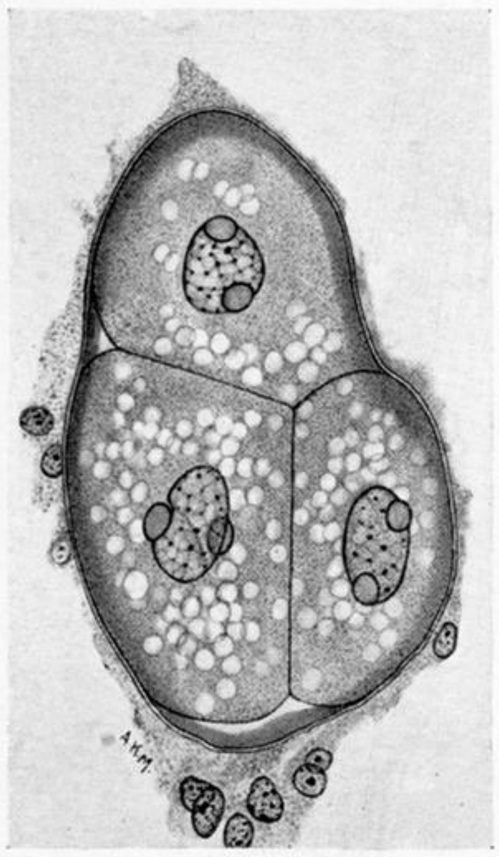

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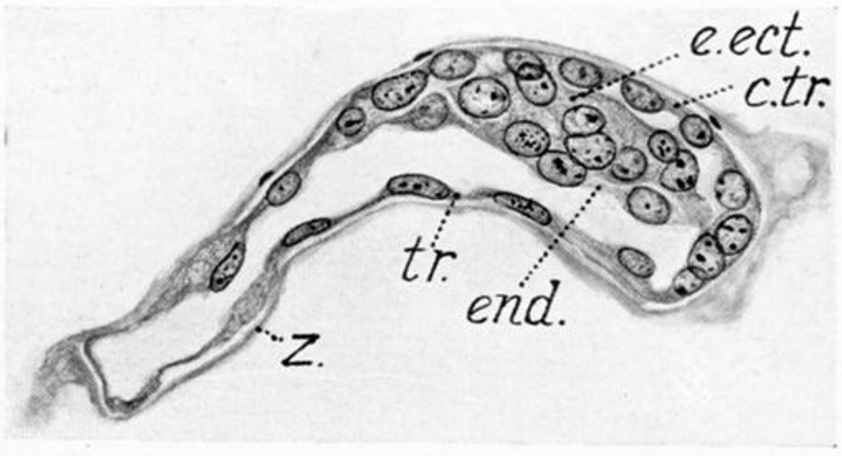

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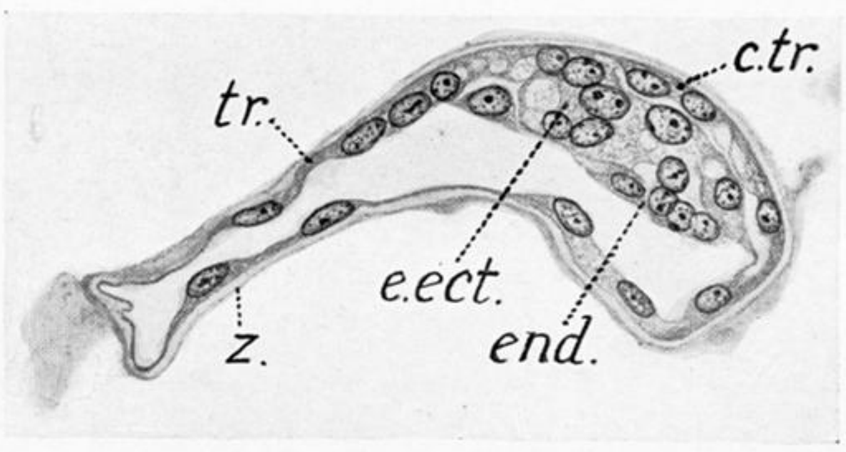

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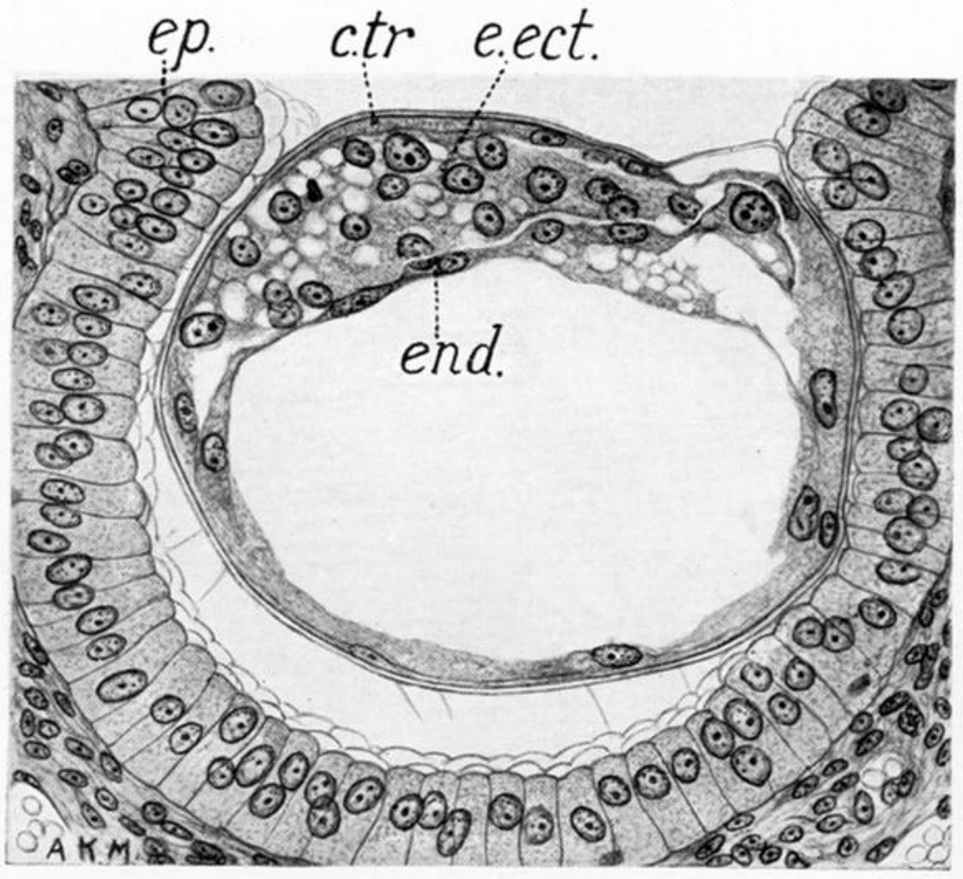

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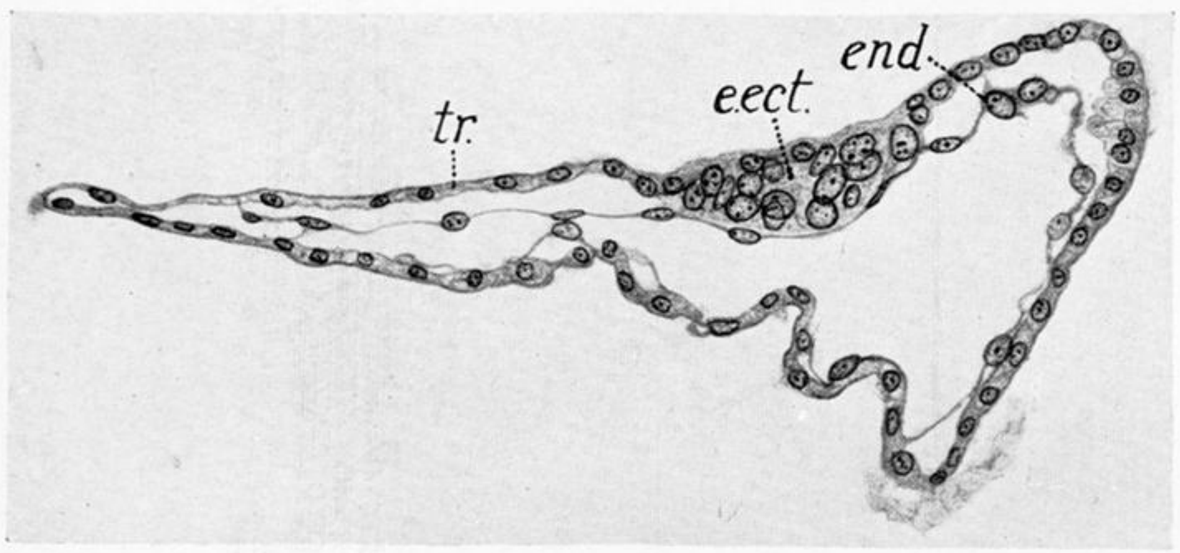

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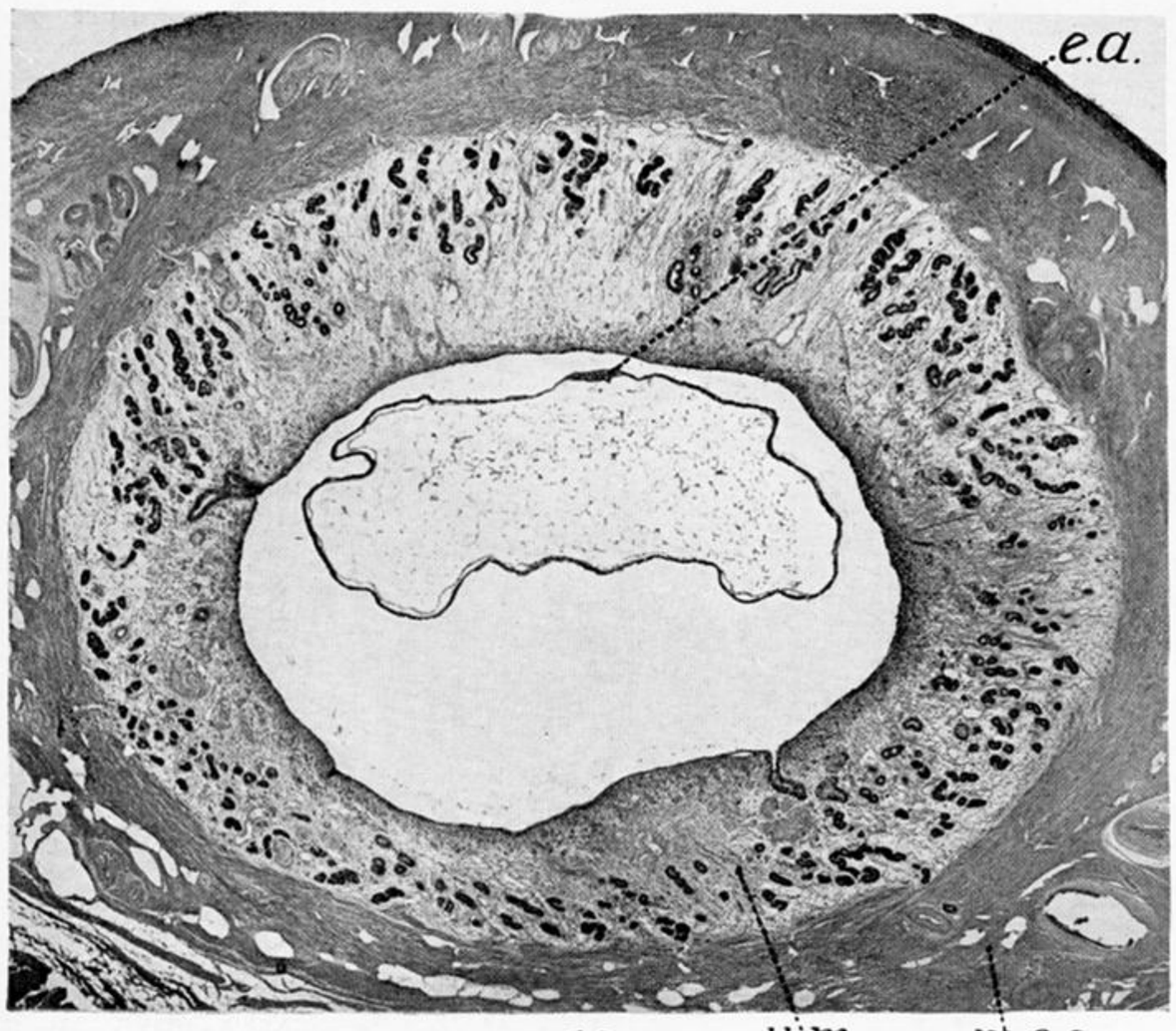

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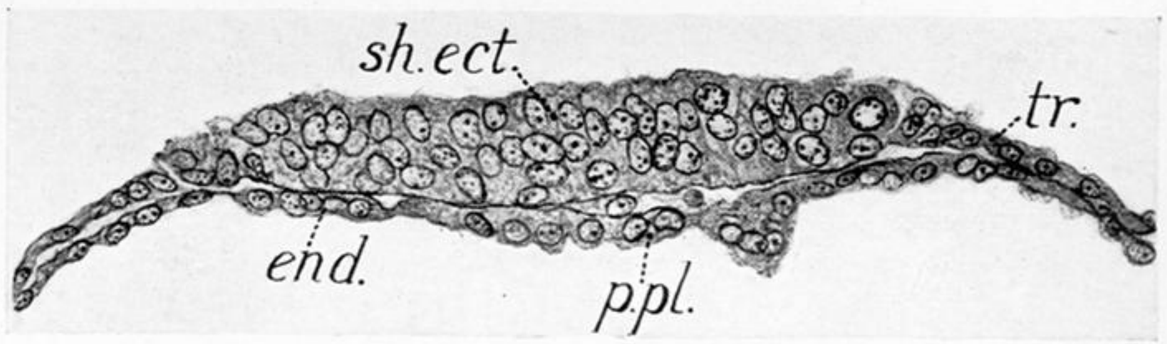

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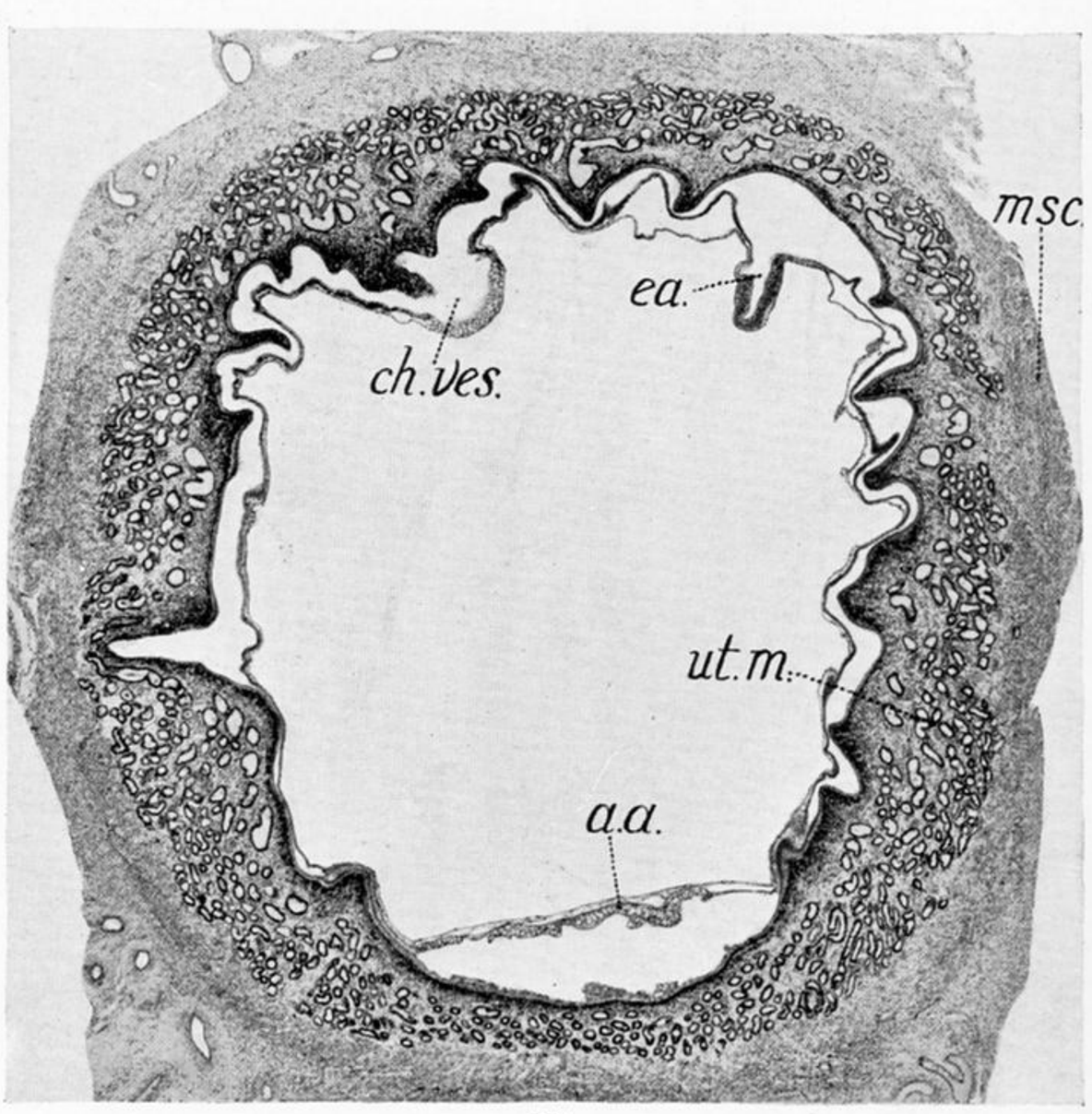


12

PLATE 1.

FIGS. 1–4.—Ovarian Oocytes of Loris (from a preparation by Professor C. R. NARAYAN RAO), Tarsius, *Hapale jacchus* and *Macacus rhesus*. Fig. 1, × 366. Fig. 2, × 567. Fig. 3, × 456. Fig. 4, × 470.

FIG. 5.—Loris 4. Section of 4-celled egg (Egg A). × 484.

FIGS. 6 & 7.—Nycticebus 241. H.C. Sections of blastocyst from the Fallopian tube. × 430.

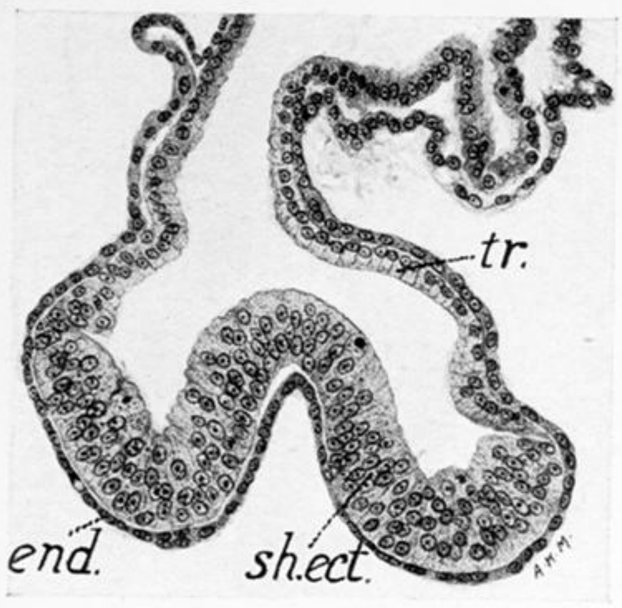
FIG. 8.—Loris 45. Section of blastocyst here seen occupying a bay in the endometrium. × 337.

FIG. 9.—Nycticebus 264. H.C. Section of blastocyst. × 237.

FIG. 10.—Nycticebus 190. H.C. Section of uterus with blastocyst *in situ*. *e.a.* embryonal area. × 19.

FIG. 11.—Nycticebus 190. H.C. Section passing through embryonal area. *p.pl.* prochordal plate. × 280.

FIG. 12.—Loris 5. Section of uterus with blastocyst (A) *in situ*. The folded embryonal area (*e.a.*) is seen on the right upper side of the figure and, on the left, a developing chorionic vesicle (*ch.ves.*). Below is an absorptive area (*a.a.*), with thickened and folded trophoblast. × 18.



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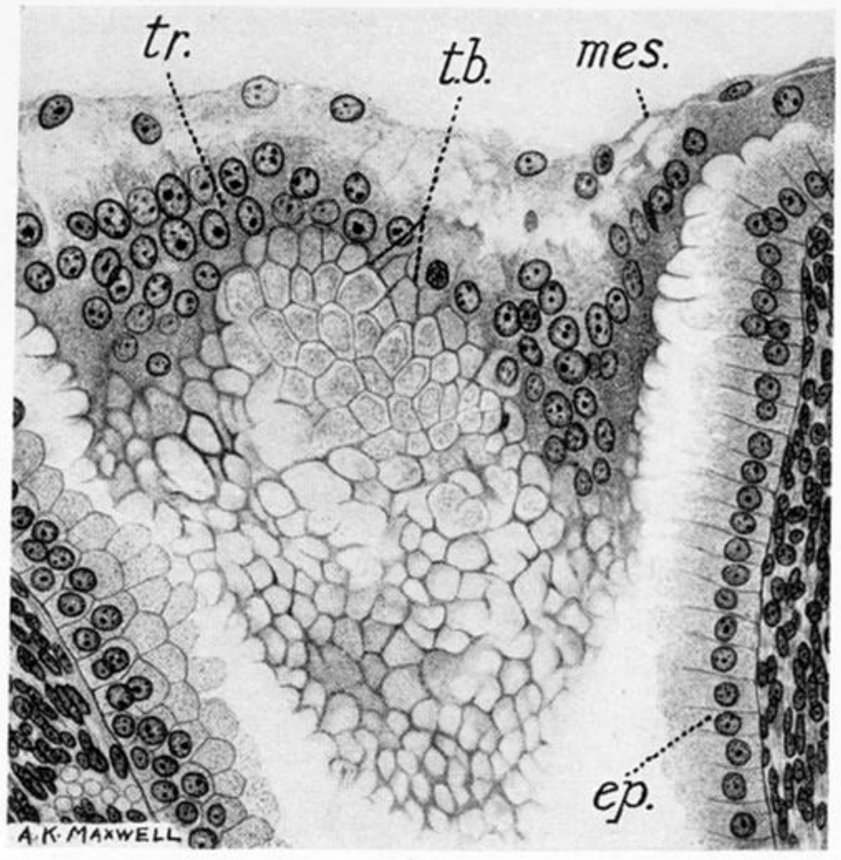

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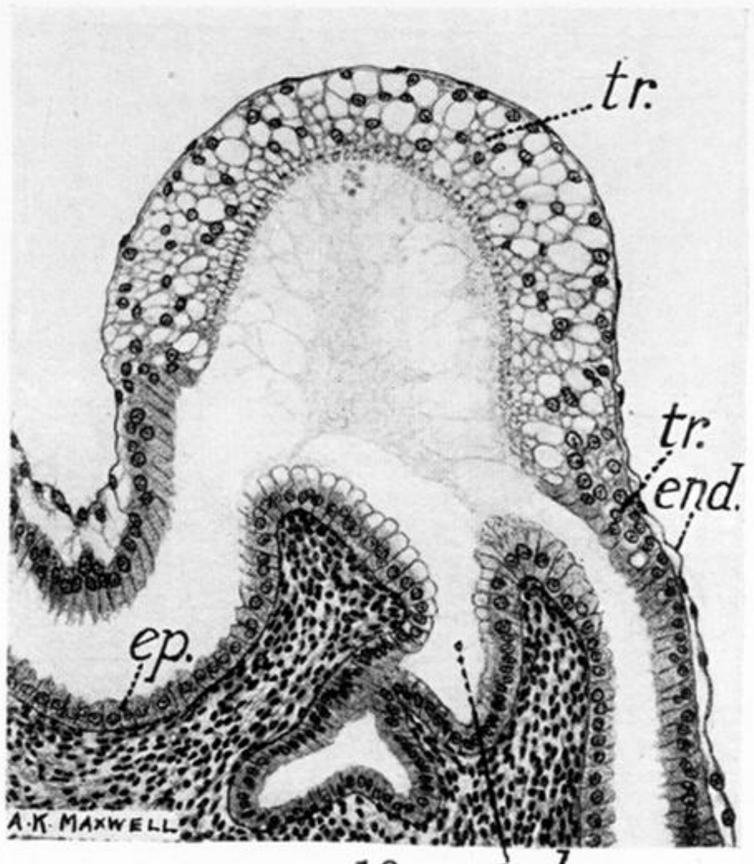

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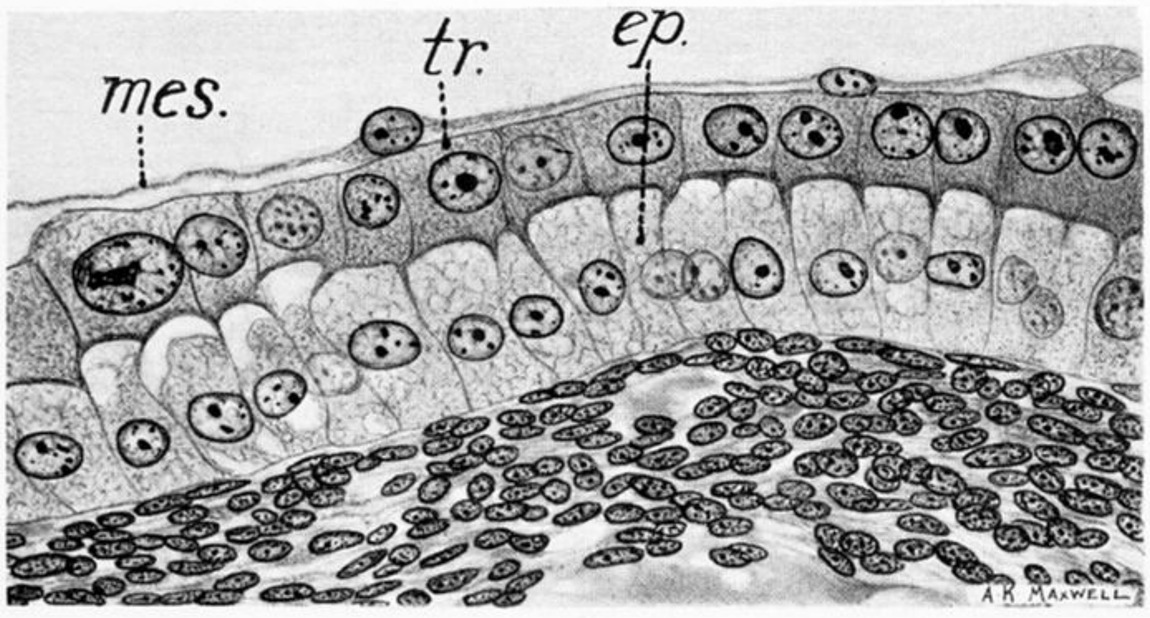

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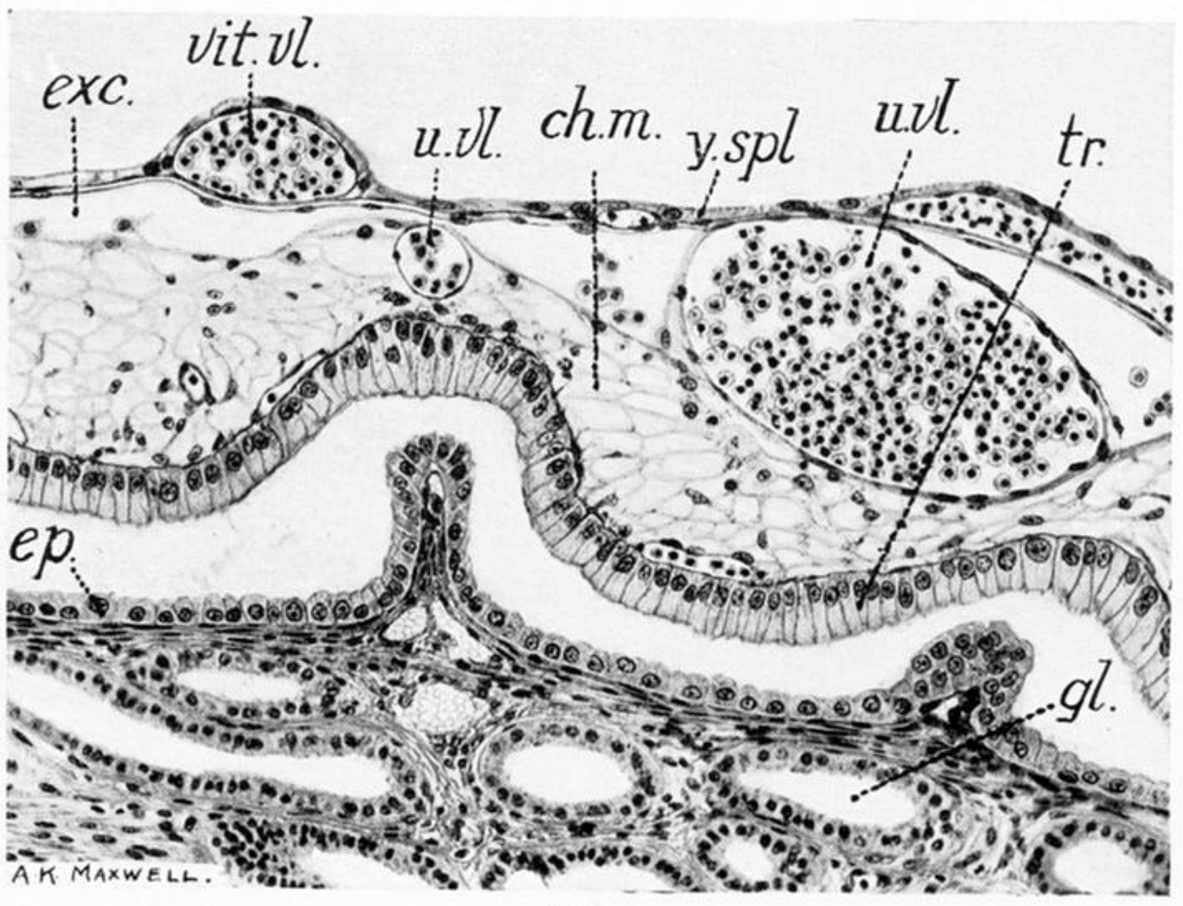

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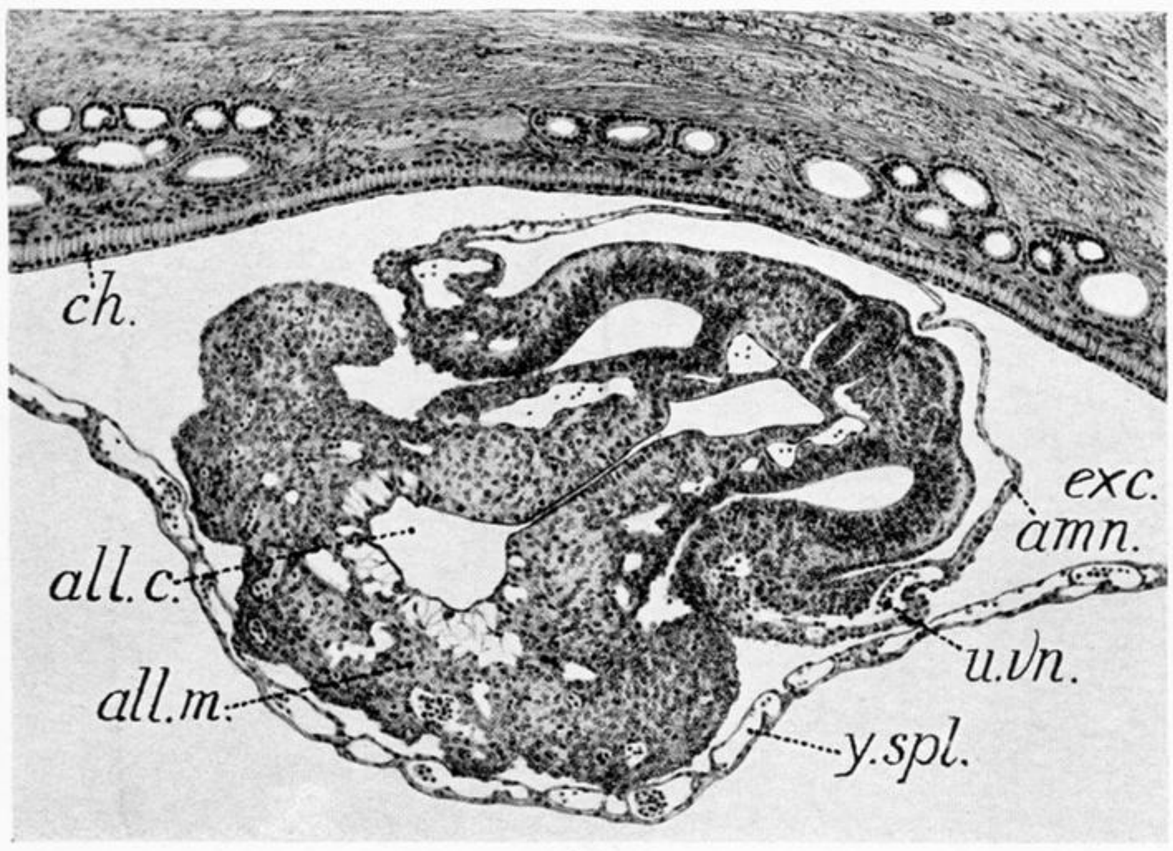

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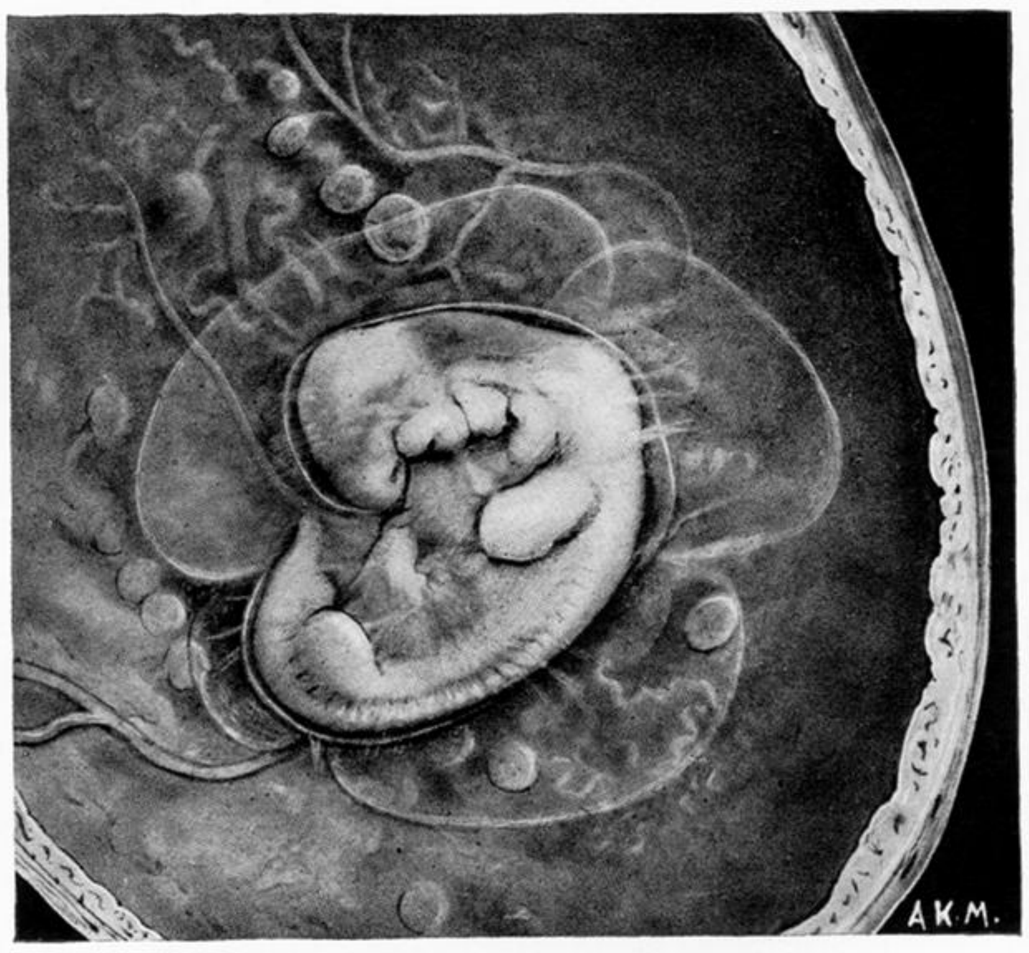

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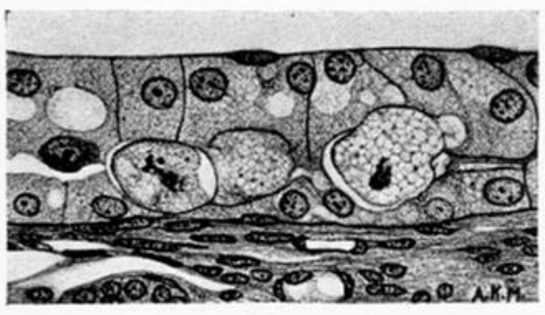

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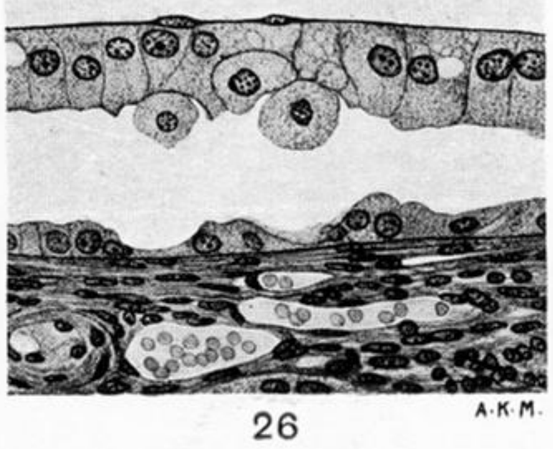

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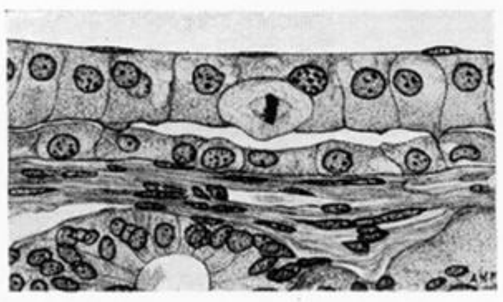

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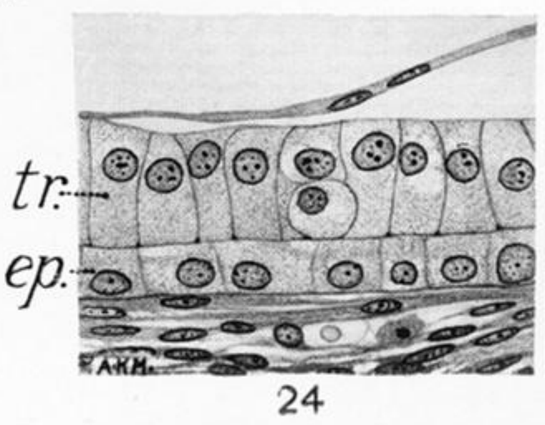

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PLATE 2.

FIG. 13.—Loris 5. Section through embryonal area of blastocyst. × 115.

FIG. 14.—Loris 5. Section through the bilaminar omphalopleure and the uterine wall, showing the mode of attachment of the trophoblast (*tr.*) to the uterine epithelium (*ep.*). See text, p. 52. × 515.

FIG. 15.—Loris 5. Tangential section through the trophoblast of the bilaminar omphalopleure to show the presence of terminal bars (*t.b.*) separating the outer ends of its cells. × 267.

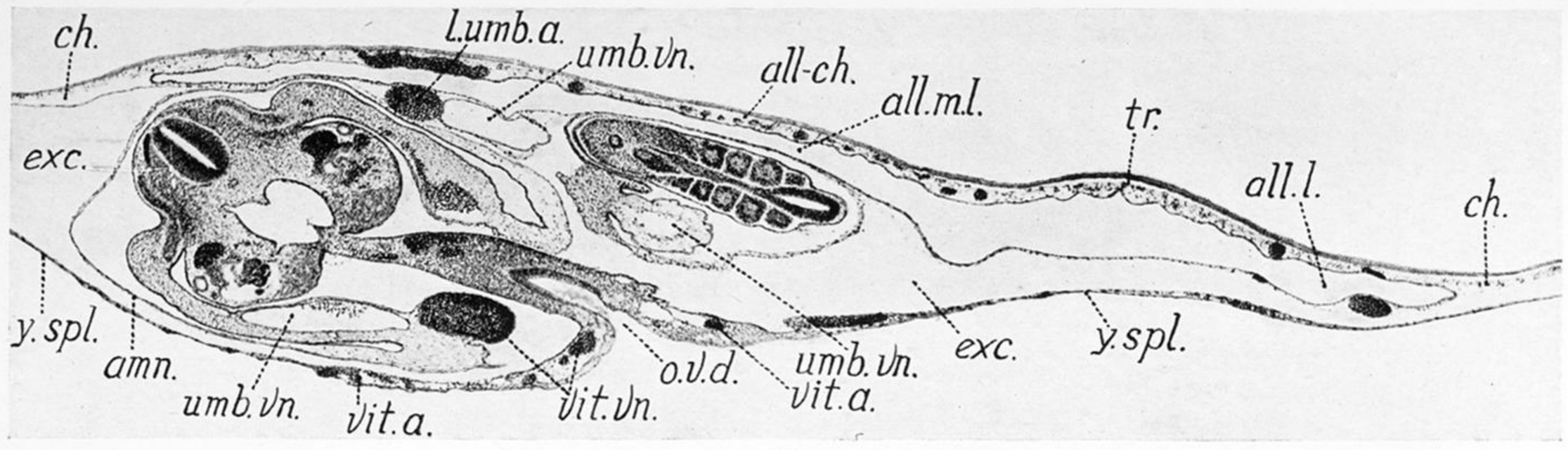
FIG. 16.—Loris 5. Section through a developing chorionic vesicle. Note its position opposite the common opening (*o.gl.*) of a group of uterine glands, the presence of secretion in its concavity and the vacuolated trophoblast cells (*tr.*) which line it. × 120.

FIG. 17.—Loris 8. Section passing through the yolk-sac wall (*y.spl.*) with its vitelline vessels (*vit.vl.*), the extra-embryonal cœlom (*exc.*), the chorion, in the mesenchyme (*ch.m.*) of which are situated the umbilical vessels (*u.vl.*), and the superficial portion of the endometrium. The trophoblast (*tr.*) of the chorion and the uterine epithelium (*ep.*) are here artificially separated. × 138.

FIG. 18.—Loris 9A. Trans. section of embryo showing the freely projecting, thick walled allantois, *all.c.* allantoic cavity, *all.m.* allantoic mesoderm. × 63.

FIG. 19.—Loris 8. Embryo *in situ* in the opened uterine horn. Note the outline of the four subequal accessory allantoic lobes, and the rounded chorionic vesicles, showing through the fœtal membranes (*cf.* text-fig. 3, p. 58). × 6·4.

FIGS. 24, 25, 26 & 27.—Loris 33. Sections through the bilaminar omphalopleure and the adjoining portion of the endometrium, showing the occurrence of cells at the free surface of the trophoblast, destined to degenerate (figs. 26 & 27) and their probable mode of origin (figs. 24 & 25). Fig. 24, × 365. Fig. 25, × 310. Fig. 26, × 310. Fig. 27, × 350.



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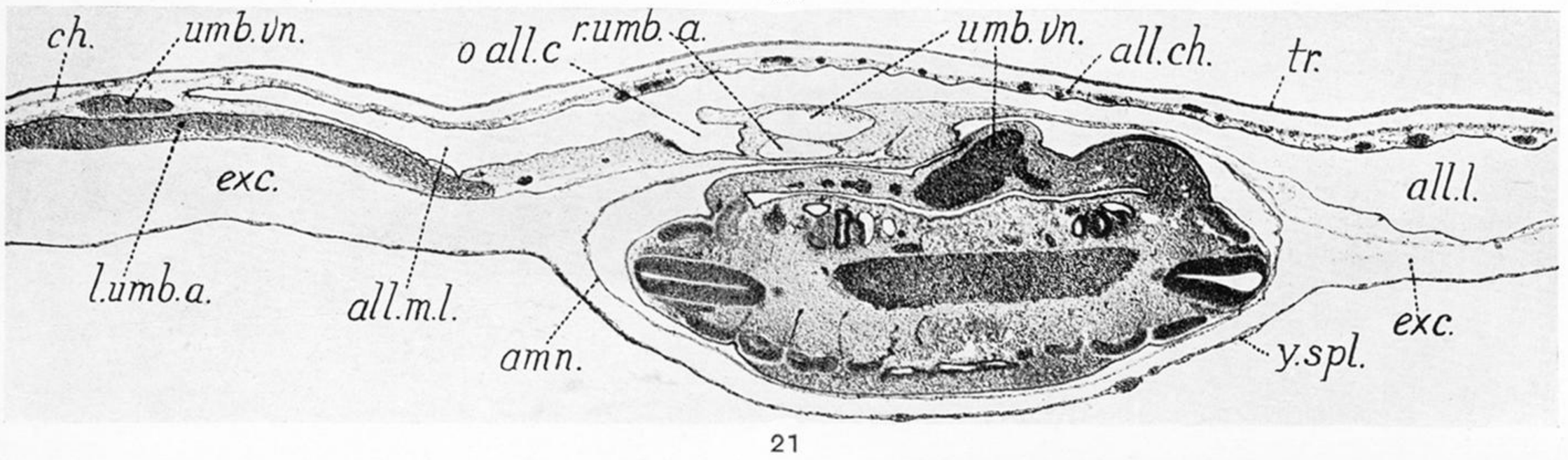

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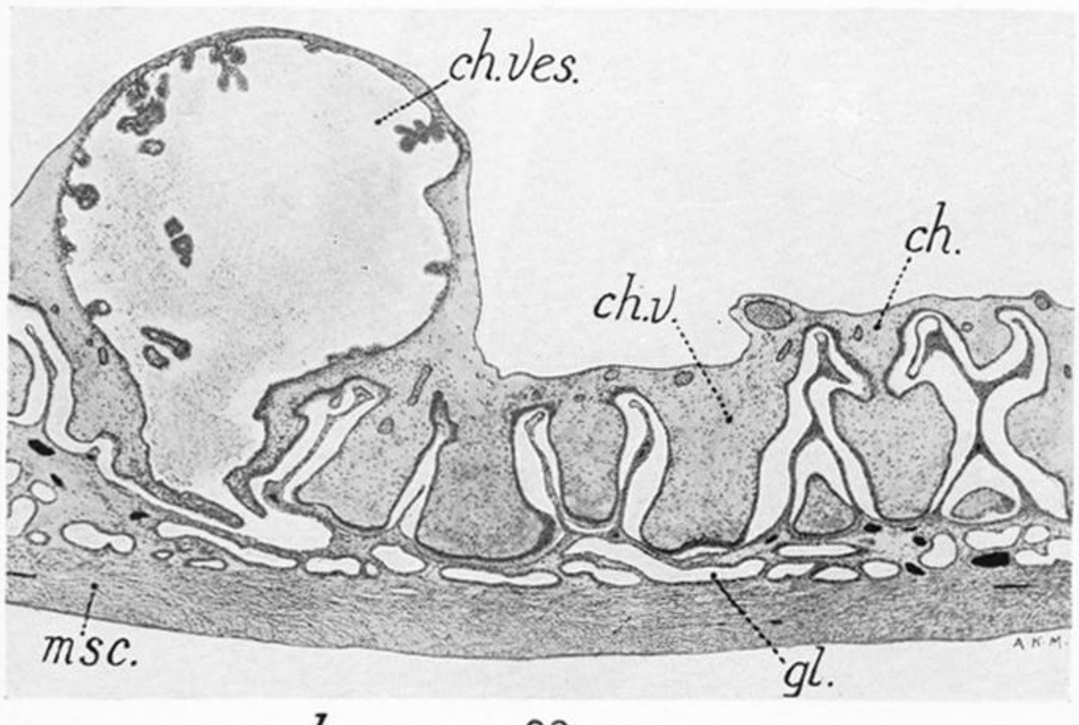

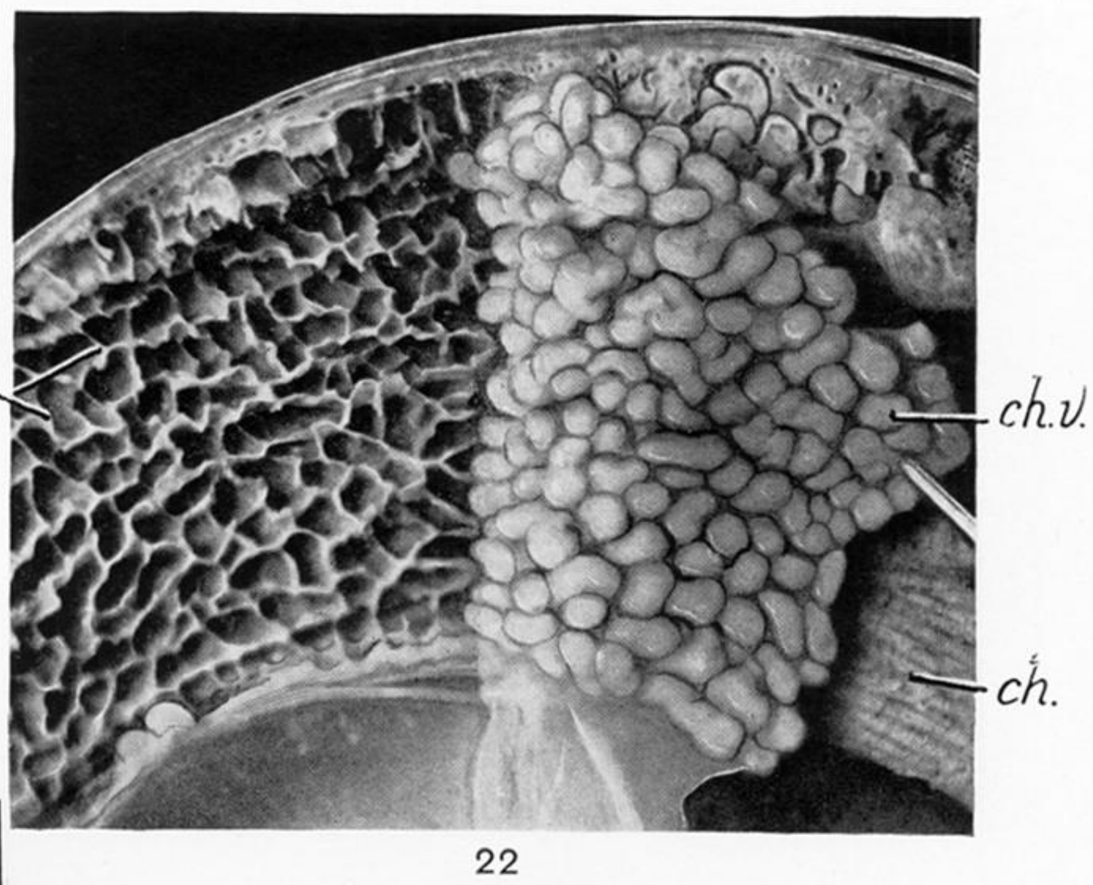

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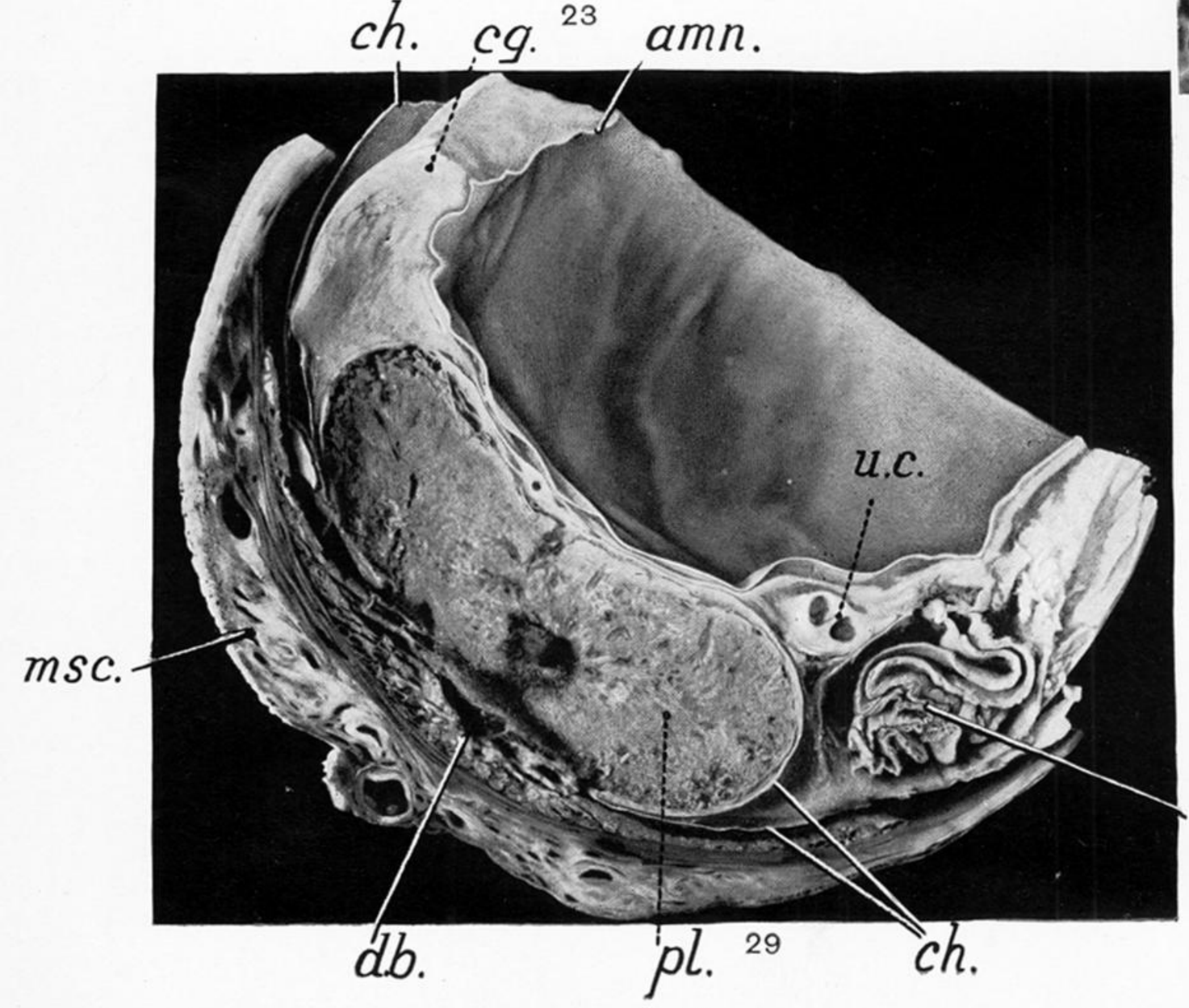

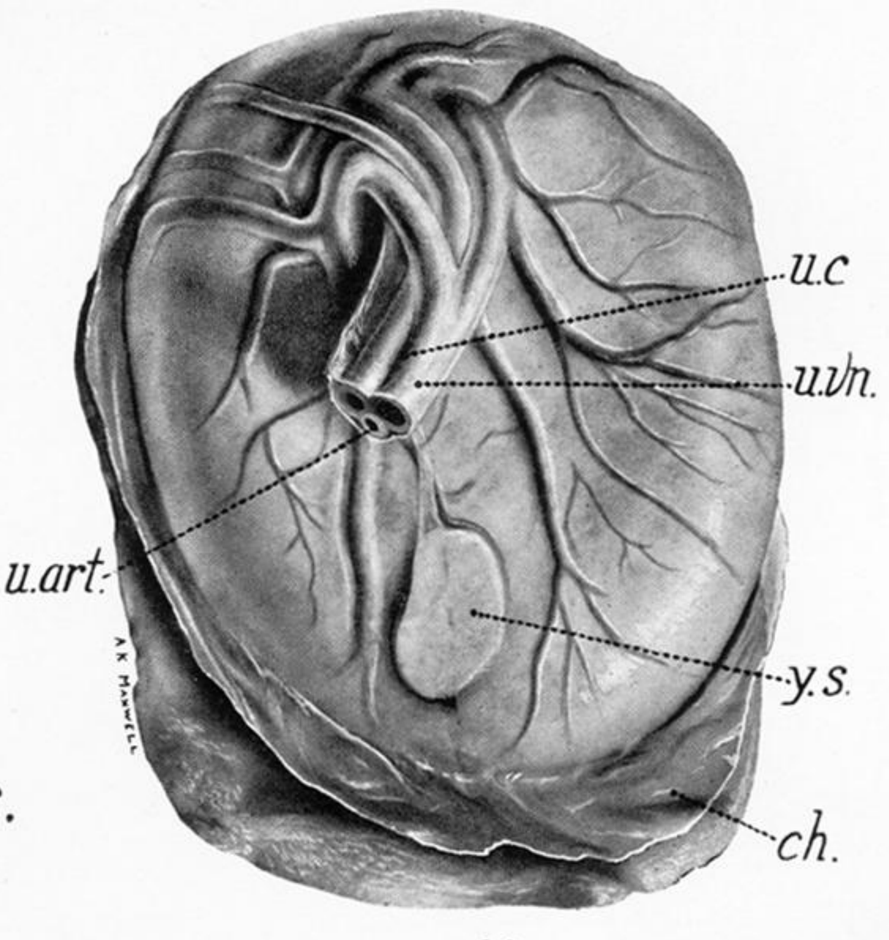

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PLATE 3.

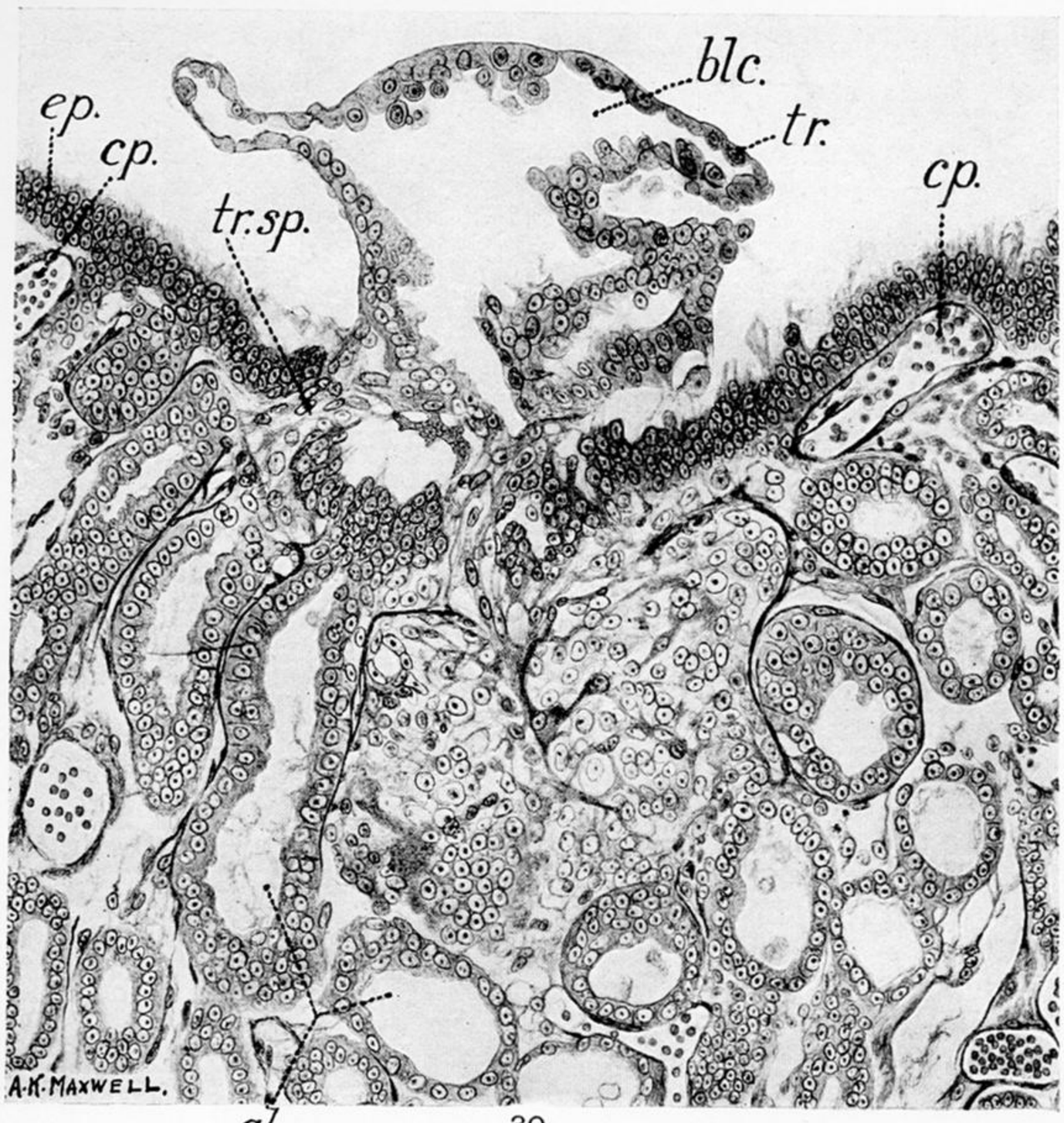
FIGS. 20 & 21.—Nyticebus 302. H.C. Trans. sections through the embryo and its fœtal membranes, fig. 20 being at the level of the opening of the yolk-stalk (*o.v.d.*) into the yolk-sac and fig. 20 at the level of the opening of the allantoic canal (*o.all.c.*) into the primary sac or main lobe of the allantois (*all.m.l.*). Note the chorion (*ch.*), the allanto-chorion (*all.ch.*), the allantois (*all.m.l.* main lobe, *all.l.* accessory lobe), amnion (*amn.*), the yolk-sac splanchnopleure (*y.spl.*) and the exocœlom (*exc.*), and in fig. 21, the direct passage of umbilical vessels (*umb.vn.* umbilical vein, *l.umb.a.* left umbilical artery) from the inner or cœlomic wall of the allantois into and from the chorion (*ch.*). *tr.* trophoblast (in fig. 21, artificially separated from the underlying allantochorionic mesenchyme). *l.umb.a.*, *r.umb.a.*, left and right umbilical arteries, *umb.vn.* umbilical vein. *vit.a.* vitelline artery. *vit.n.* vitelline vein. × 31.

FIG. 22.—Loris 19. Total view of portion of the placenta from the region of the cornual septum. The chorion has been turned back towards the right in the figure, exposing its villi (*ch.v.*) and the honeycomb-like system of crypts (*cr.*) in the endometrium, into which they fit. × 7·3.

FIG. 23.—Loris 19. Section of the placenta, showing the chorion (*ch.*) with its villi (*v.*) and a single chorionic vesicle (*ch.ves.*), with a narrow spout-like opening and its lining produced into sparse, slightly branched processes and also the thin uterine wall, the glands (*gl.*) of the endometrium and the muscularis (*msc.*). Note between the villi the extremely thin walls of the uterine crypts. × about 24.

FIG. 28.—Tarsius 405. H.C. Total view of the placenta seen from the fœtal surface. Placenta 15 × 12 mm. in diameter × 7·5 mm. in thickness. Fœtus D.C.L. 8·7 cm. H.L. 2·8 cm. Note the umbilical cord (*u.c.*) cut across, the umbilical vessels on the placental surface, the yolk-sac (3·5 × 2 mm. in diameter) with its stalk, and the reflection of the chorion (*ch.*) from the lower border of the placenta. *u.art.* umbilical artery. *u.vn.* umbilical vein. × 4.

FIG. 29.—Tarsius 72. H.C. Total view of a section through the placenta. Placenta, 10 mm. in diameter × 3 mm. in thickness. Fœtus G.L. 20 mm. Note the constricted base of attachment of the placenta (*pl.*) to the uterine wall (decidua basalis, *d.b.*), the umbilical cord (*u.c.*) seen in section and to the right of it the folded yolk-sac (*ys.*). Between the amnion (*amn.*) and the chorion (*ch.*) is a dense mass of coagulum (*cg.*) occupying the exocœlom. × about 5·5.



gl.

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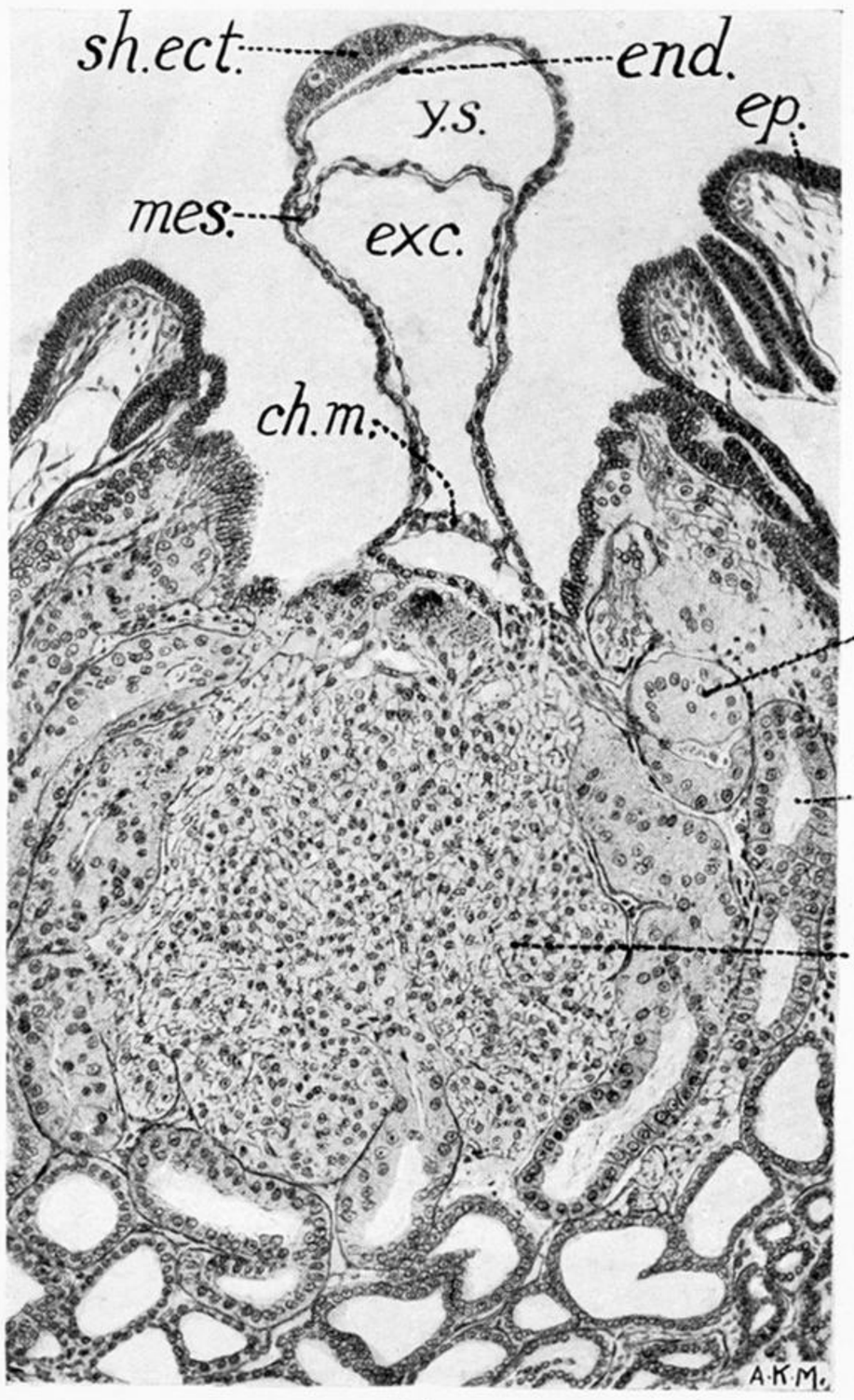

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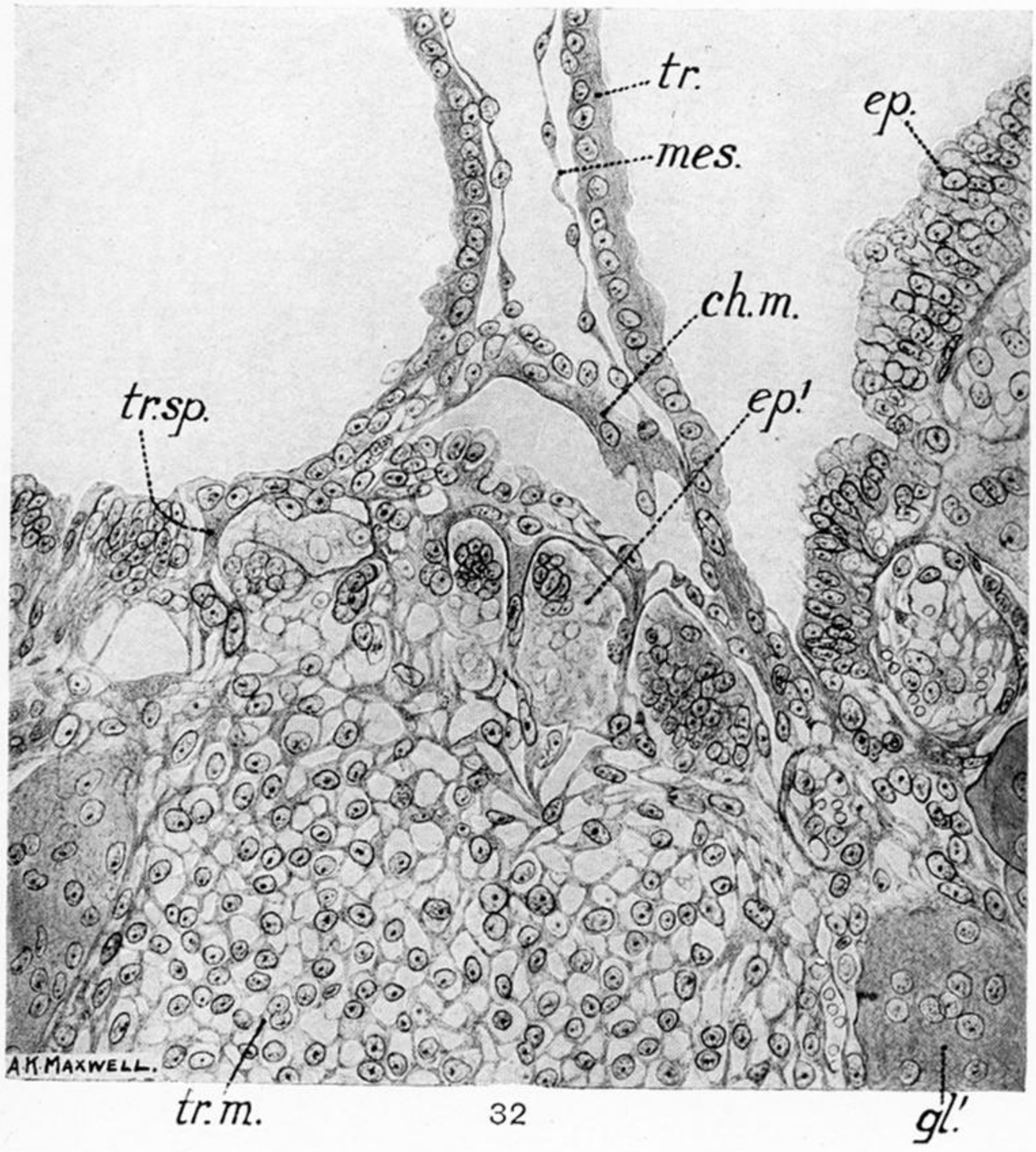
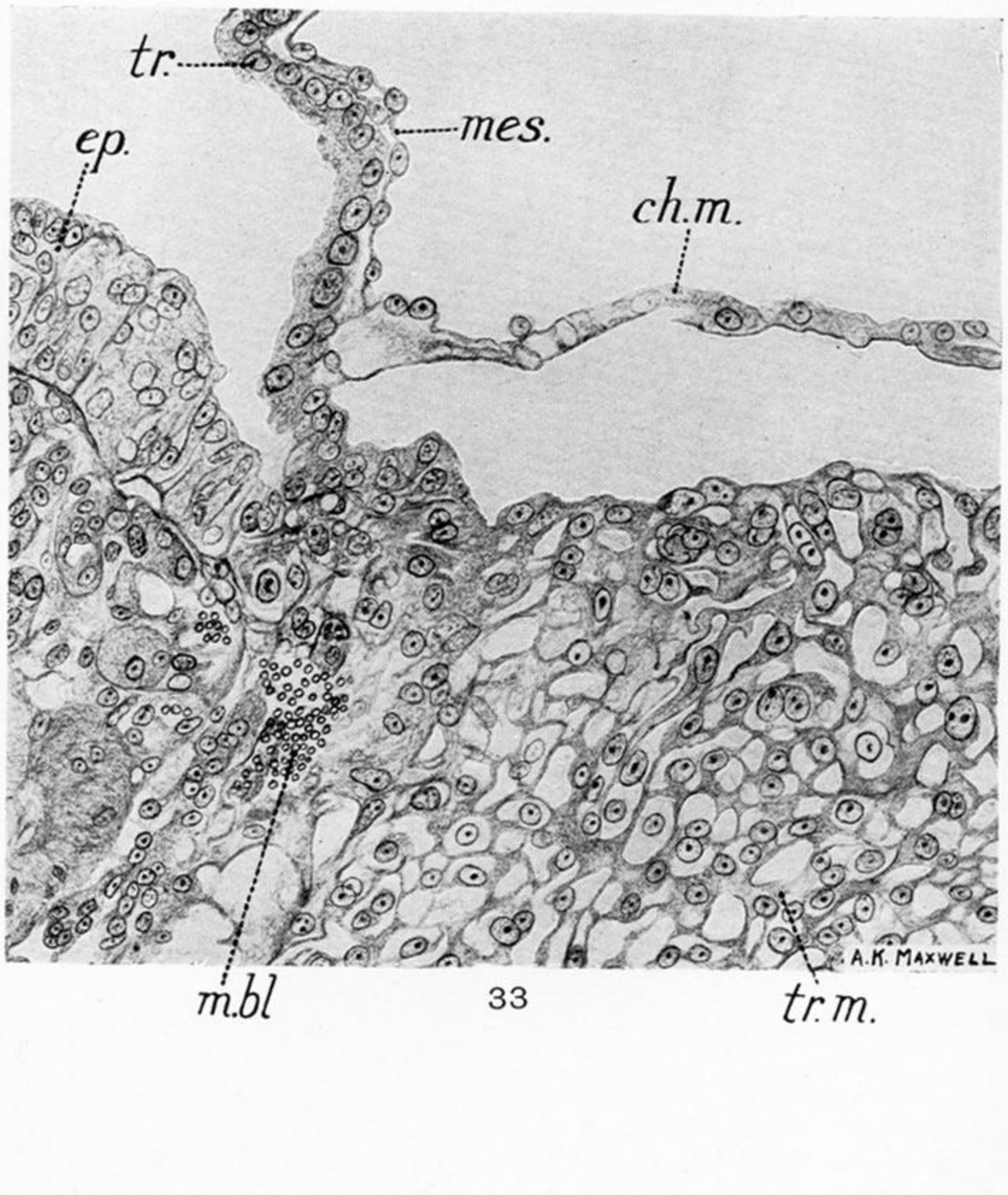


tr.m. 32 gl.'



m.bl 33 tr.m.

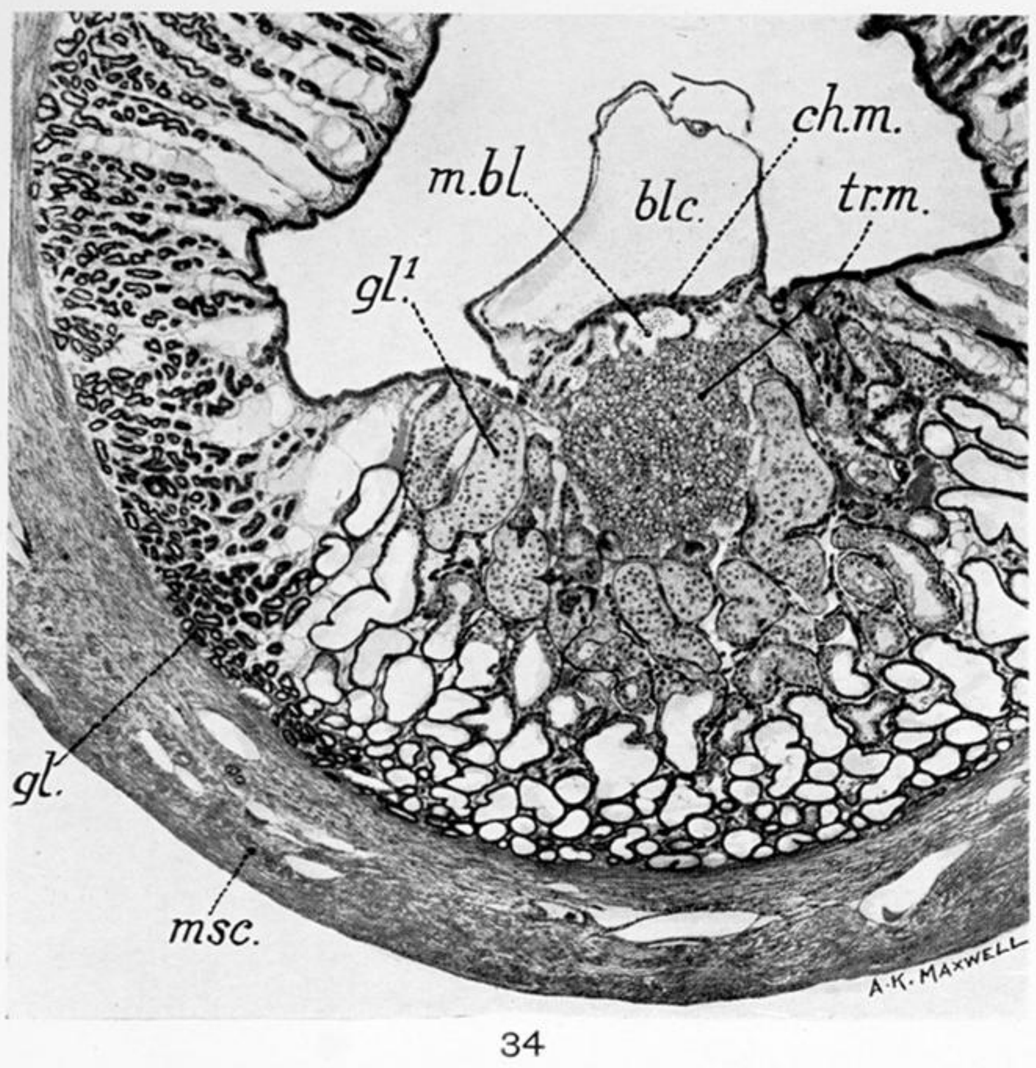
PLATE 4.

FIG. 30.—Tarsius 110*b*. H.C. Blastocyst, shortly after attachment to the endometrium; combination figure from two sections (*cf.* HUBRECHT, '99, Pl. 7, fig. 55). Two trophoblastic sprouts (*tr.sp.*) are seen arising from the trophoblast (*tr.*) of the blastocyst (*blc.*). They penetrate through the uterine epithelium (*ep.*) which is thickened, to terminate in contact with the uterine gland epithelium. The neck portions of the uterine glands (*gl.*) are enlarged and their epithelium thickened, whilst immediately below the blastocyst some of them appear already to be solid and are here separated by thin deeply staining connective tissue strands. × 108.

FIG. 31.—Tarsius 617. H.C. Blastocyst (combined from two sections) and the related portion of the endometrium to which it is attached (*cf.* HUBRECHT, '99, Pl. 7, fig. 56). The blastocyst is attached by its lower pole to the bottom of an endometrial groove. Note the shield-ectoderm (*sh.ect.*) freely exposed, the small yolk-sac (*ys.*) and the large exocœlom (*exc.*). The tropho-placental mass (*tr.m.*) is established and is surrounded by enlarged uterine glands (*gl.*), some of them solid (*gl.*[1]). × 97.

FIG. 32.—Tarsius 617. H.C. Attached pole of blastocyst and upper portion of the tropho-placental mass (*tr.m.*), showing trophoblastic processes (*tr.sp.*) from the lower polar trophoblast penetrating between degenerating masses of uterine epithelium (*ep.*[1]) to become continuous with the tropho-placental mass (*tr.m.*), *ch.m.* thickened chorionic mesoderm. × 245.

FIG. 33.—Tarsius 235. H.C. Section including margin of attached pole of blastocyst and adjoining portion of the tropho-placental mass (*tr.m.*). Note the continuity of the unattached trophoblast of the blastocyst wall (*tr.*) with the latter and the absence over the attached area of any layer of trophoblast distinct from the tropho-placental mass. *mes.* thin mesoderm of the free chorion. *ch.mes.* thickened mesoderm of the attached area, artificially detached from the surface of the tropho-placental mass. *m.bl.* maternal blood extravasation. For the general structure of the blastocyst, *cf.* text-fig. 8, p. 76. Tropho-placental mass 0·6 × 0·44 mm. in diameter. × 290.



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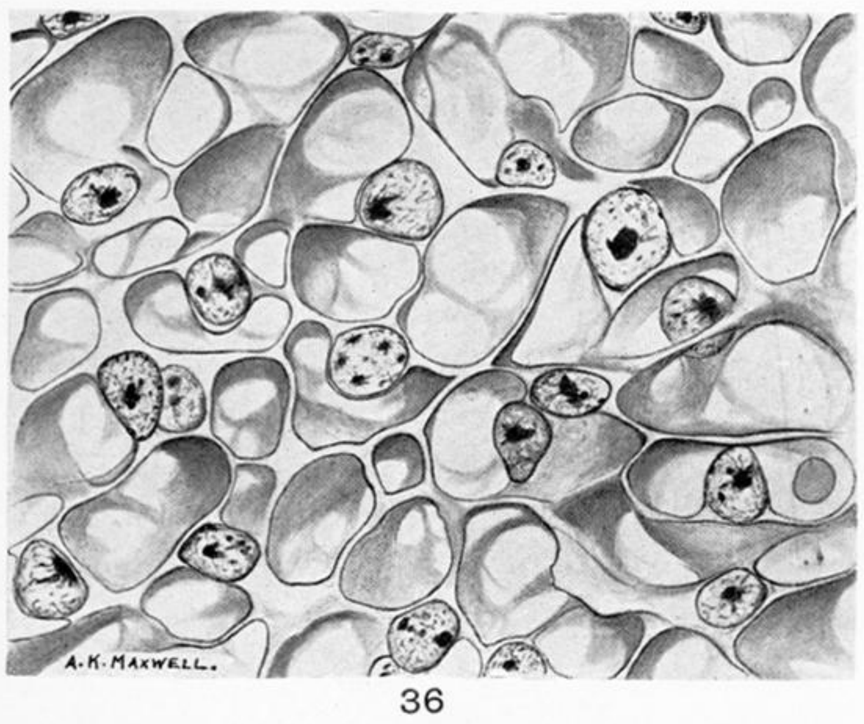

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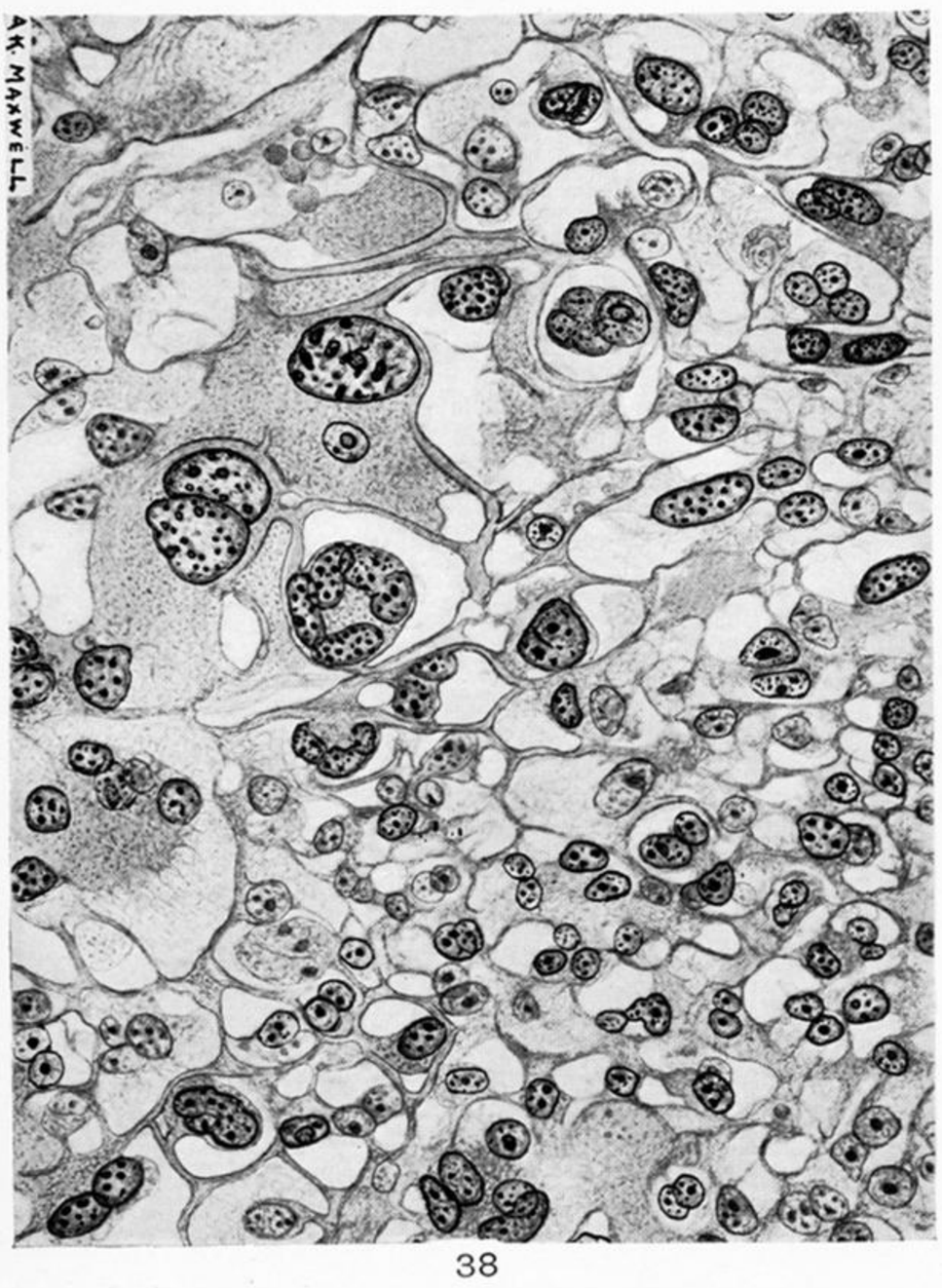

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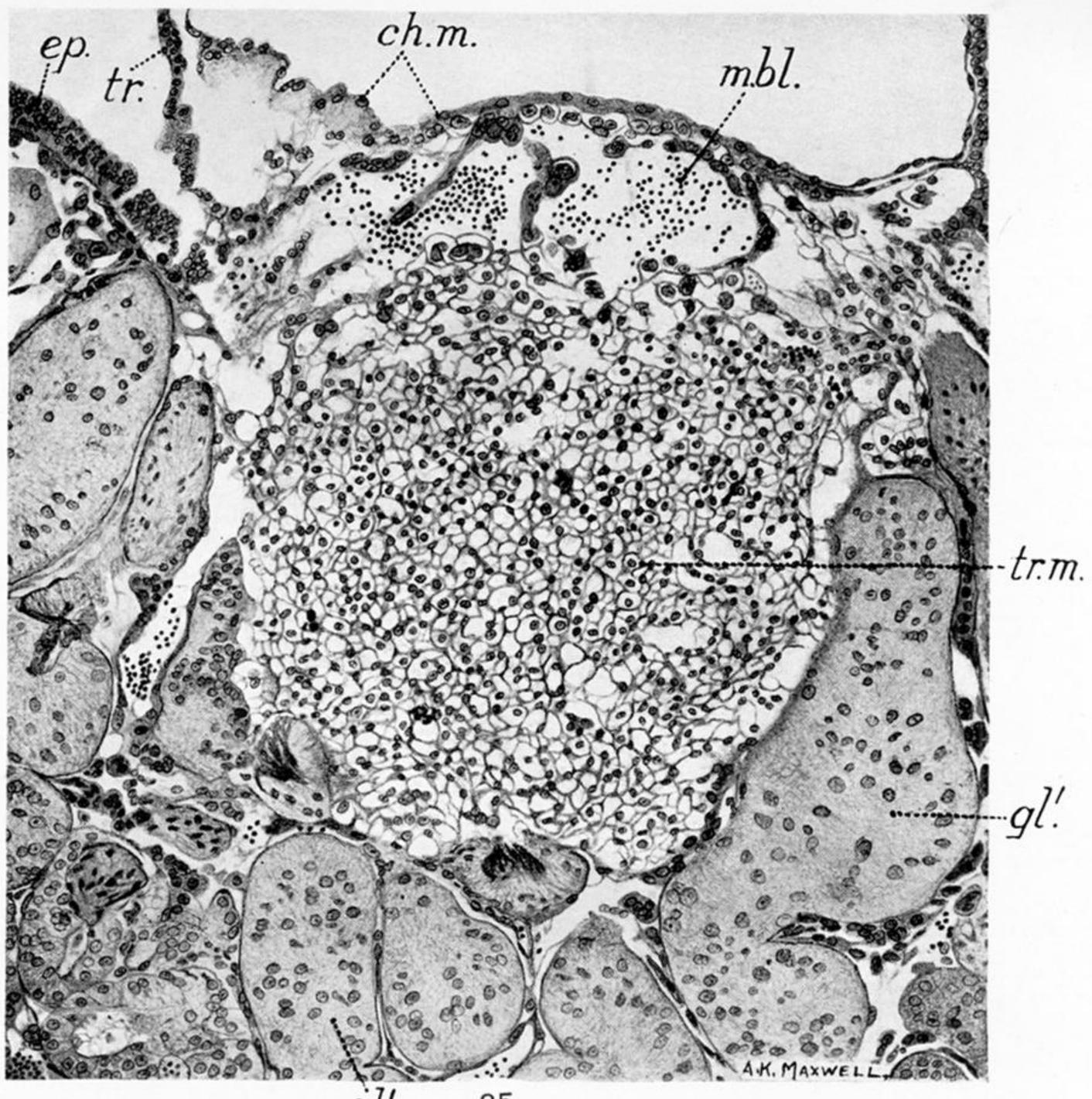

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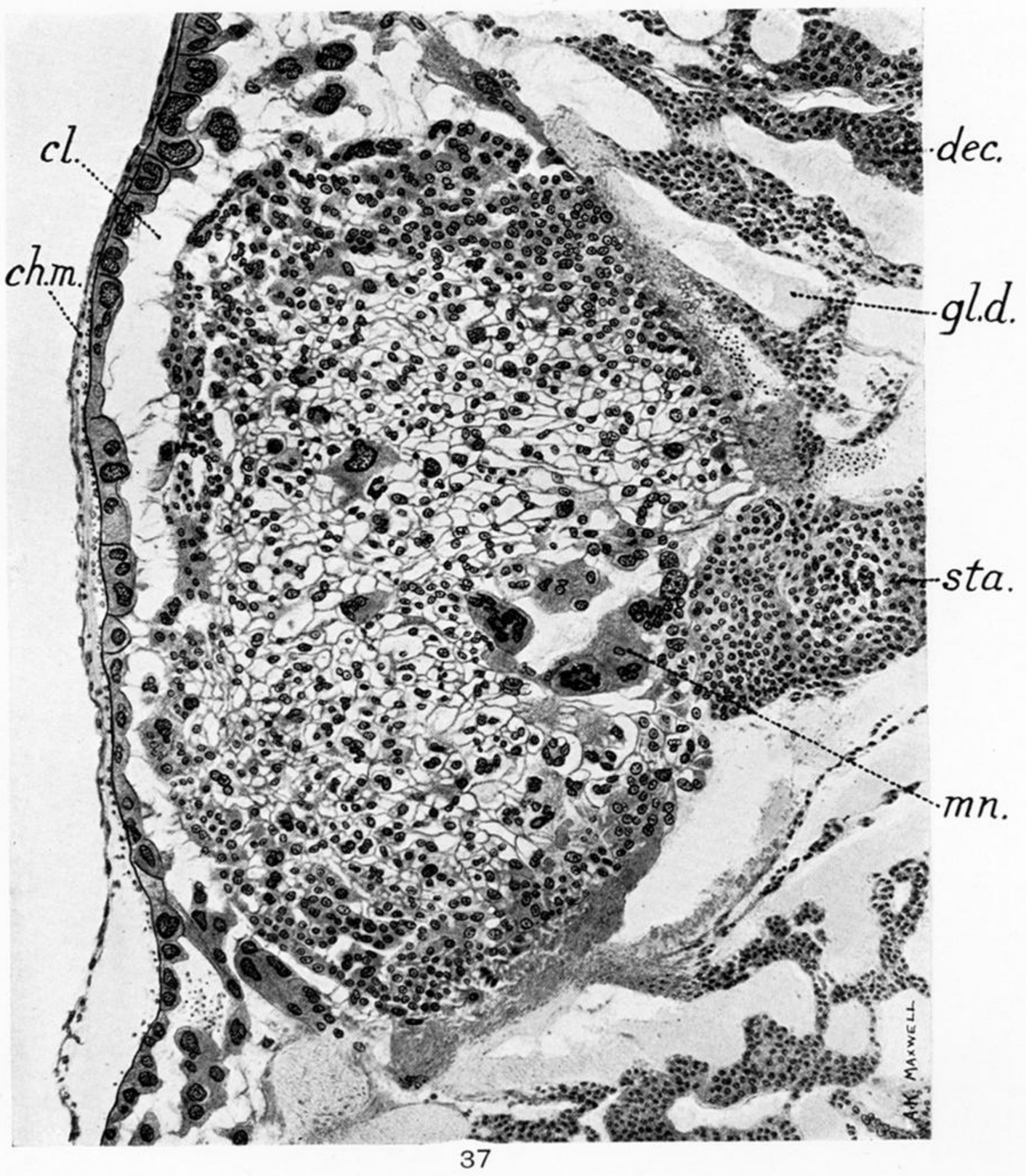

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PLATE 5.

FIG. 34.—Tarsius 622. H.C. Section of uterine cornu with blastocyst *in situ*. (Blastocyst, 0·83 × 0·76 mm. in diameter, shield-ectoderm about 0·3 mm. in diameter, tropho-placental mass, 0·67 × 0·51 mm. in diameter). Note the latter mass, surrounded by the solid degenerating glands (*gl.*¹) peripherally to these are much enlarged glands and more laterally still, normal glands in club-shaped groups. In the upper part of the tropho-placental mass are large lacunæ, containing maternal blood (*m.bl.*), here present exceptionally early. × 32.

FIG. 35.—Tarsius 622. H.C. The tropho-placental mass of the preceding figure under higher magnification, to show its characteristic parenchyma-like appearance and the lacunæ in its upper part containing maternal blood. Note the characters of the solid degenerating glands (*gl.*¹) and the commencing enlargement of the interglandular connective tissue cells, well seen on the right side of the figure. × 121.

FIG. 36.—Tarsius 622. H.C. Sectional view of small area of the tropho-placental mass as seen under the stereo-binocular microscope. Note the characteristic frame-work in the compartments or "cells" of which the nucleated units of the mass are situated.

FIG. 37.—Tarsius 175*a*. H.C. Section of the tropho-placental mass and its surroundings at a stage considerably later than that of Tarsius 622. The mass has increased in bulk, now measuring 1·24 × 0·86 mm. in diameter and possesses a stalk-like prolongation (*sta.*) (0·4 mm. in length × 0·27 mm. in thickness), regarded by HUBRECHT as maternal (trophospongial) in origin. The mass is now beginning to lose its original uniform character, owing to the enlargement of certain of its units and the formation of multinucleate syncytial masses (*mn.*). Note the irregular network of decidual strands (*dec.*) surrounding the mass and enclosing the degenerate remains of the uterine glands (*gl.d.*) in its meshes. *cl.* cleft formed by the artificial separation of the superficial layer of the mass (together with the chorionic mesoderm (*ch.m.*) adherent to it) from the remainder.

For details of the blastocyst *v.* text-fig. 9, p. 78. *Cf.* also for the tropho-placental mass, HUBRECHT ('99), Pl. 9, fig. 62. × 80·5.

FIG. 38.—Tarsius 175*a*. H.C. Portion of the tropho-placental mass under higher magnification, showing the commencing enlargement of its nucleated units, the increase in number of their nuclei and the formation of multinucleate syncytial masses. × 241.

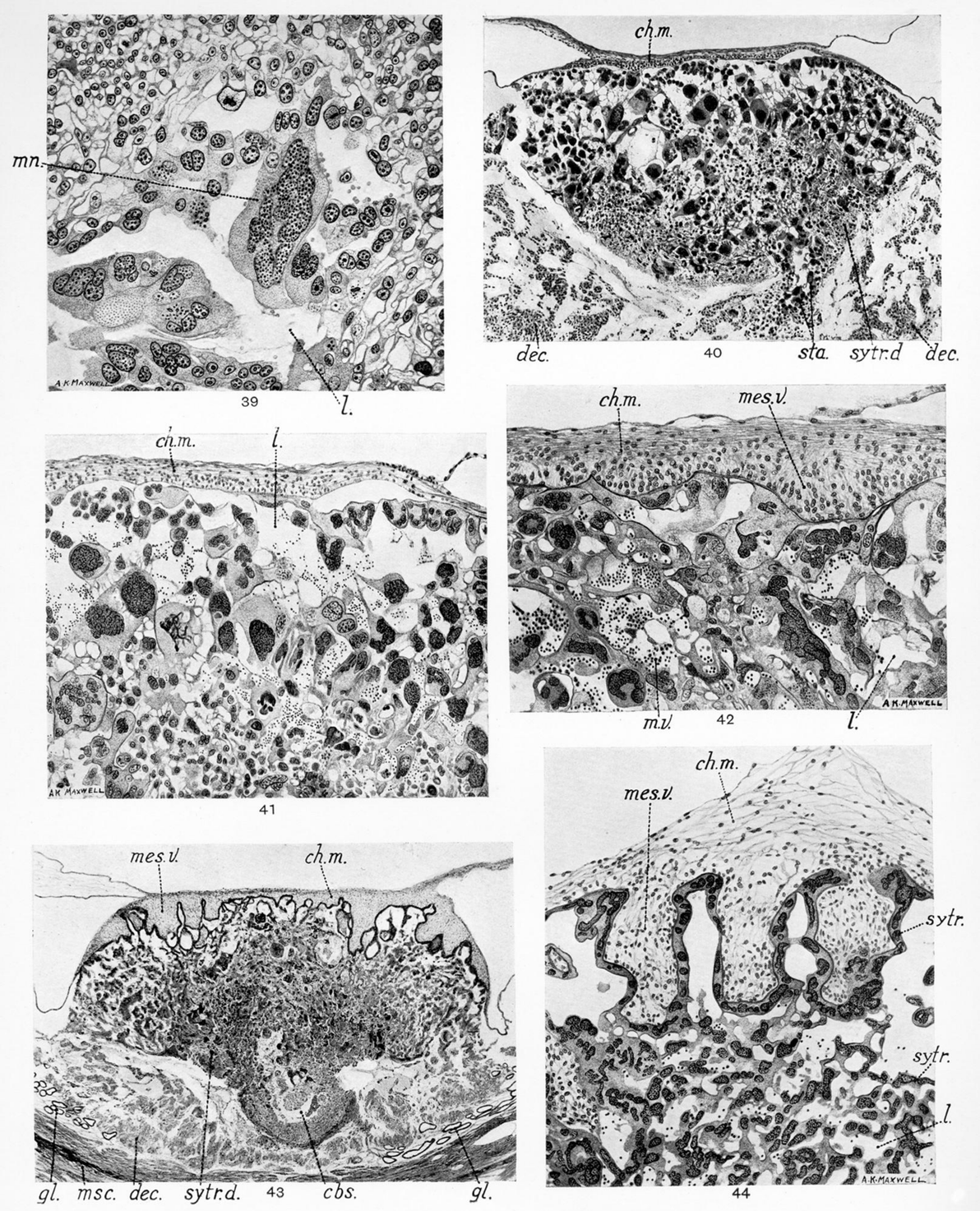


PLATE 6.

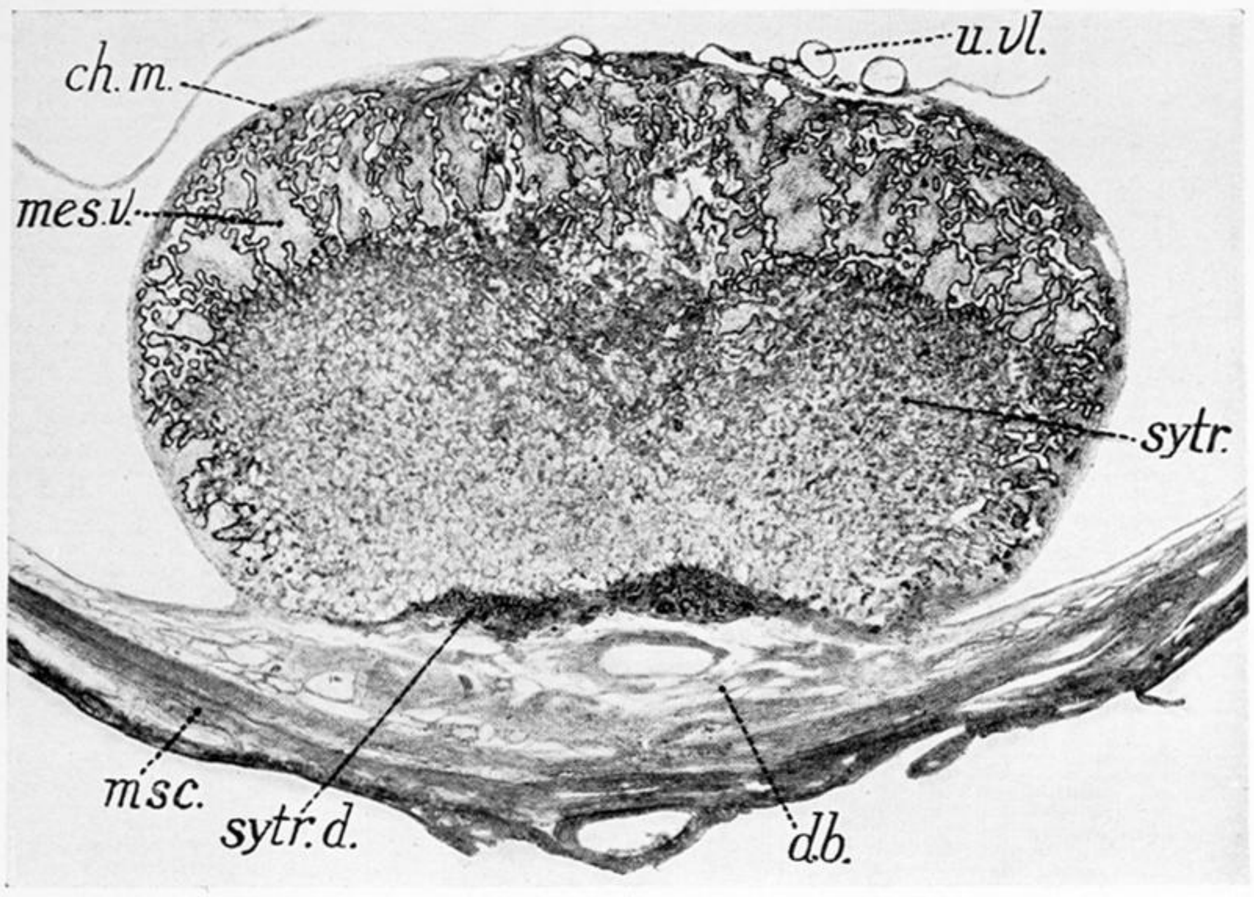
FIG. 39.—Tarsius 262*b*. H.C. Later stage than 175*a*. Blastocyst ± 2 mm. in diameter, tropho-placenta mass 1·39 × 1·0 mm. in diameter. The figure shows a portion of the latter mass, distinctly more advanced in differentiation than that depicted in the preceding figure. A large multinucleate mass (*mn.*) is visible near the centre of the figure, containing numerous large darkly stained nuclei, extremely rich in chromatin granules and around it other masses in process of formation by the fusion of the enlarged units. Note especially the large composite mass towards the lower left corner of the figure, the multinucleate constituents of which are still marked off from each other by portions of the "adenoid" frame-work. Lacunar spaces (*l.*) are present between the masses as in fig. 38, but now maternal blood in small amount is present in them both in the central and peripheral regions. × 203.

FIGS. 40 & 41.—Tarsius 261*a*. H.C. Low and high power views of the tropho-placental mass from a stage distinctly later than 262. Blastocyst ± 4·5 mm. in diameter (DE LANGE, 21, p. 58). Tropho-placental mass 2·14 × 1·3 mm. in diameter. In the latter, enlarged uni- and multinucleate masses are now abundant especially in the upper half of the primordium, their nuclei, variable in form and size, are mostly large and intensely staining and show evidence of amitotic division. Between them, occur lacunæ (*l.*) containing maternal blood as yet in small amount. The chorionic mesoderm (*ch.m.*) is beginning to thicken and possesses a wavy under surface (first indication of the mesodermal villi). Round the base of the primordium is a tract of what appears to be degenerating trophoblast (*sytr.d.*). The decidual strands (*dec.*) of the basalis are reduced and the gland-remains have largely disappeared. *sta.*, stalk of the primordium, here eccentric. Fig. 40, × 40. Fig. 41, × 98.

FIG. 42.—Tarsius 22*a*. H.C. *v.* text-fig. 11, p. 80. Portion of the upper region of the tropho-placental primordium (2·4 × 1·9 mm. in diameter), showing the thickened chorionic mesoderm (*ch.m.*) produced into localised down-bulgings, the primordia of the mesodermal villi (*mes.v.*). The tropho-placental primordium is assuming the character of an irregular syncytium enclosing lacunæ (*l.*) containing maternal blood, though many of its constituent multinucleate elements still appear individualised and separated by remains of the "cuticular" frame-work. × 157.

FIG. 43.—Tarsius 164*c*. H.C. Entire view of placenta and uterine wall. Placental mass 3·28 × 1·9 mm. in diameter. As the result partly of its own growth in thickness, partly of the progressive reduction in the thickness of the decidual tissue underlying it, the placenta now projects so that its base lies practically on a level with the surface of the surrounding endometrium. The chorionic mesodermal villi (*mes.v.*) are now beginning to grow into the tropho-placental primordium as thick finger-like processes. *cbs.* central blood-sinus in the placental stalk. *sytr.d.* degenerating trophoblast. *dec.* strands and masses of decidual cells, the gland-remains originally enclosed by them having largely disappeared. Embryonal area of blastocyst ± 1·8 mm. (DE LANGE, '21, p. 56). × 25.

FIG. 44.—Tarsius 164*c*. H.C. Portion of the placenta under higher magnification showing the chorionic mesodermal villi penetrating into what is now the definitive syncytium (*sytr.*) of the tropho-placental primordium, a thin layer of syncytium enveloping each villous outgrowth. As yet there are no umbilical capillaries in the mesodermal villi, though maternal blood is present in the lacunæ of the syncytium. × 116.



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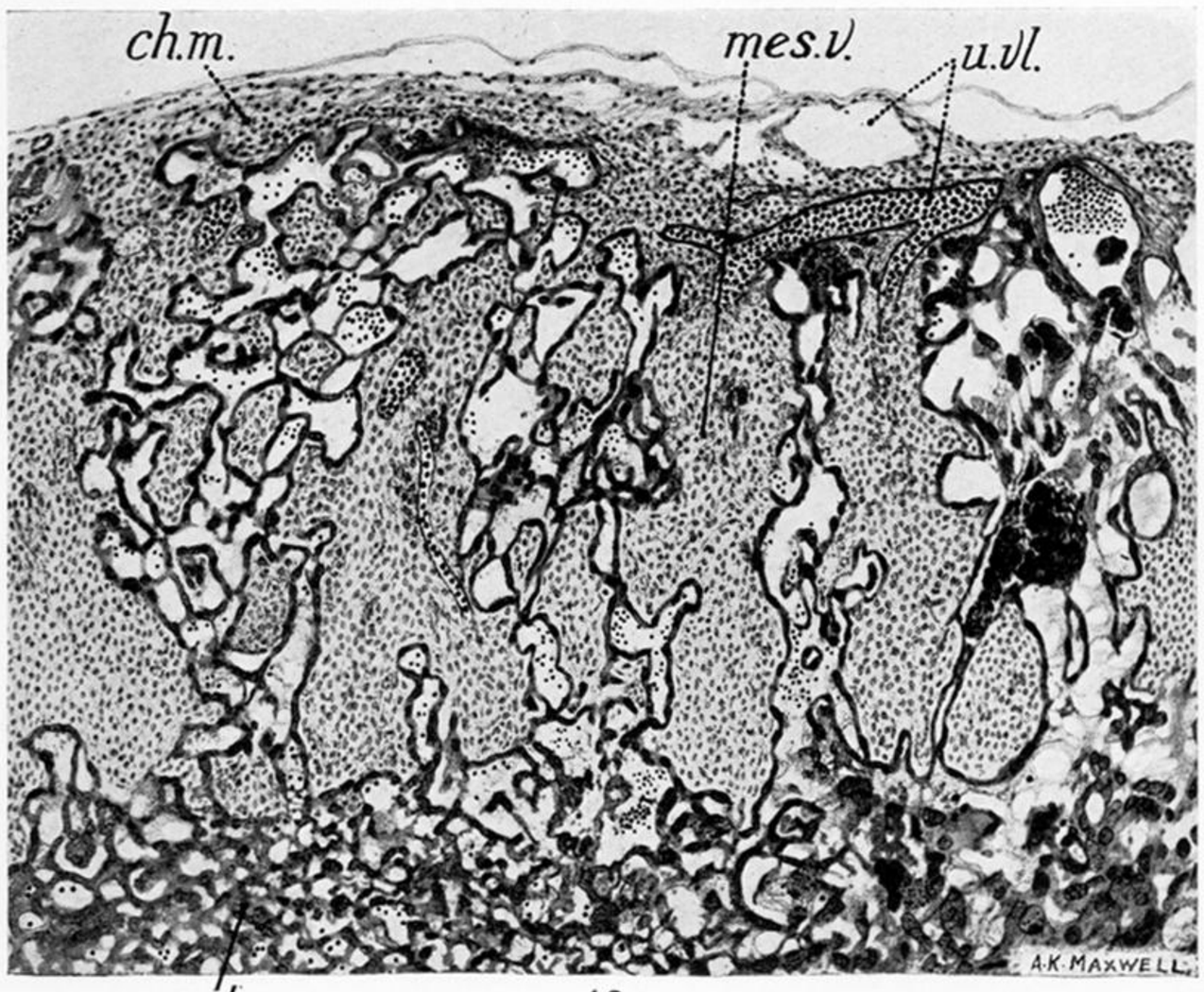

sytr.

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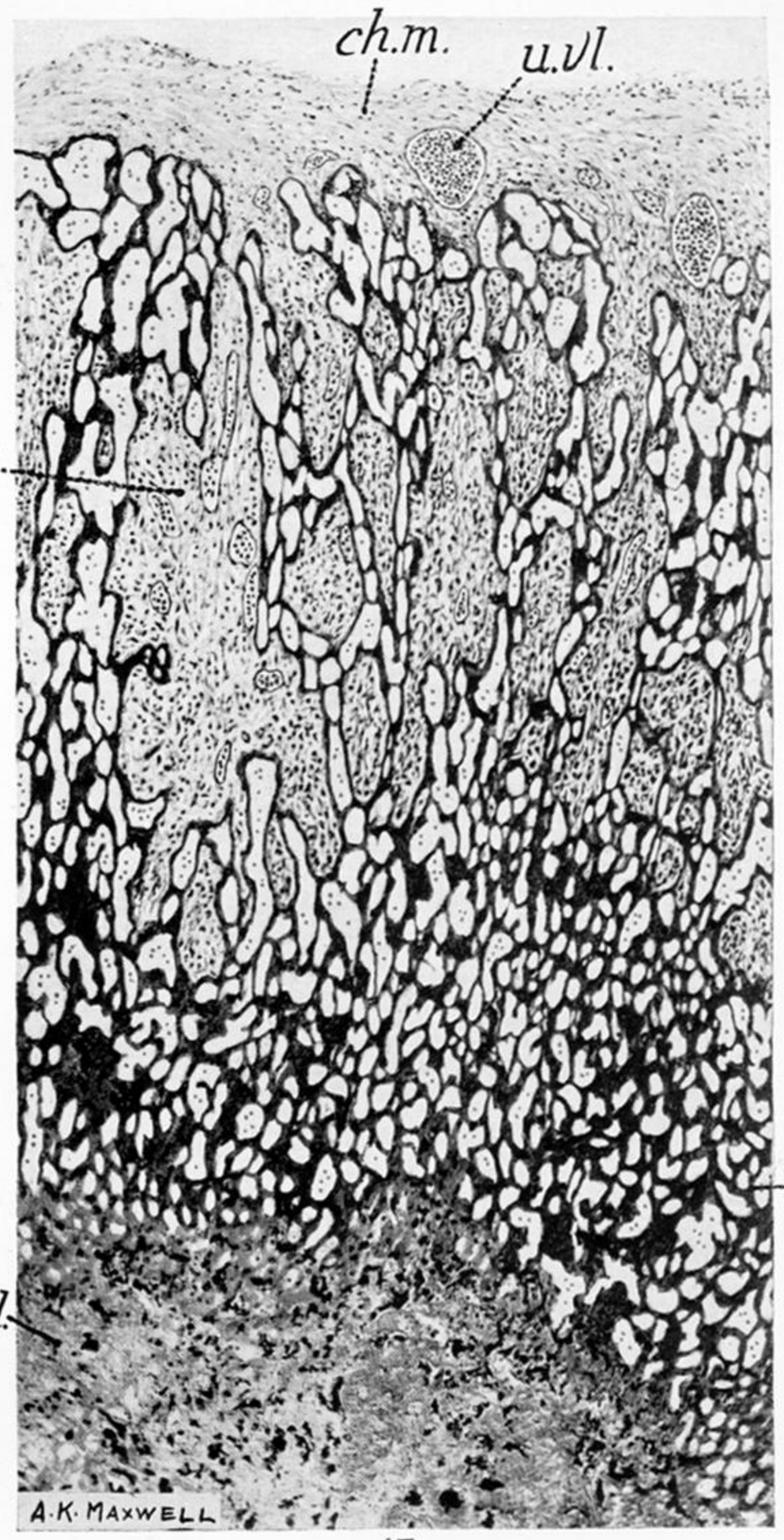

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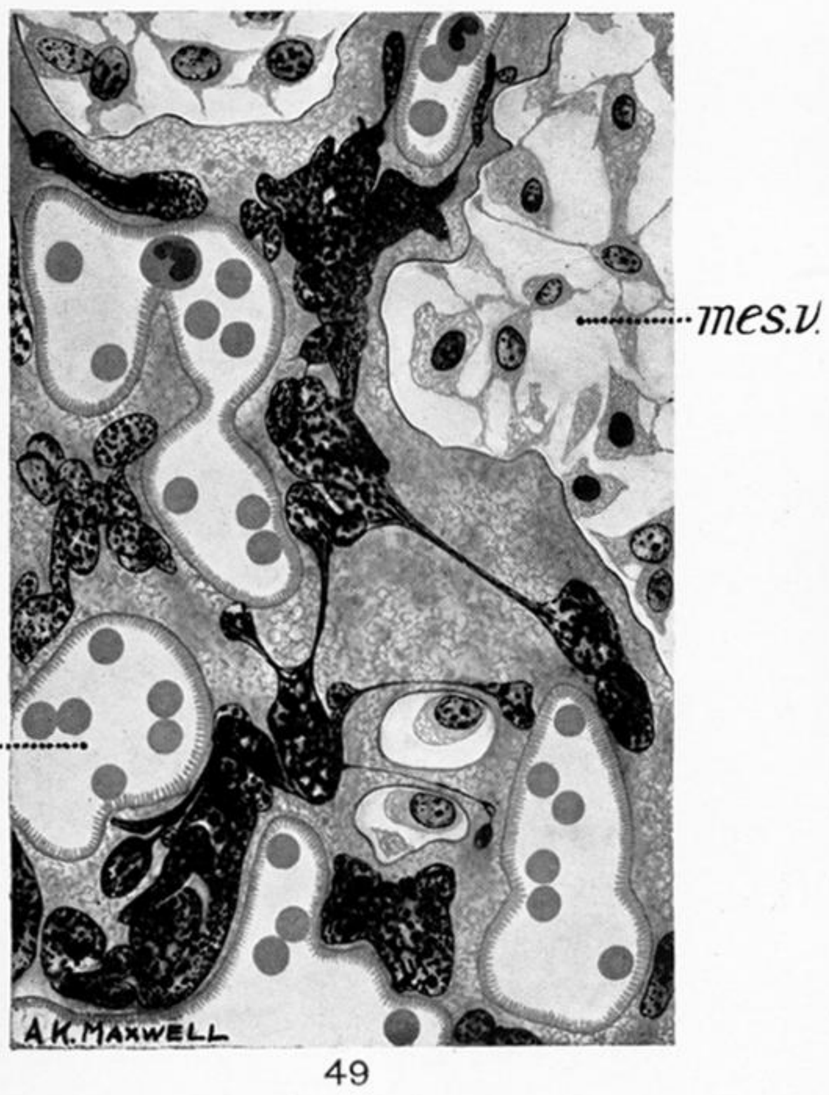

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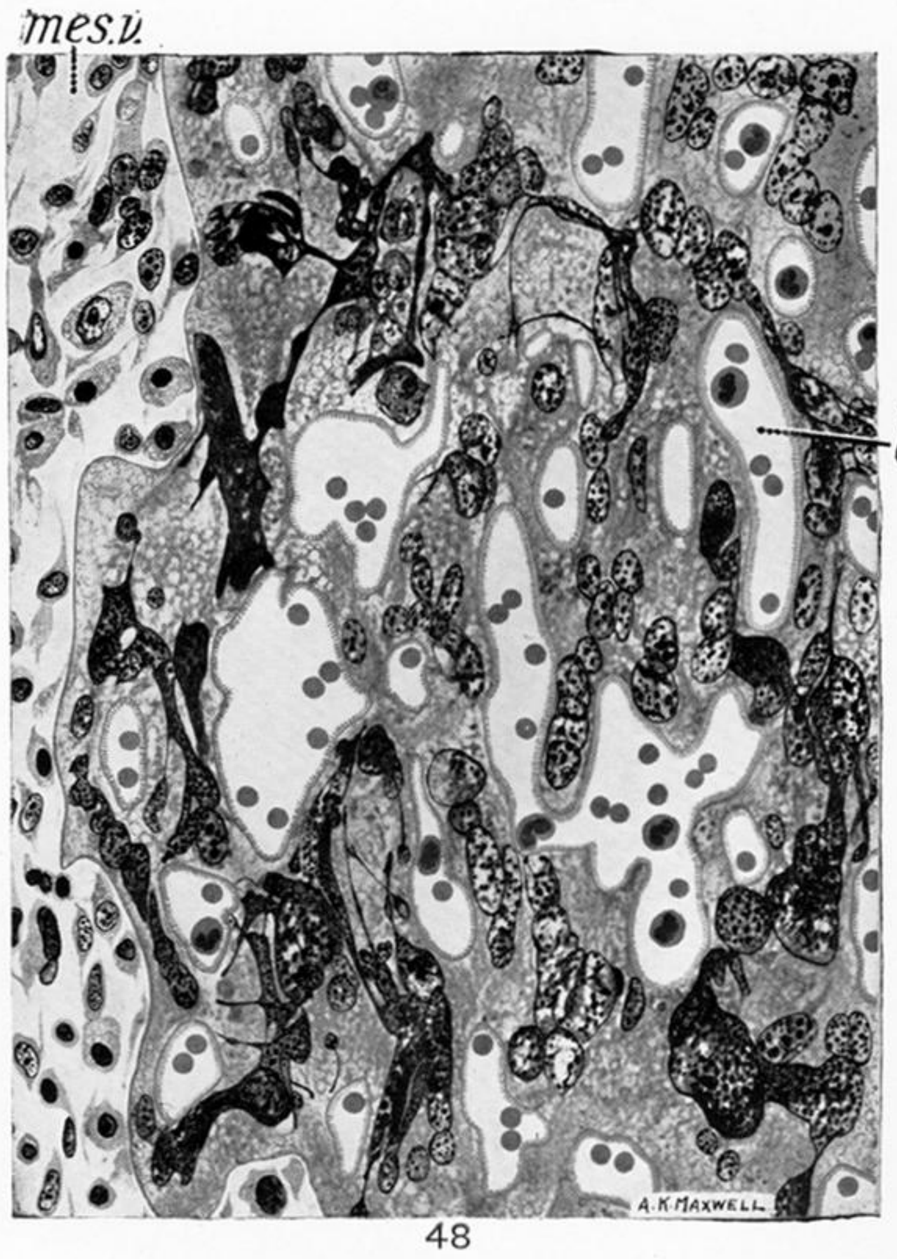

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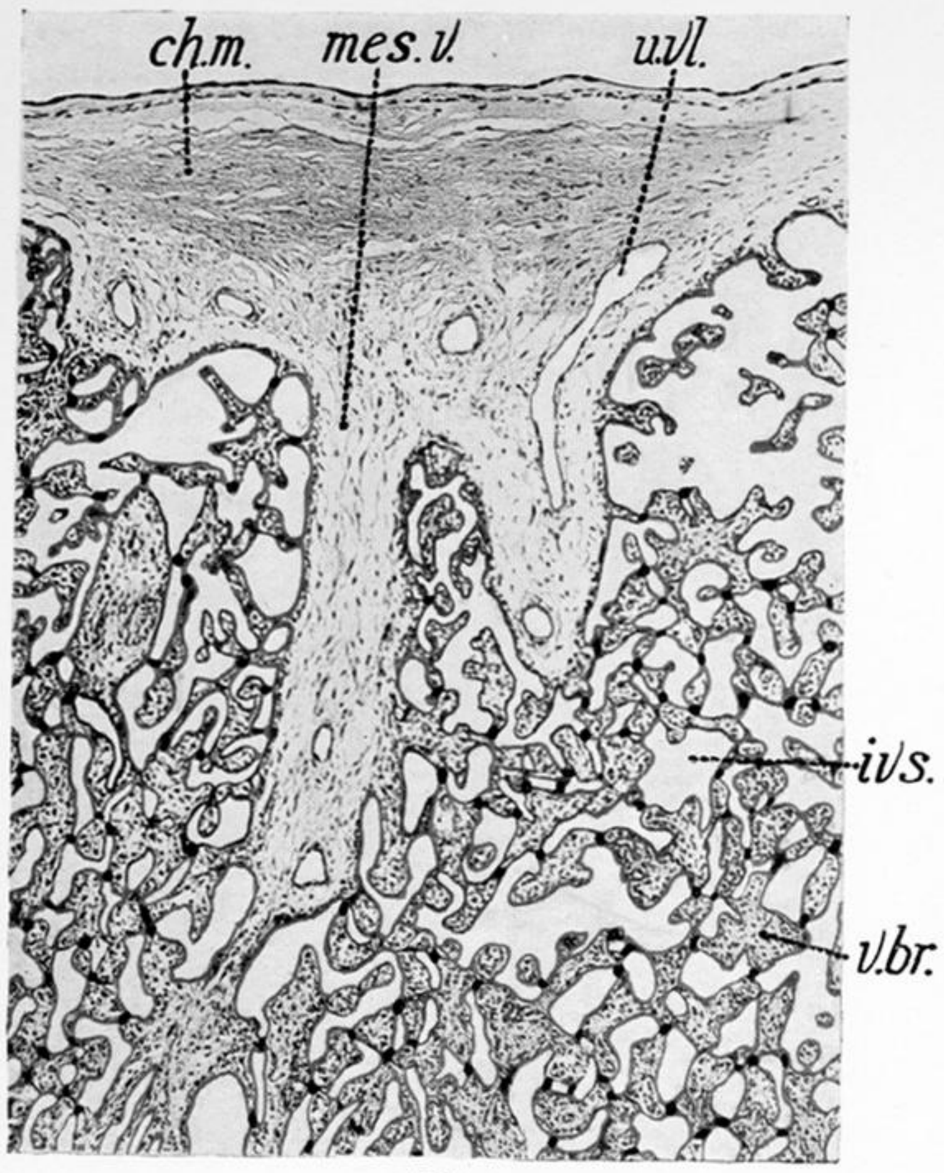
Plate 7.

Fig. 45.—Tarsius 595*c*. H.C. Blastocyst + 8 mm. in diameter (de Lange, '21, p. 63). Placenta 4·6 × 2·6 mm. in diameter. The figure shows a sectional view of the entire placenta. It now forms a knob-like projection with a broad base of attachment to the underlying decidual tissue (*d.b.*) which is much reduced. Between the latter and the syncytio-trophoblast (*sytr.*) is a deeply staining zone (*sytr.d.*) of what appears to be degenerate trophoblast. *u.vl.*, umbilical vessel in the chorionic mesoderm. × 16·5.

Fig. 46.—Tarsius 595*c*. H.C. Superficial zone of the same placenta, showing the mesodermal villous outgrowths (*mes.v.*) now much increased in length and beginning to branch. Umbilical vessels (*u.vl.*) are present in the chorionic mesoderm (*ch.m.*) and are penetrating into its villous outgrowths. *sytr.*, syncytiotrophoblast. × 79·5.

Fig. 47.—Tarsius Cl. 1. Later stage (placenta 6 mm. in diameter). The mesodermal villi (*mes.v.*) have increased in length and are more branched as compared with those of 595. The syncytiotrophoblast (*sytr.*) into which they are growing forms a very distinct network. It provides the syncytial investment of the villous outgrowths and is also present between them. *sytr.d.* degenerate trophoblast. × 66.

Figs. 48–50.—Tarsius Cl. 1. Portions of the syncytiotrophoblast of the same placenta. Note its lacunæ bounded by what appears to be a " brush " border comparable with that on the surface of the syncytiotrophoblast of the human chorionic villi and especially the remarkable branching forms assumed by its nuclei, evidently preparatory to direct division. Fig. 49, × 545. Fig. 50, × 534.



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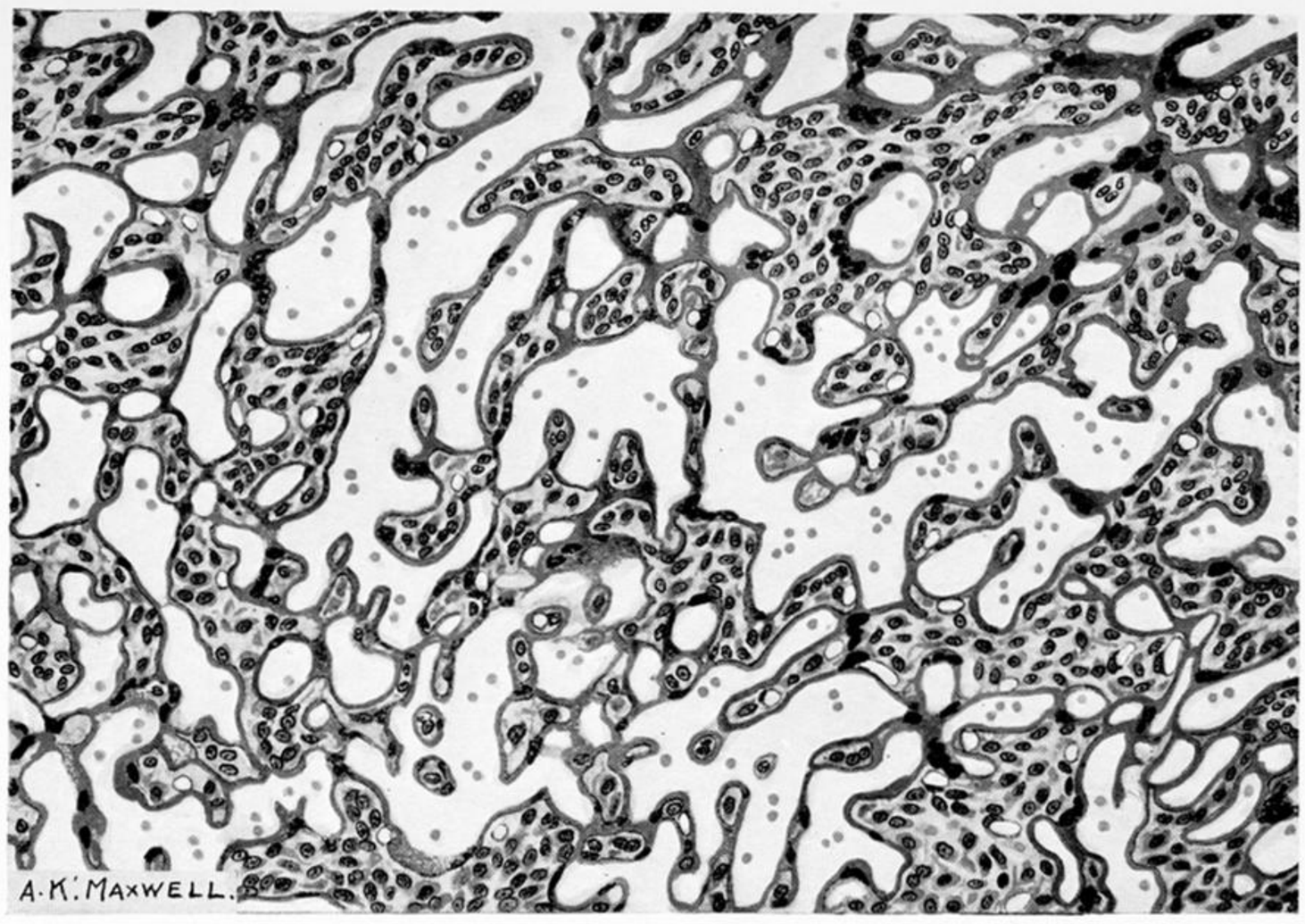

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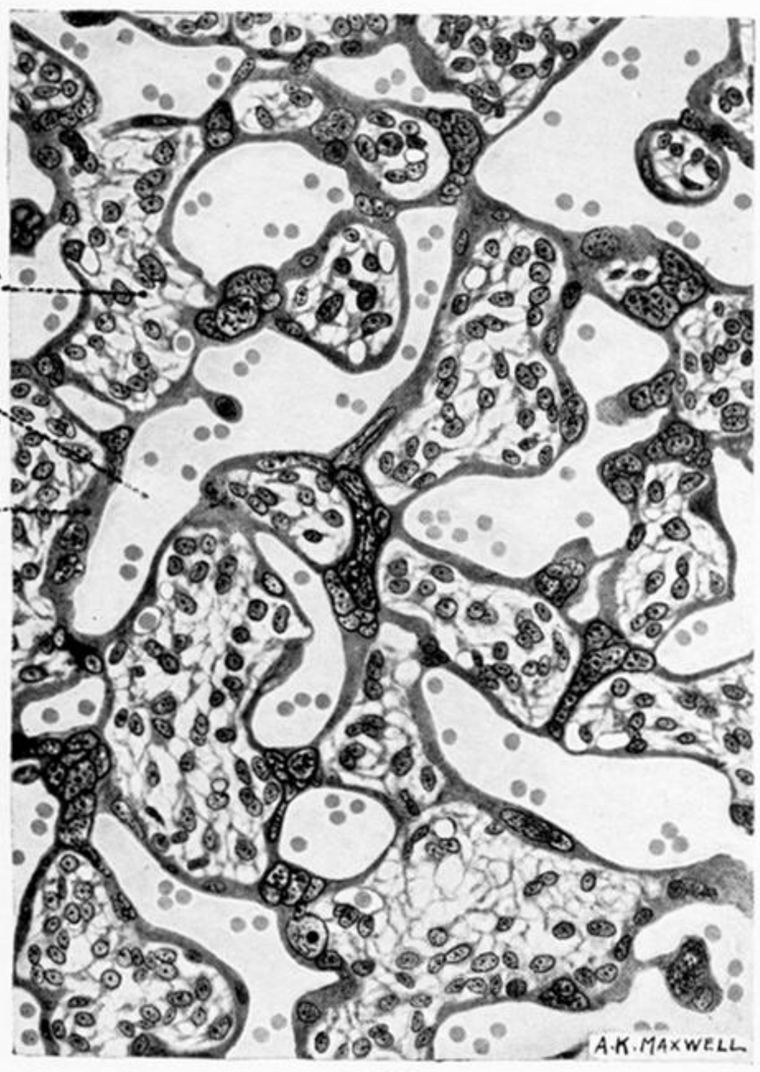

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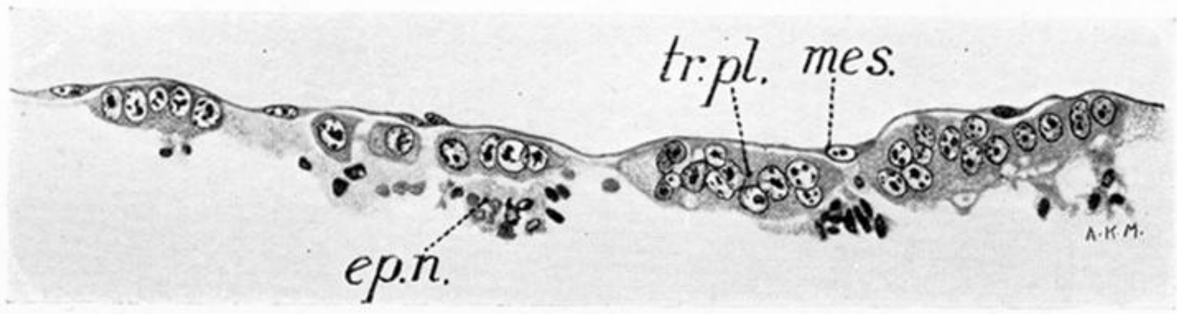

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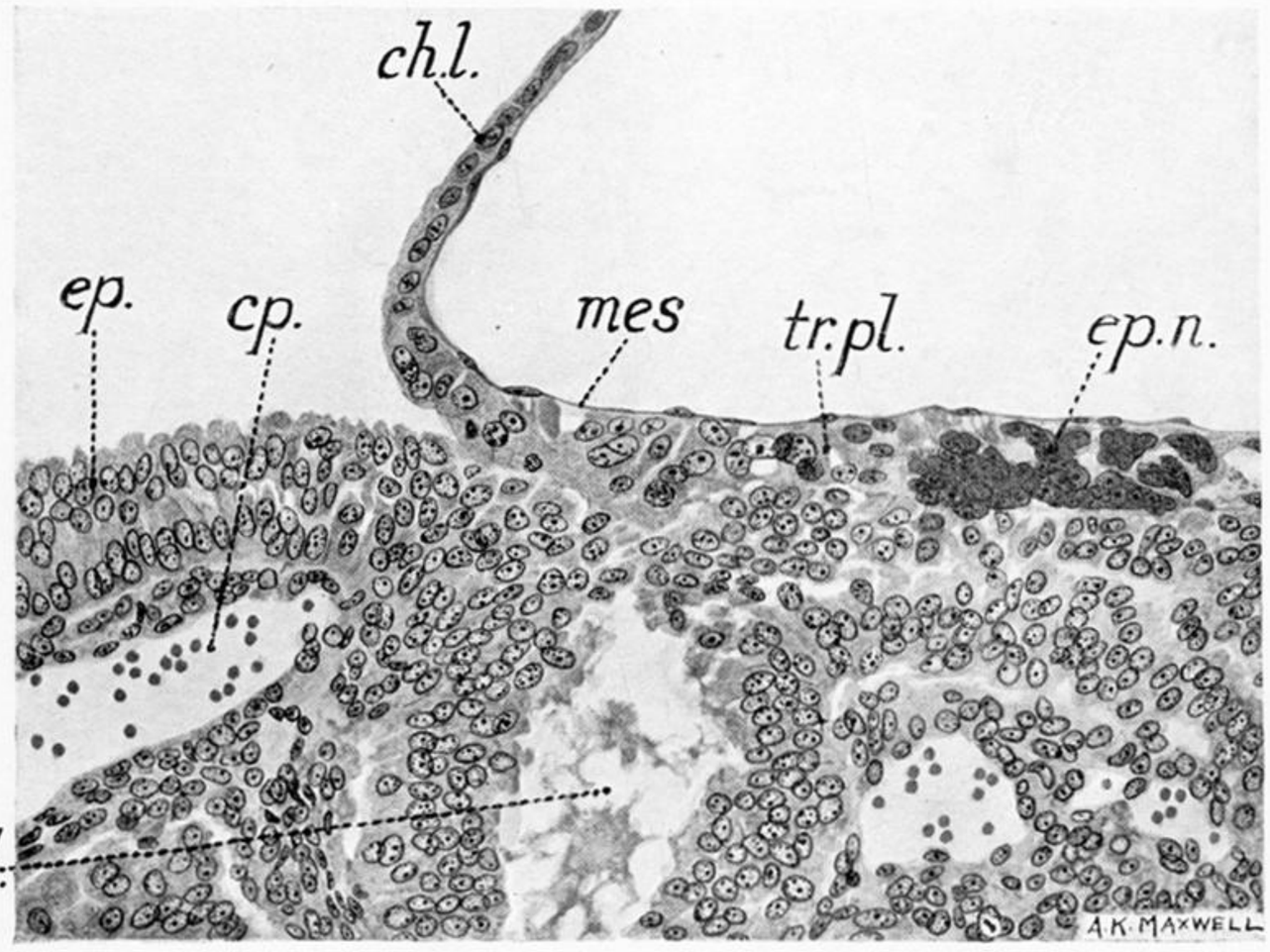

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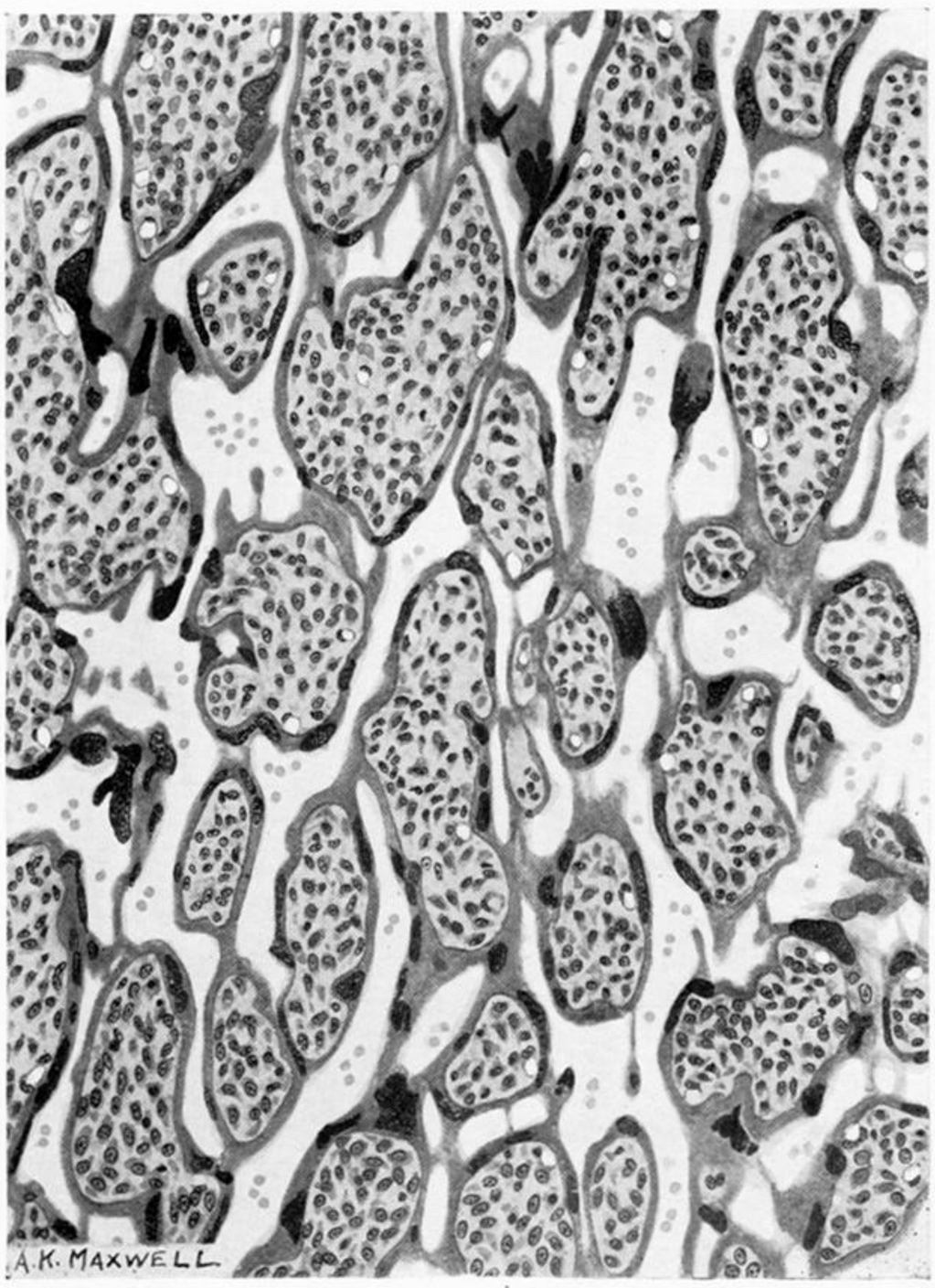

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Plate 8.

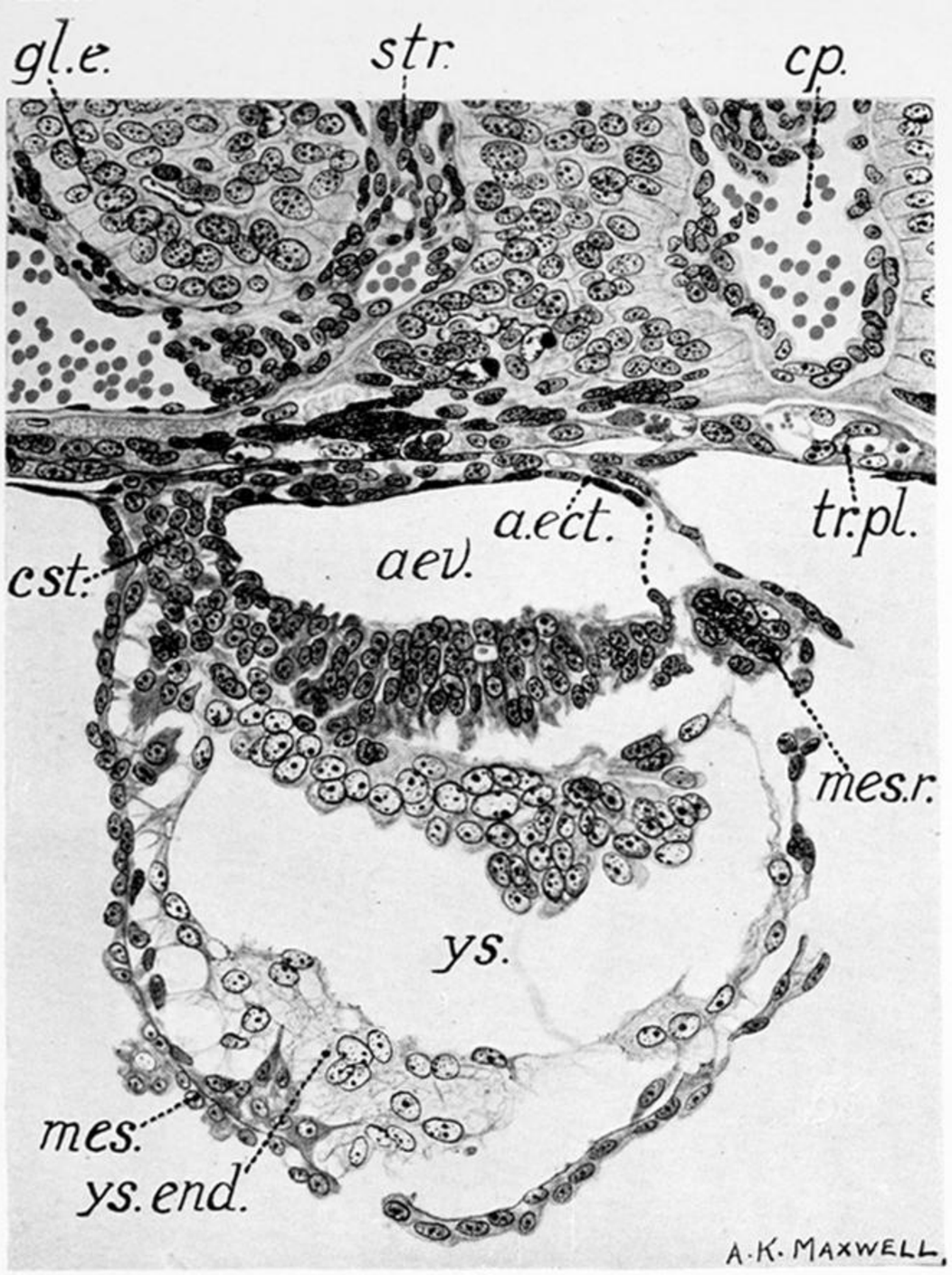
Figs. 51 & 52.—Tarsius 76. H.C. Placenta, conical, 10 × 11 mm. in diameter. Embryo G.L. 29 mm. The placenta is now well established and essentially consists of villous branches or trabeculæ (*v.br.*), connected up by syncytial junctions so as to form a coarse network, the meshes of which constitute the intervillous lacunar blood-spaces (*ivs.*) occupied by the maternal blood. Each villous branch consists of an axis of chorionic mesenchyme, carrying the umbilical capillaries and a thin investing layer of nucleated syncytium. *ch.m.* chorionic mesoderm. *mes.v.* a main villous stem arising from the chorion. *u.vl.* umbilical vessel. Fig. 51, × 56. Fig. 52, × 260.

Fig. 53.—Tarsius 812. H.C. Placenta 13·5 × 9 mm. in diameter × 4 mm. in thickness. Portion of the villous (trabecular) network, the villous branches being still relatively thick. × 188.

Fig. 54.—Tarsius 405. H.C. The fœtal surface of the intact placenta is shown in fig. 28, Pl. 3. Placenta 15 × 12 mm. in diameter × 7·5 mm. in thickness. Portion of the villous network, the villous (trabecular) branches being now much finer than those of 812. × 192.

Fig. 57.—Hapale 2. Section through marginal region of the attachment of the blastocyst. *ch.l.* free wall of blastocyst (chorion læve). *ep.* greatly thickened uterine epithelium. *ep.n.* pycnotic nuclei of the latter, in process of degeneration. *tr.pl.* attaching (ectoplacental) trophoblast. × 266.

Fig. 58.—Hapale 2. Isolated portion of the attaching (ectoplacental) trophoblast. × 275.



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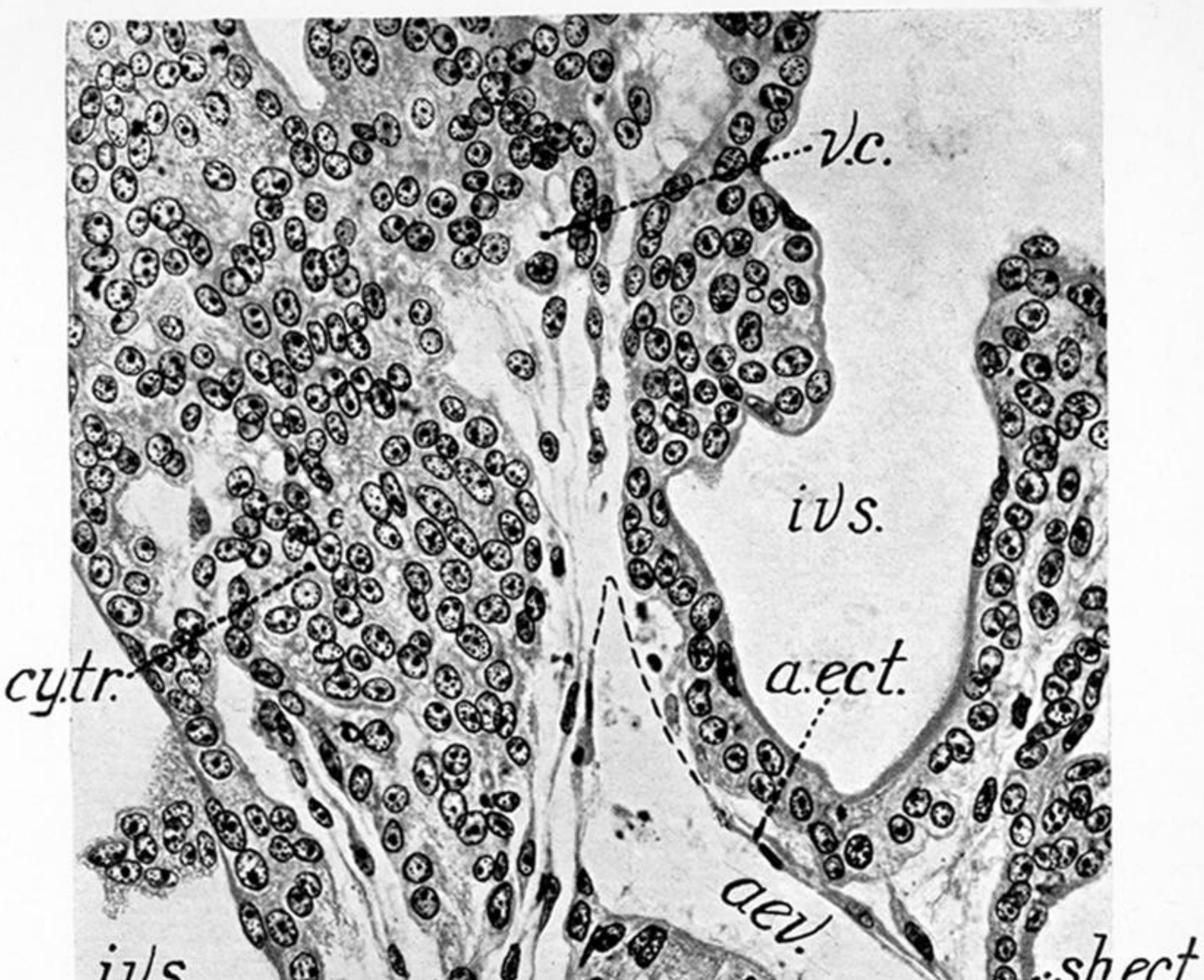

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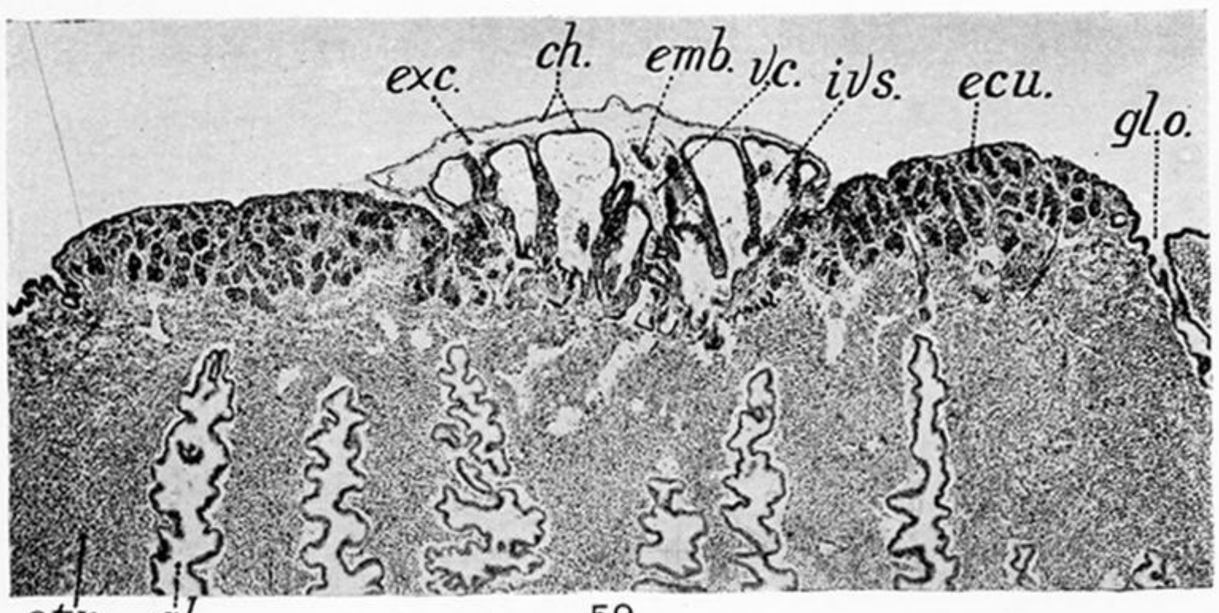

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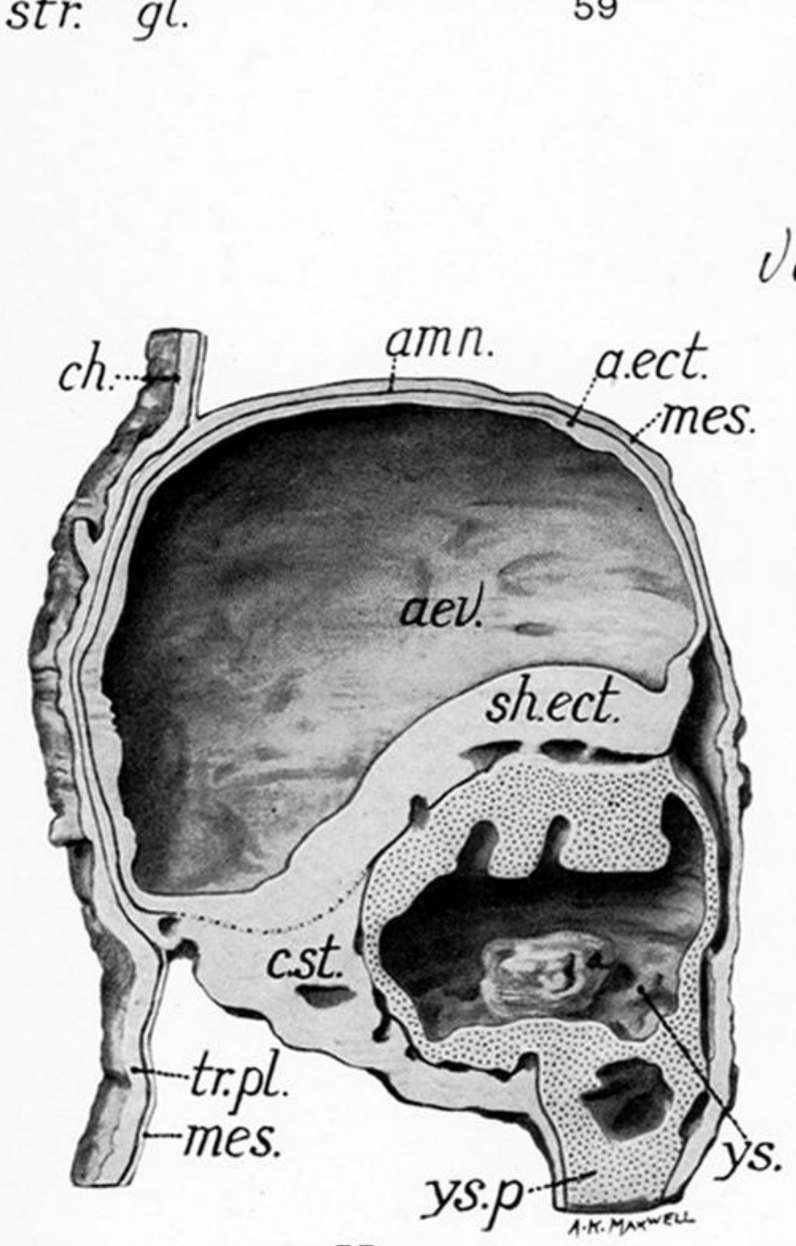

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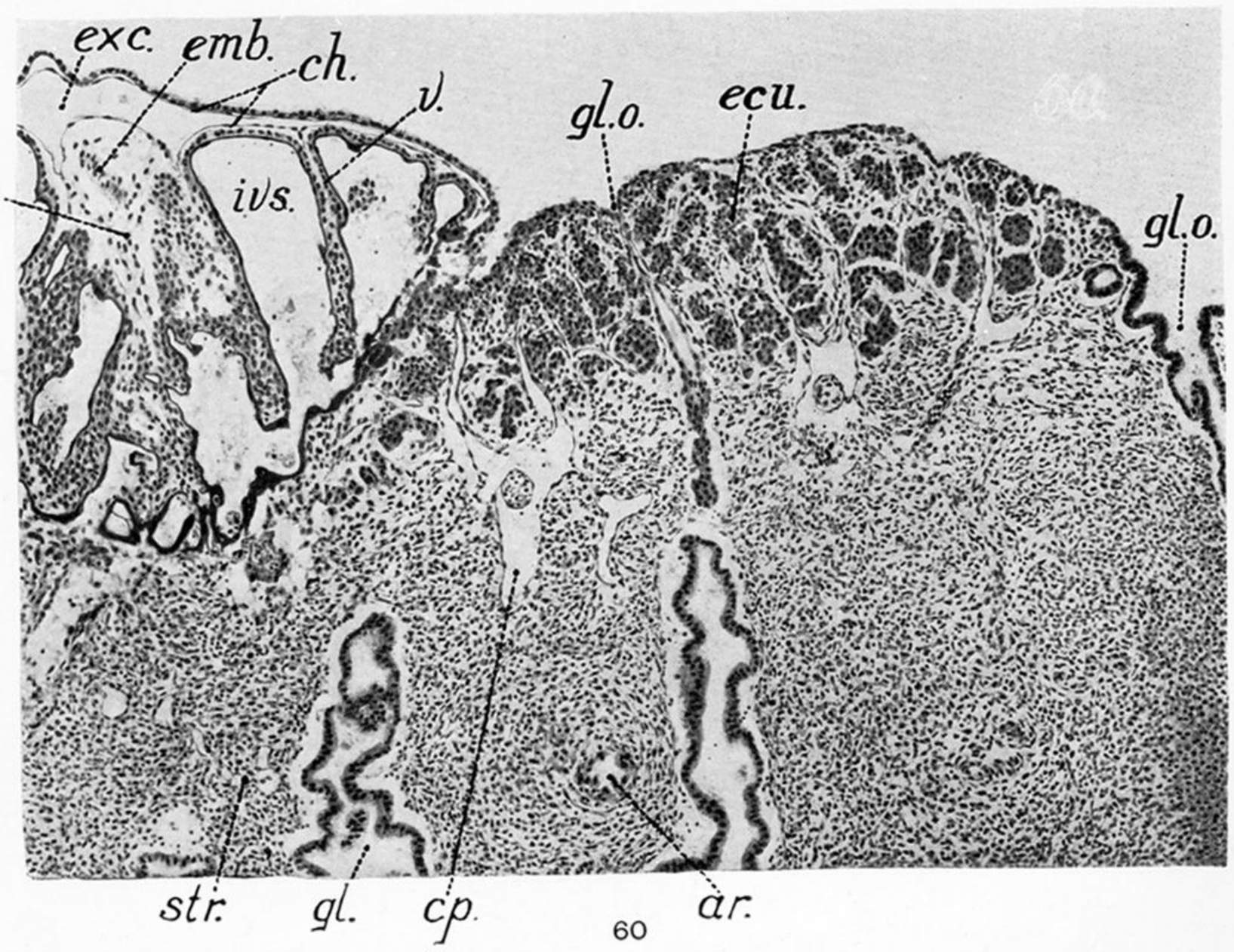

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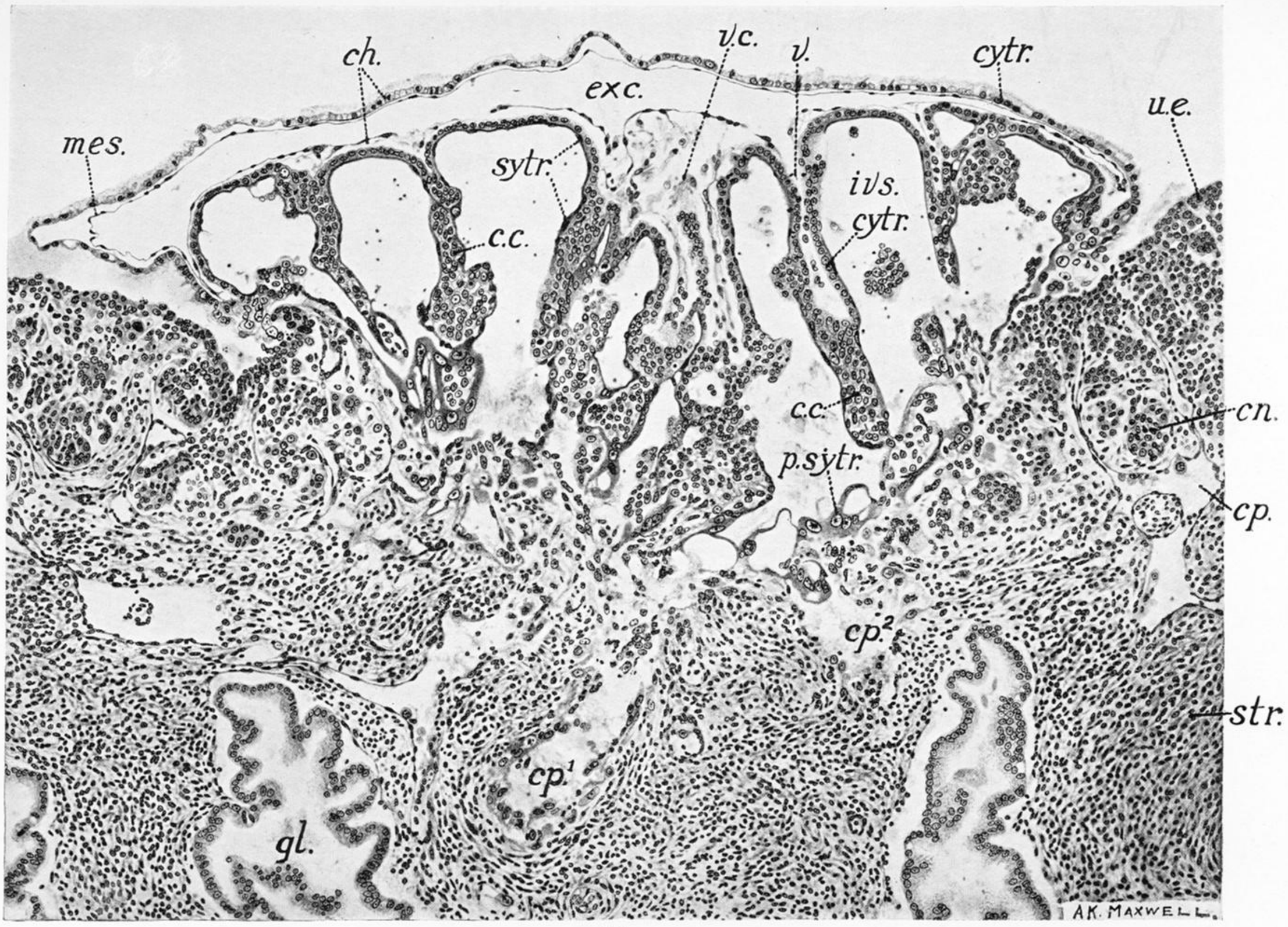
PLATE 9.

FIG. 55.—Hapale 2. Wax-plate model of embryo B (prepared by Dr. C. J. HILL), seen in median longitudinal section. *aev.* amnio-embryonal vesicle. *c.st.* connecting stalk primordium. *ys.* yolk-sac vesicle. *ys.p.* yolk-sac process.

FIG. 56.—Hapale 2. Median longitudinal section through embryo A. Lettering as in fig. 55. *gl.e.* gland epithelium. *str.* stroma of uterine mucosa. *mes.* mesothelium. *mes.r.* median portion of an incomplete horseshoe-shaped band of mesoderm which is prolonged forwards from the mesoderm of the connecting stalk (*c.st.*). *ys.end.* yolk-sac endoderm, the marked thickening of the embryonal endoderm may possibly represent the prochordal plate. *tr.pl.* ectoplacental (attaching) trophoblast, note that the uterine epithelium has disappeared except for groups of darkly stained pycnotic nuclei. × 266.

FIGS. 59 & 60.—*Nasalis larvatus* (Keim S., SELENKA). H.C. Low and higher power views of blastocyst and the related endometrium, showing the attached blastocyst, the position of the embryo (*emb.*) at the base of the central villus (*v.c.*) and the thickened endometrial cushion (*ecu.*). Fig. 59, × 28. Fig. 60. × 77.

FIG. 61.—*Nasalis larvatus* (Keim S., SELENKA). H.C. Longitudinal section through the embryo, *cf.* text-fig. 16, p. 106. *aev.* amnio-embryonal vesicle, note postero-dorsal prolongation of amnion. *ch.* chorion. *cytr.* cytotrophoblast, in part cut tangentially. *exc.* exocœlom. *ivs.* intervillous blood-space. *mes.* mesothelium. *ys.end.* yolk-sac endoderm. *v.c.* central villus. × 323.



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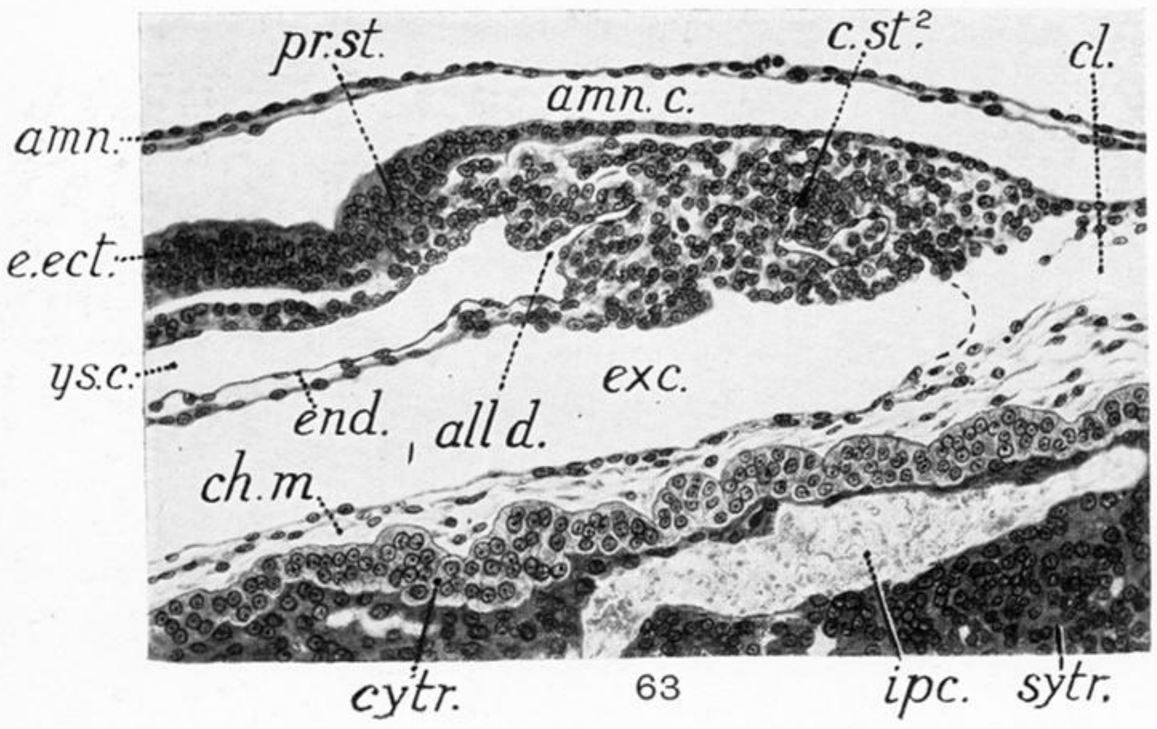

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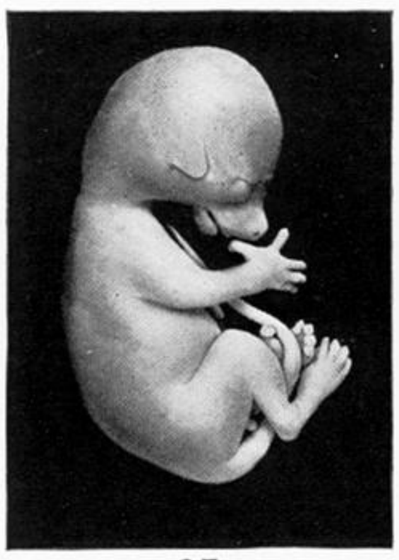

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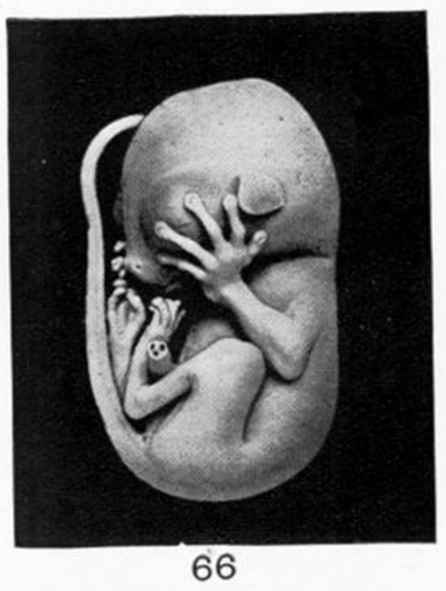

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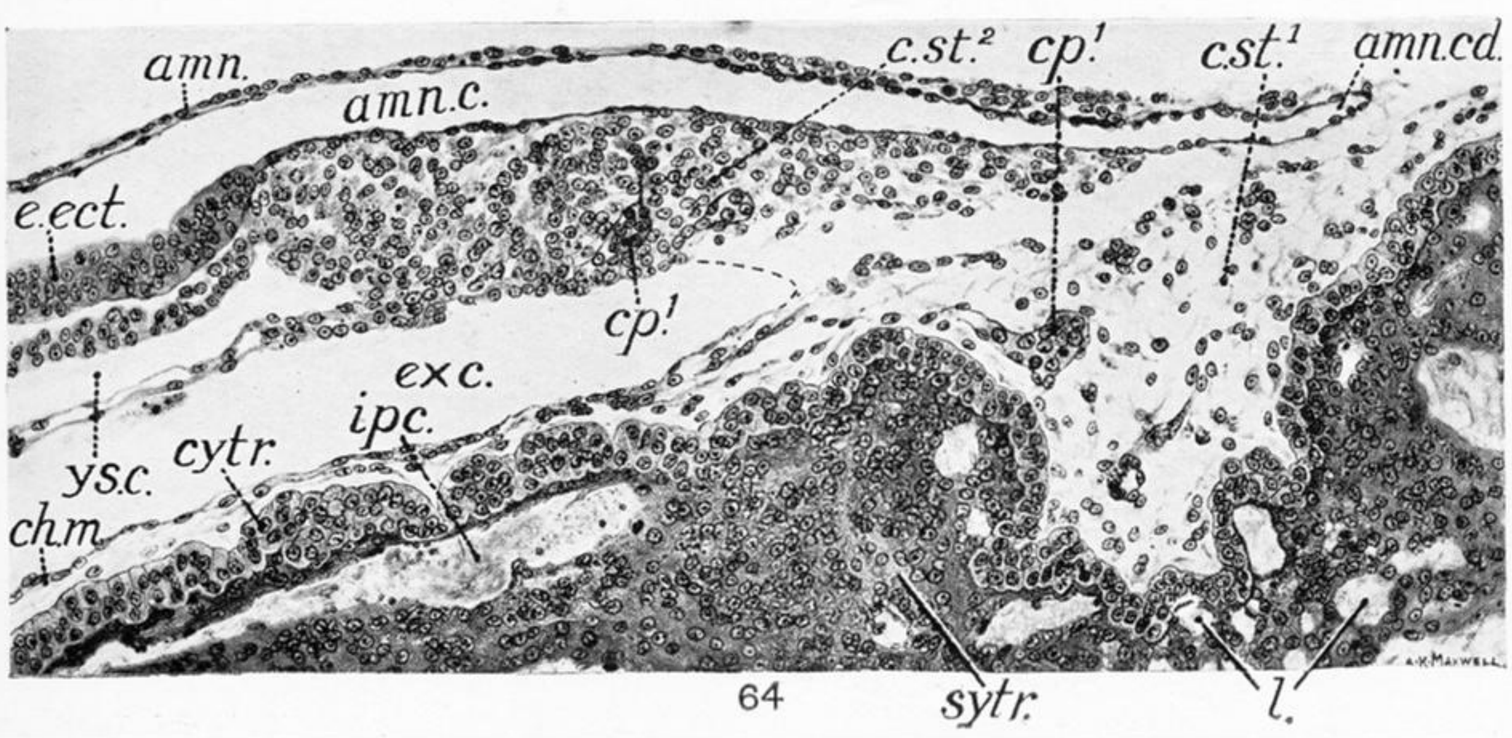

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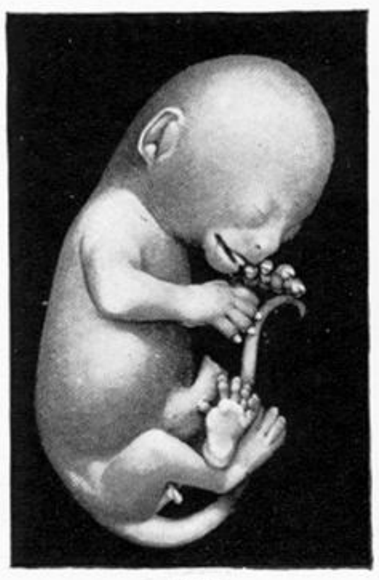

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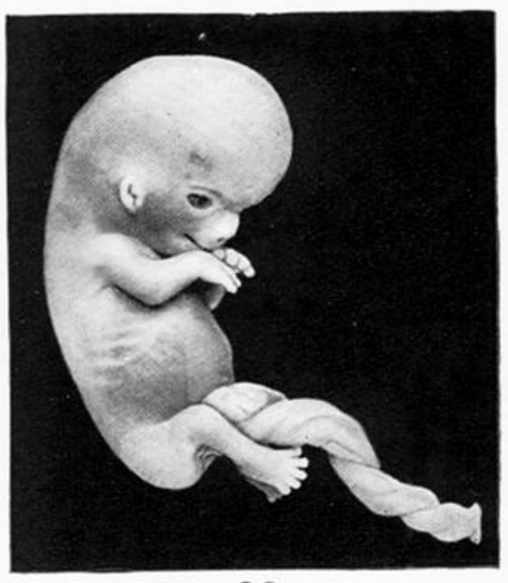

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PLATE 10.

FIG. 62.—*Nasalis larvatus* (Keim S., SELENKA). H.C. Section of the blastocyst and the related endometrium, to show the details of the structure of the blastocyst and its villi (*v.c.*, *v.*) and the changes in the endometrium. For description, see text, pp. 136–140. Note especially the cell-columns (*c.c.*) of the villi, the intervillous blood-space (*ivs.*) which is filled by maternal blood, the irregular peripheral (basal) syncytium (*p.sytr.*). In the endometrium, note the stroma (*str.*), dense in its deeper zone, much looser and œdematous-looking in its superficial zone. *cp.* greatly enlarged capillary. *cp.*¹ capillary, the endothelium of which has proliferated. *cp.''* lumen of capillary into which projects a prolongation of the peripheral syncytium. *cn.* cell-nest or epithelial ingrowth of endometrial cushion (*ecu.*). *gl.* enlarged uterine gland. × 120.

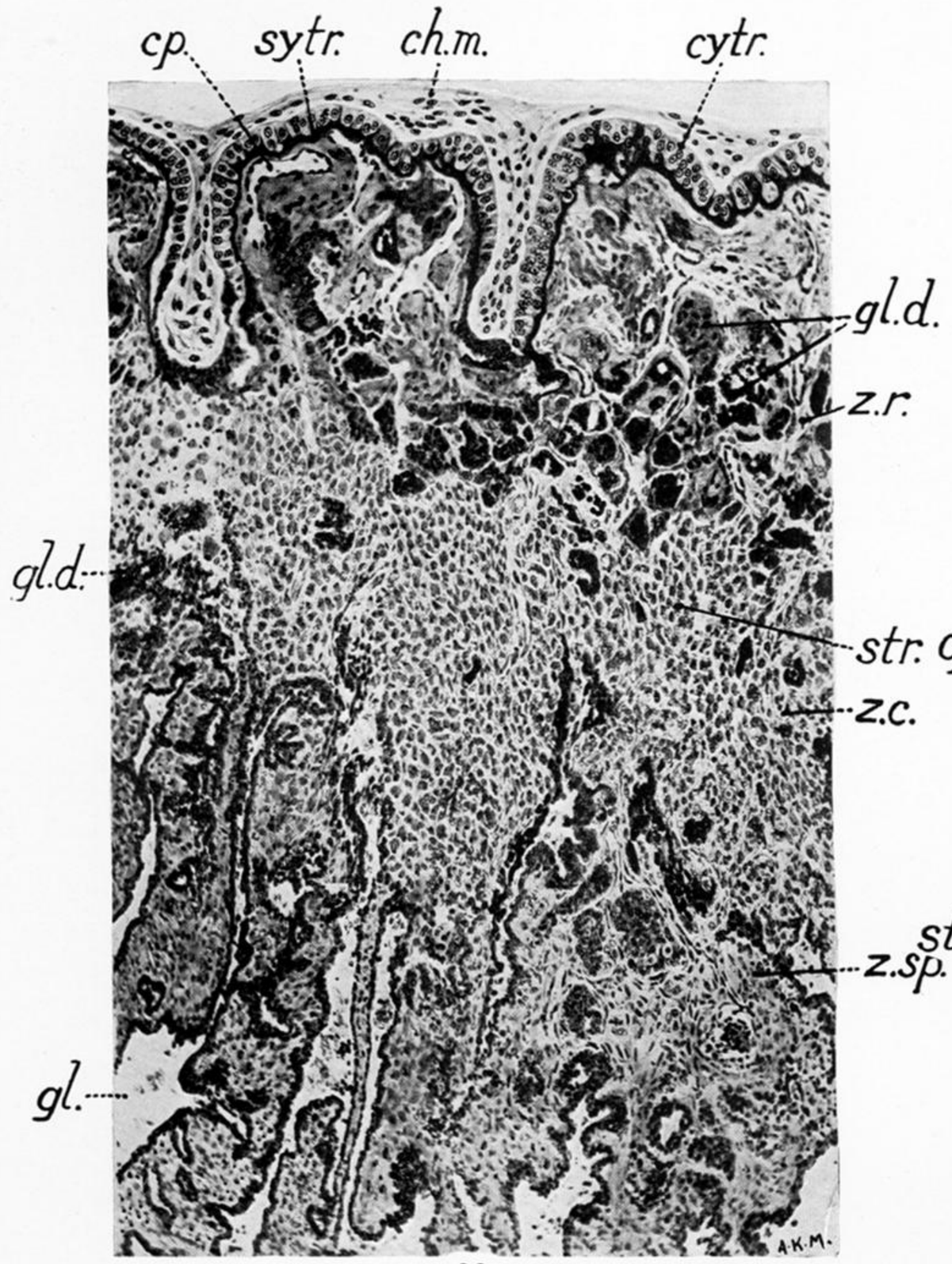
FIGS. 63 & 64.—*Chrysothrix sciureus* 467. B.C. Longitudinal sections through the caudal extremity of the embryo (0·978 mm. in length, blastocyst 6 mm. diameter), *cf.* fig. 18*a*, Pl. 21. *c.st.*¹ and *c.st.*² the two parts of the connecting stalk (*v.* text, pp. 113, 114). *all.d.* (?) allantoic canal (?). *amn.cd.* caudal prolongation of amniotic cavity. *cp.*¹ developing capillary in mesoderm of connecting stalk. × 120.

FIG. 65.—*Galago maholi.* Fœtus 1, G.L. 24 mm., H.L. 11·5 mm.

FIG. 66.—*Tarsius spectrum.* Fœtus, G.L. 25·5 mm., H.L. 13·5 mm.

FIG. 67.—*Hapale jacchus*, H.C. 1. Fœtus B, G.L. 34 mm., H.L. 13·75 mm.

FIG. 68.—Homo H.H. 12. Fœtus, G.L. 25 mm., H.L. 12 mm.



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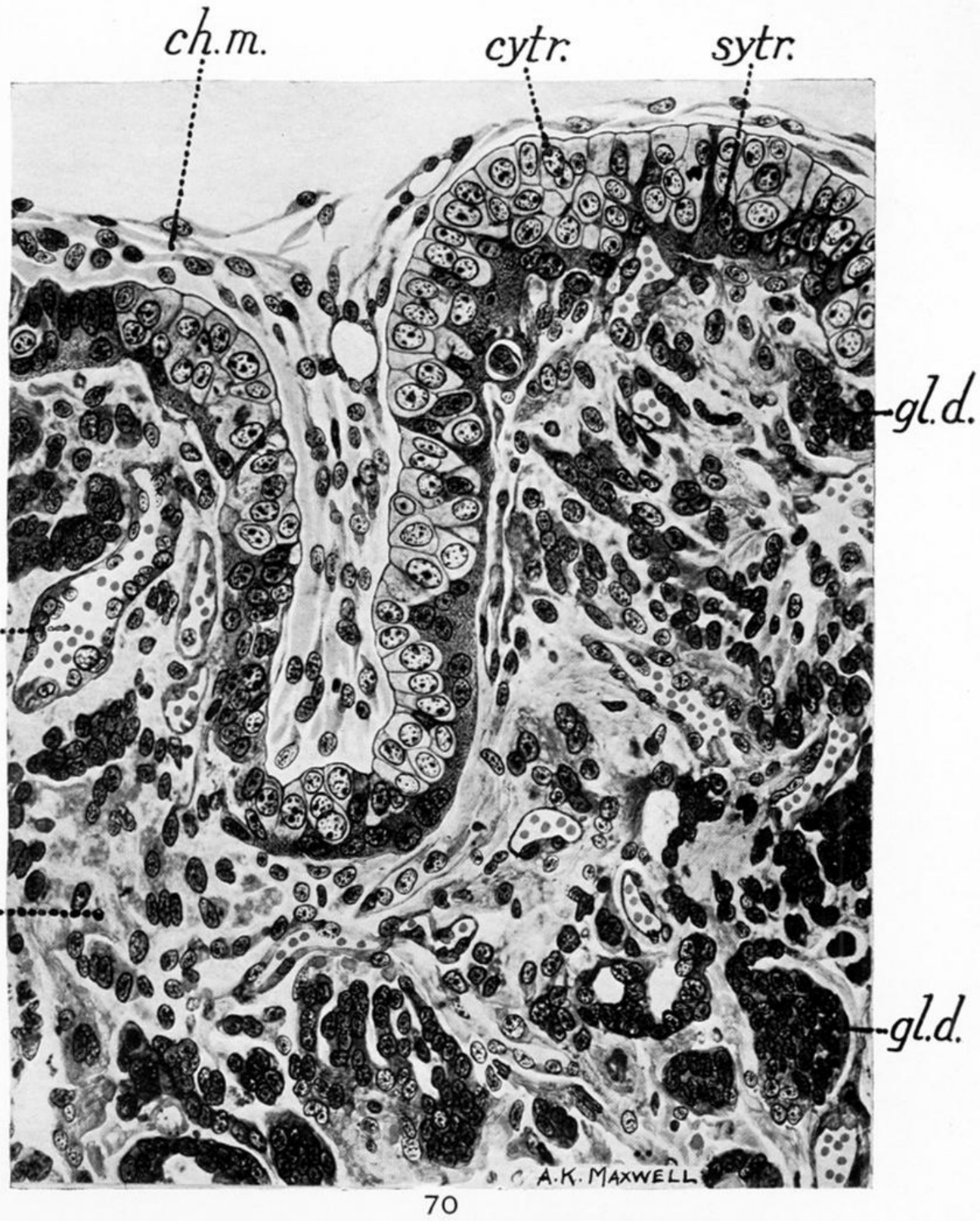

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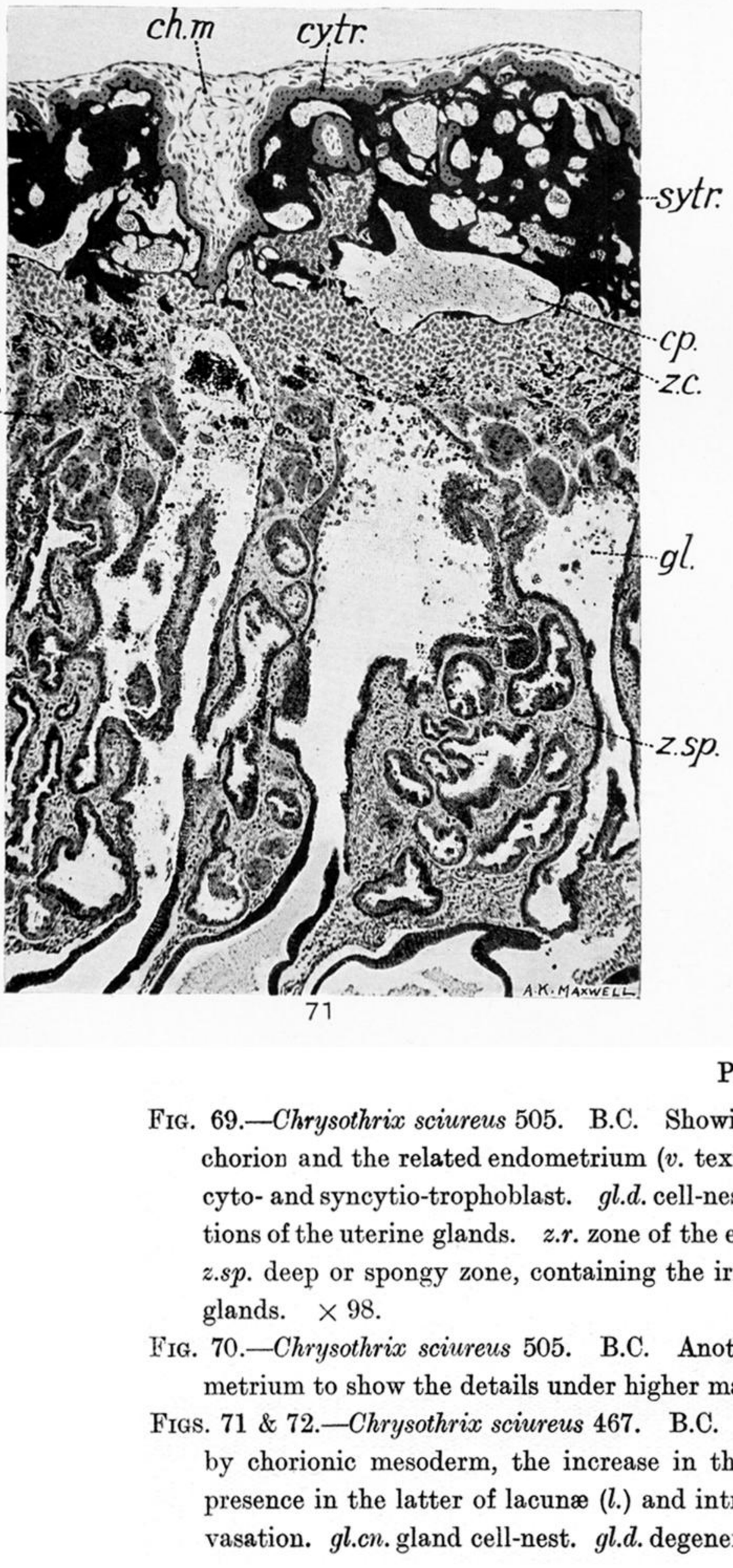

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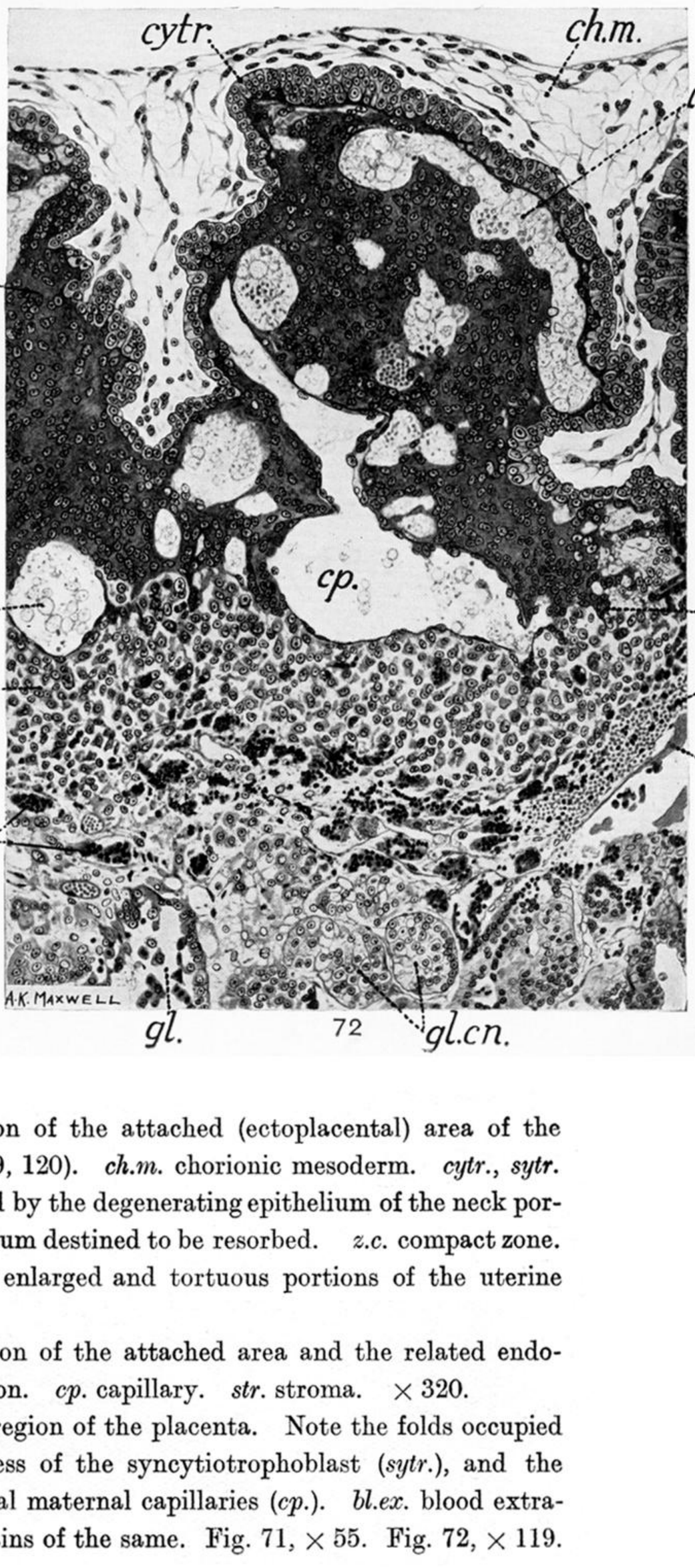

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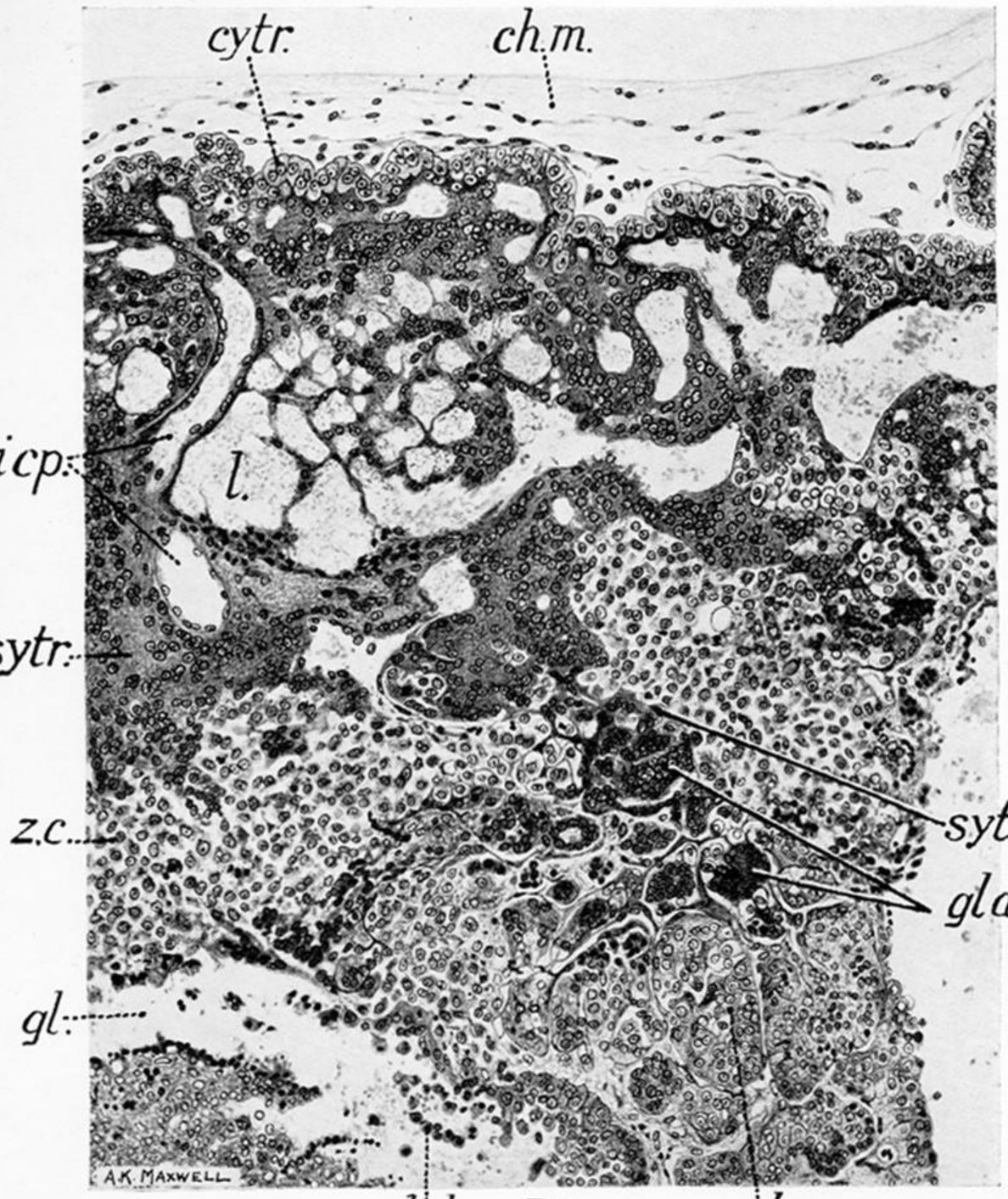
Plate 11.

Fig. 69.—*Chrysothrix sciureus* 505. B.C. Showing portion of the attached (ectoplacental) area of the chorion and the related endometrium (*v.* text, pp. 119, 120). *ch.m.* chorionic mesoderm. *cytr.*, *sytr.* cyto- and syncytio-trophoblast. *gl.d.* cell-nests formed by the degenerating epithelium of the neck portions of the uterine glands. *z.r.* zone of the endometrium destined to be resorbed. *z.c.* compact zone. *z.sp.* deep or spongy zone, containing the irregularly enlarged and tortuous portions of the uterine glands. × 98.

Fig. 70.—*Chrysothrix sciureus* 505. B.C. Another portion of the attached area and the related endometrium to show the details under higher magnification. *cp.* capillary. *str.* stroma. × 320.

Figs. 71 & 72.—*Chrysothrix sciureus* 467. B.C. Caudal region of the placenta. Note the folds occupied by chorionic mesoderm, the increase in the thickness of the syncytiotrophoblast (*sytr.*), and the presence in the latter of lacunæ (*l.*) and intraplacental maternal capillaries (*cp.*). *bl.ex.* blood extravasation. *gl.cn.* gland cell-nest. *gl.d.* degenerate remains of the same. Fig. 71, × 55. Fig. 72, × 119.



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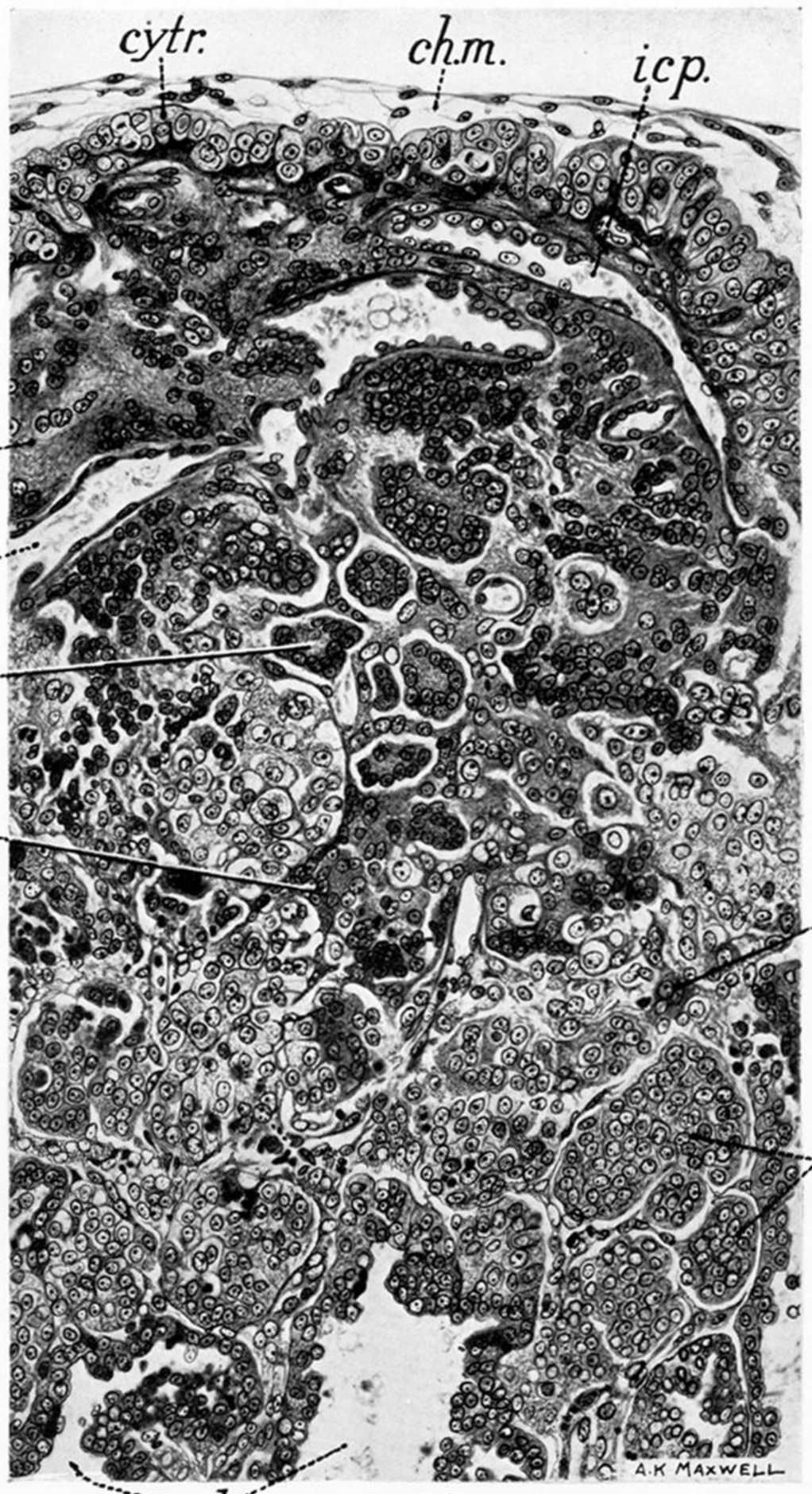
gl.d. gl.cn.



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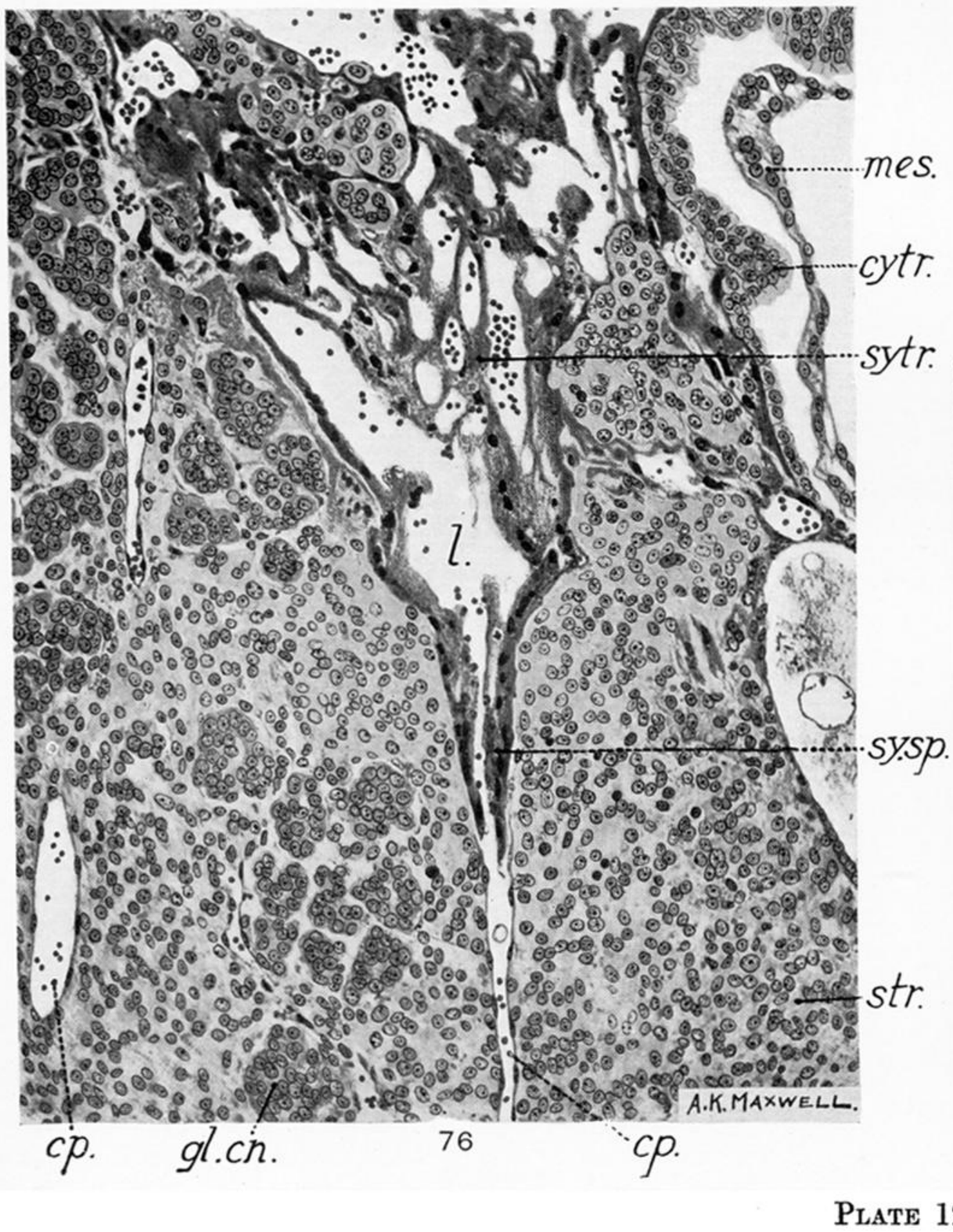
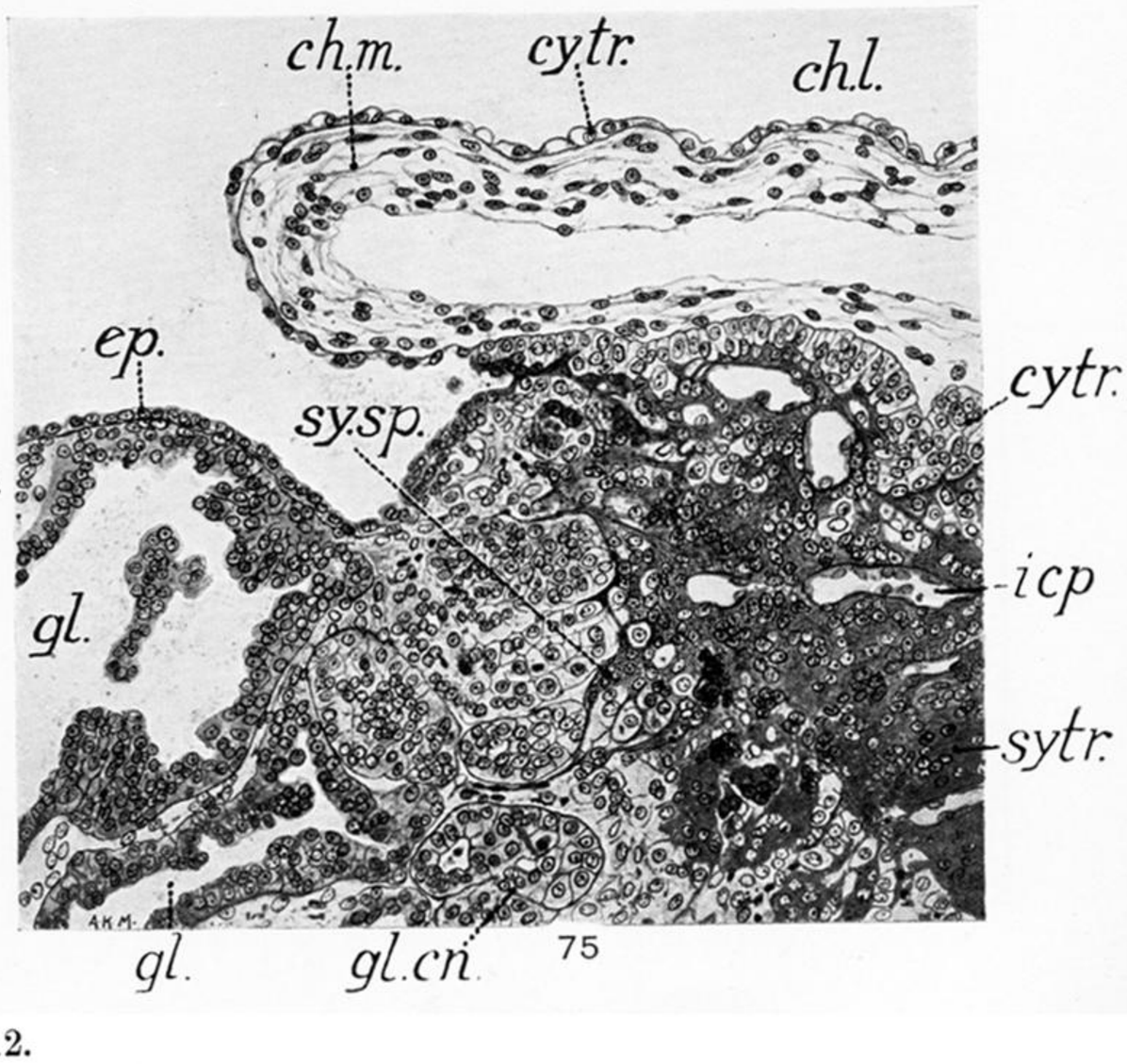


cp. gl.cn. 76 cp.



gl. gl.cn. 75

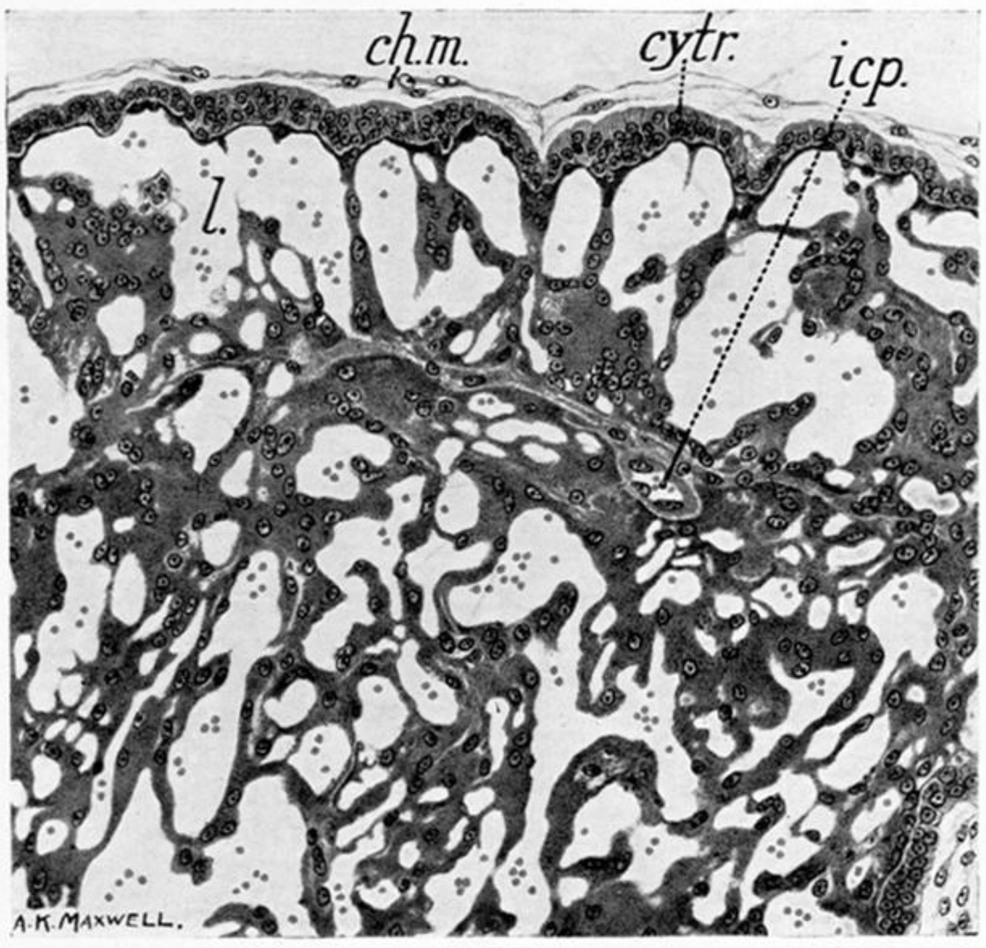
PLATE 12.

FIG. 73.—*Chrysothrix sciureus* 467. B.C. Portion of the anterior region of the placenta well in front of attachment of connecting stalk. Note the absence of the large "folds" or outgrowths met with in the posterior region, the reticular area of syncytiotrophoblast, and the irregular prolongations of the latter into the compact zone (*z.c.*), one such prolongation enclosing degenerate masses of gland-epithelium (*gl.d.*). × 119.

FIG. 74.—*Chrysothrix sciureus* 467. B.C. Another portion of the placenta from its anterior region. The syncytiotrophoblast is here less massive, but is seen to be produced into a well-marked prolongation enclosing degenerate remains of the uterine glands (*gl.d.*). In the lower part of the section note the numerous gland cell-nests (*gl.cn.*). × 198

FIG. 75.—*Chrysothrix sciureus* 467. B.C. Margin of placenta. Note the abrupt junction of the cyto-trophoblast of the placental area with that of the unattached chorion (chorion læve) (*ch.l.*), the greatly enlarged glands outside the placental area (*gl.*) and the gland cell-nests (*gl.cn.*). × 147·5

FIG. 76.—*Cebus macrocephalus* 509. B.C. Portion of marginal region of placenta, showing the invasion of a maternal capillary by a hollow sprout (*syn.sp.*) of the reticular syncytiotrophoblast (*sytr.*). × 153.



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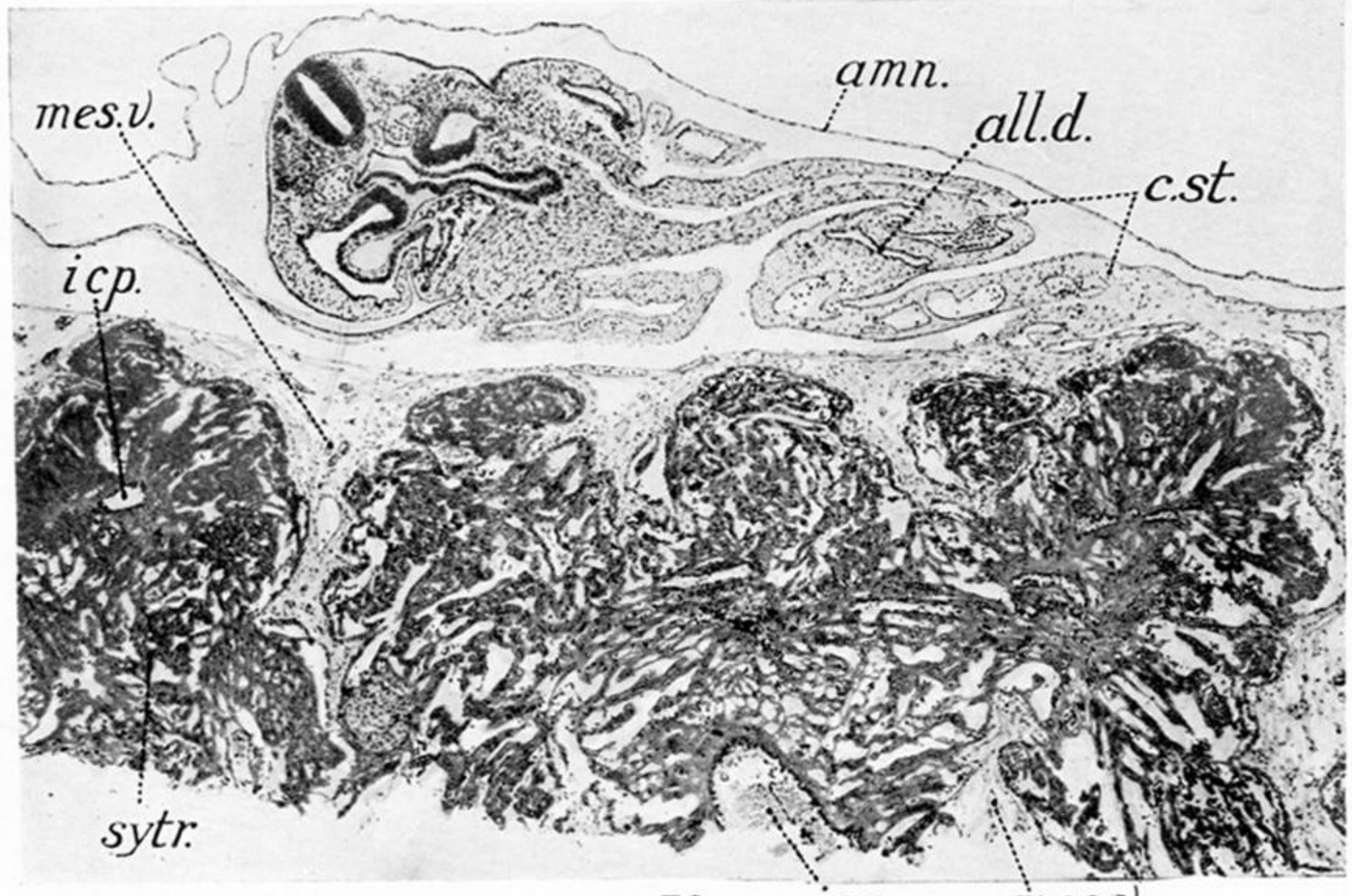

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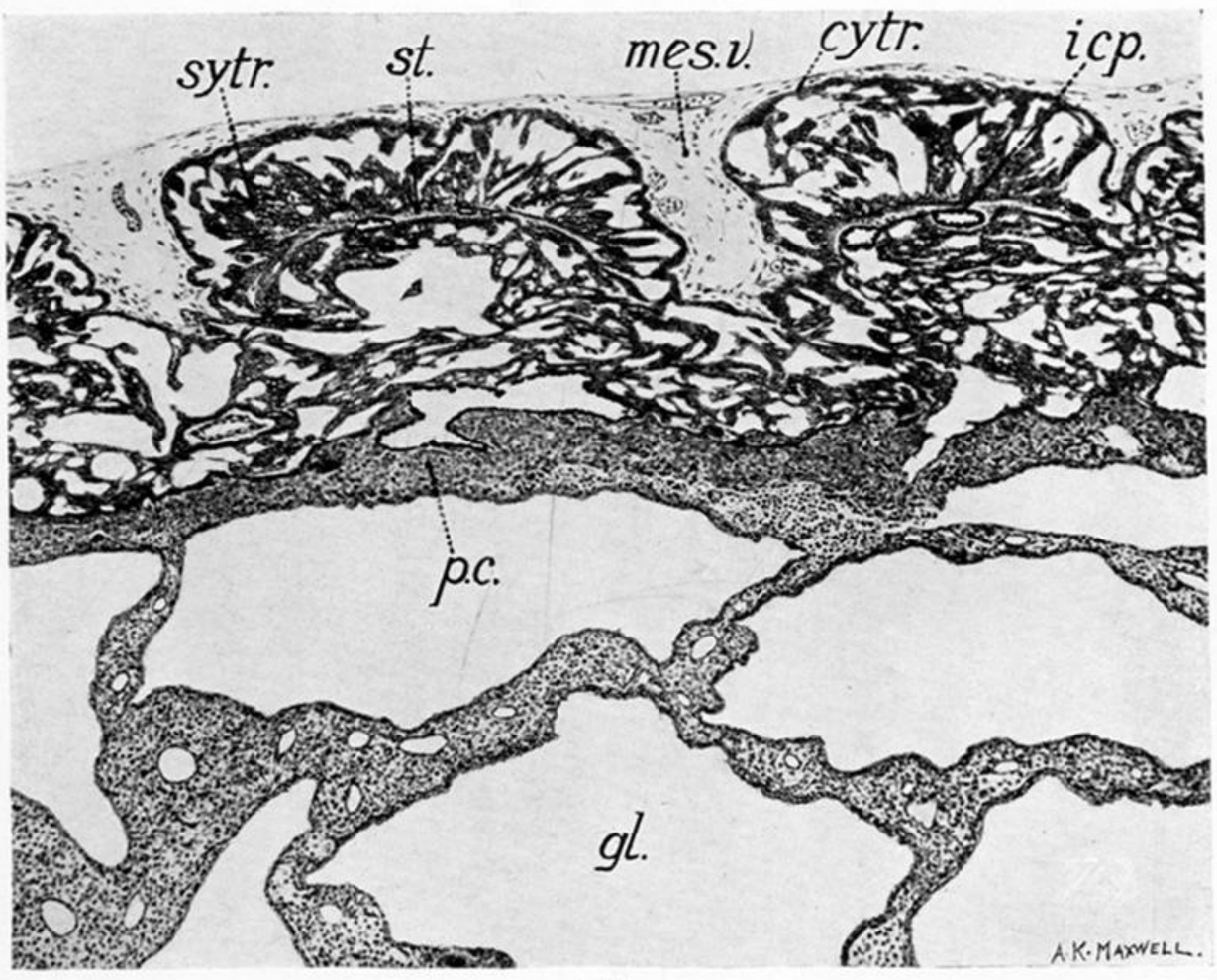

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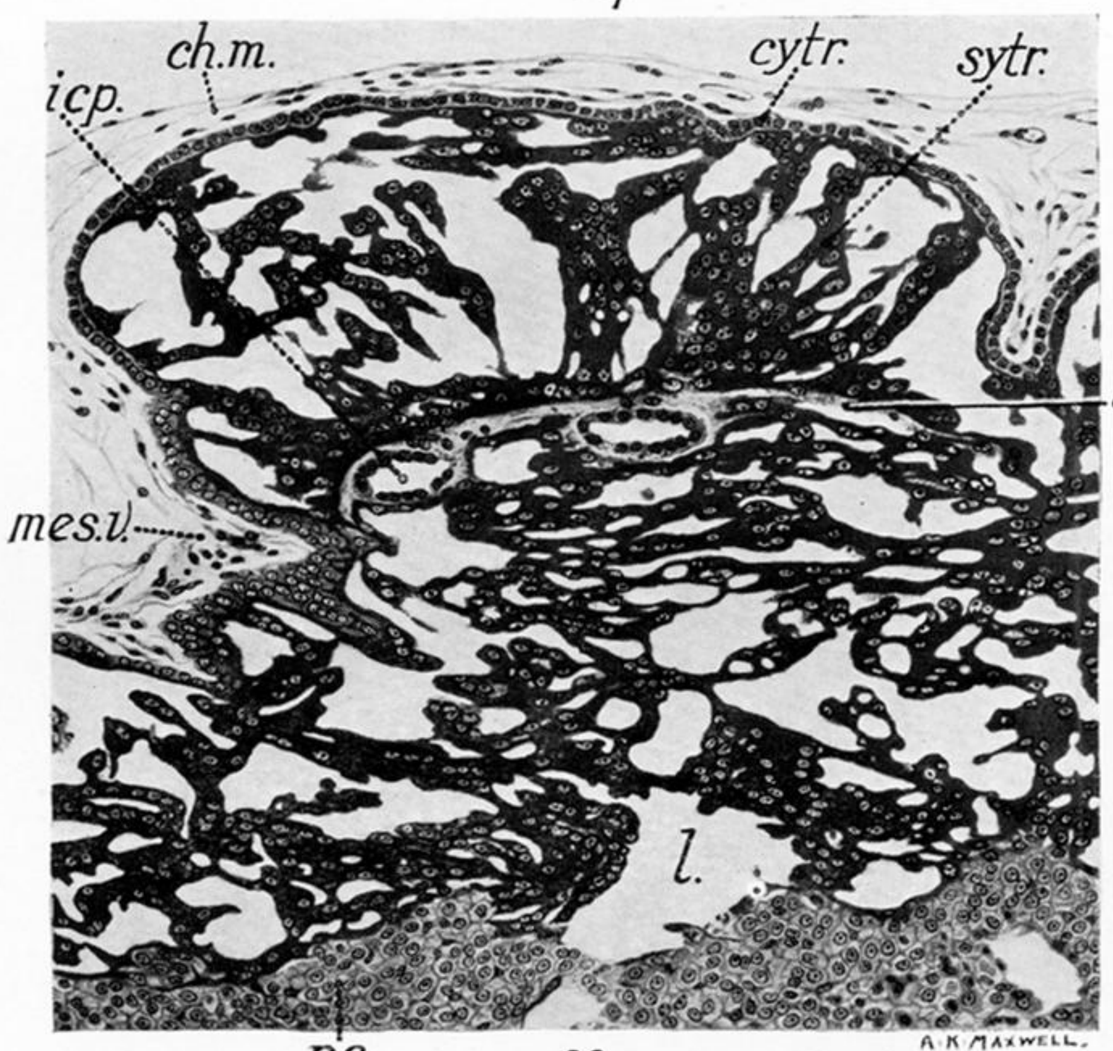

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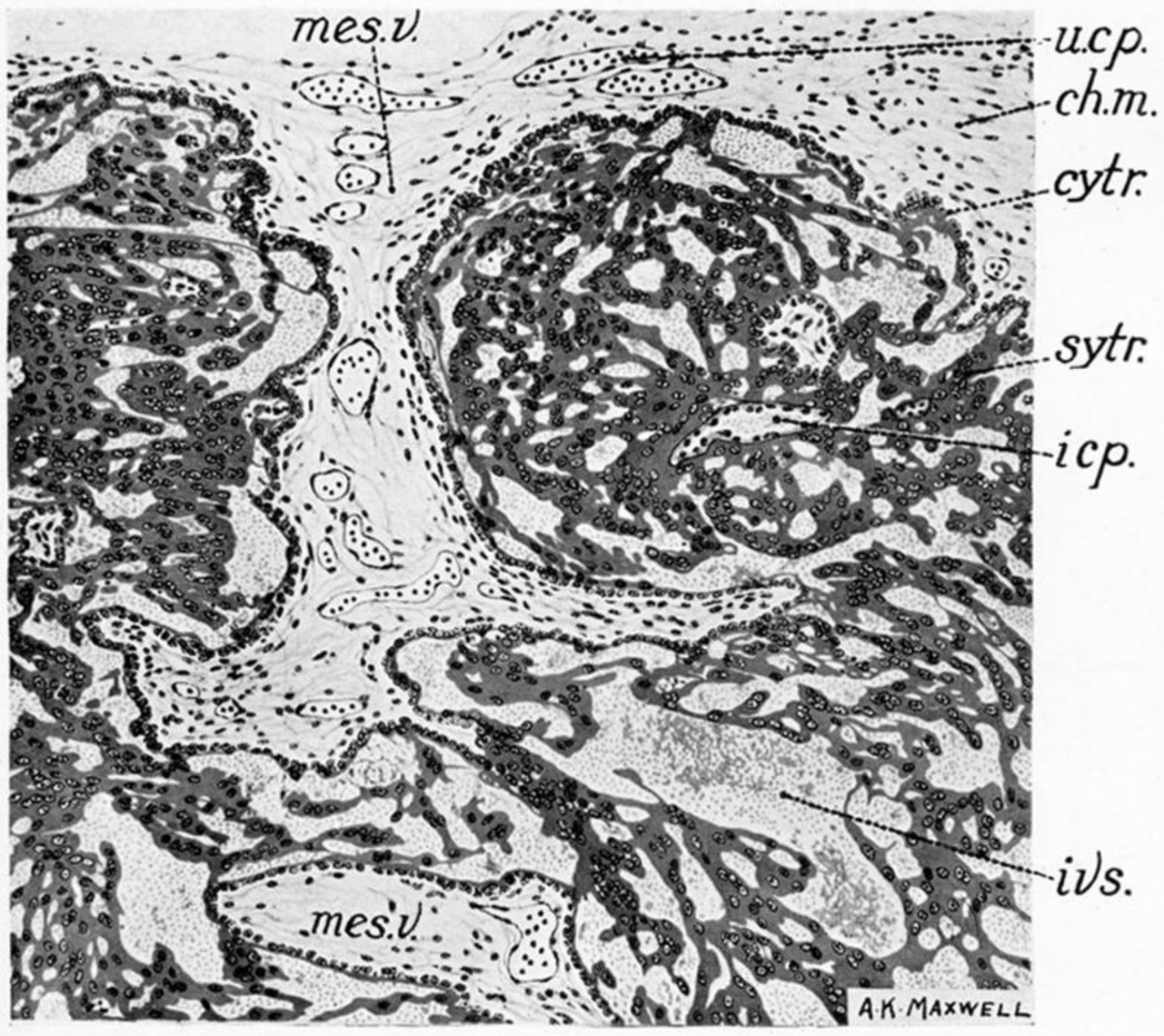

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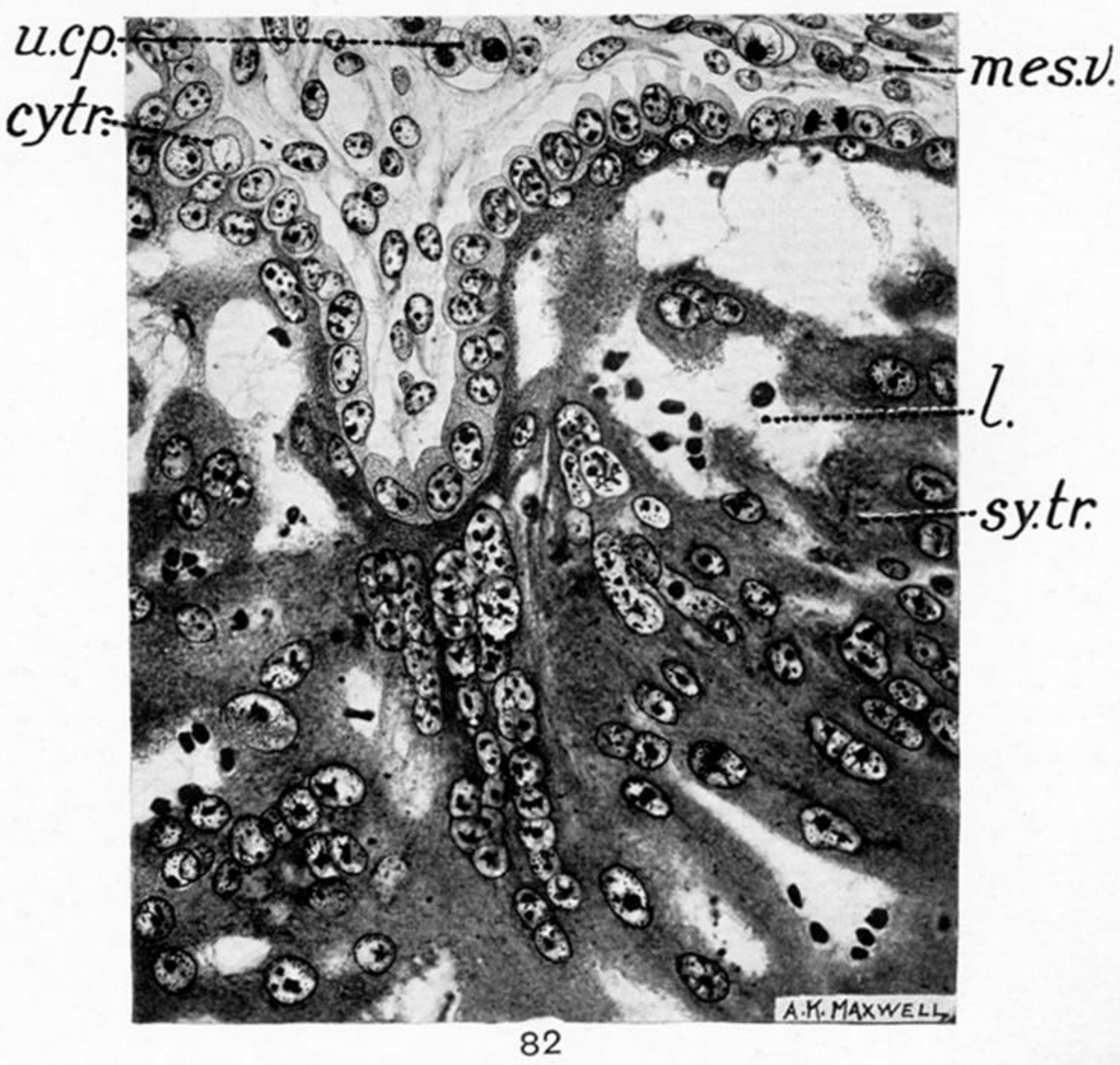

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PLATE 13.

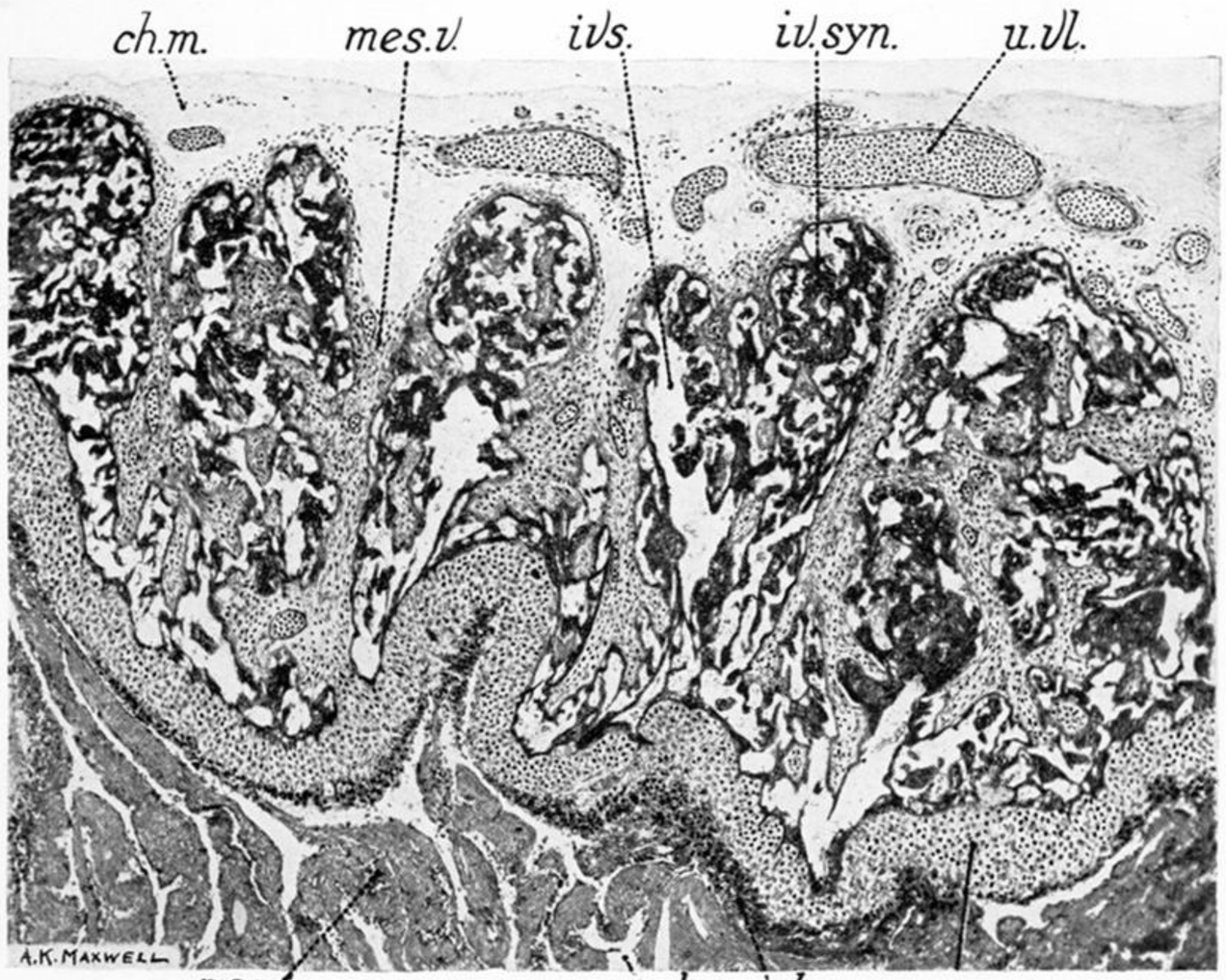
FIG. 77.—*Cebus macrocephalus* 509. B.C. Superficial zone of the ectoplacental trophoblast showing the cytotrophoblast (*cytr.*) and the syncytiotrophoblast which is coarsely reticular in character, its lacunæ (*l.*) containing maternal blood. *icp.* intraplacental capillary. × 123.

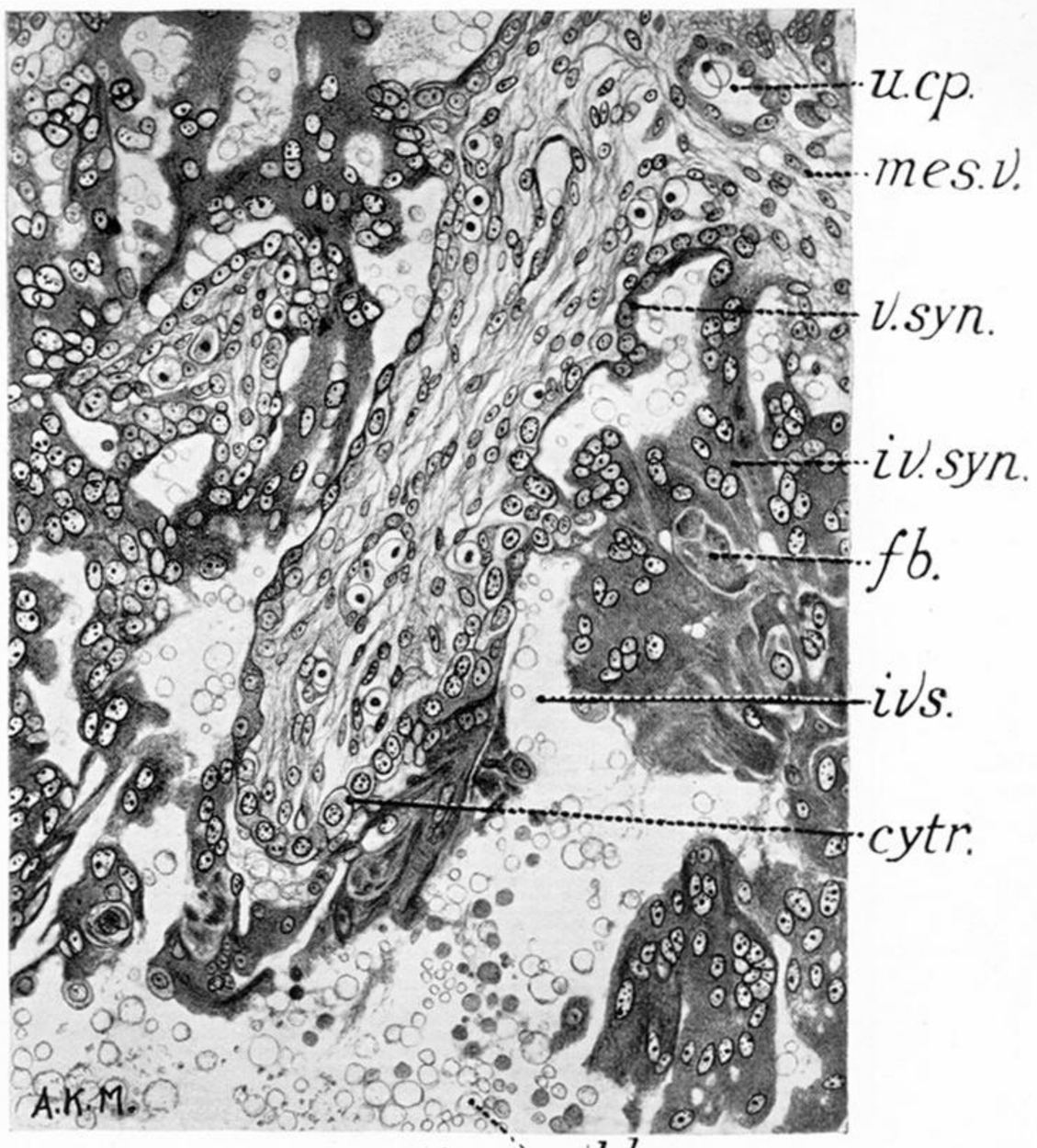
FIG. 78.—*Cebus gracilis* 475. B.C. Transverse section of embryo and adjoining portion of the placenta fœtalis, showing its lobulation and the massive character of the syncytiotrophoblast (*sytr.*). *all.d.* allantoic canal. *c.st.* connecting stalk. *icp.* intraplacental capillary. *mes.v.* mesodermal axis of chorionic villus. ×32·5.

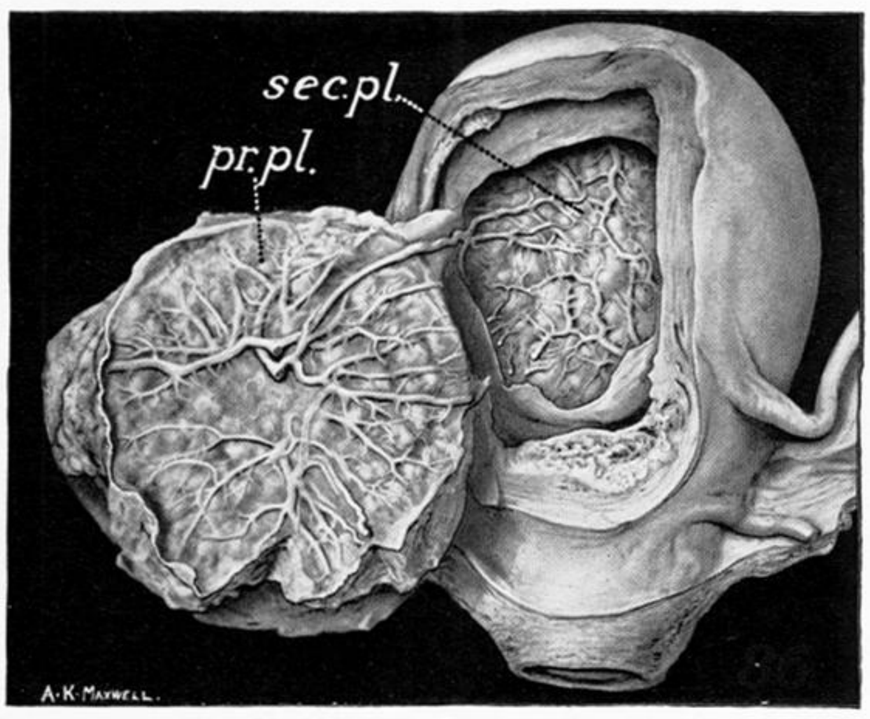
FIGS. 79 & 80.—*Cebus gracilis* 475. B.C. Low and high power views of portion of secondary placenta. Note its lobulated character, the pars compacta (*p.c.*) containing large numbers of degenerate cells and the greatly enlarged glands (*gl.*) of the pars spongiosa. *st.* syncytial tract in proximity to which intraplacental capillaries (*icp.*) and small masses of decidual cells are situated (see text, p. 125). Fig. 79, × 41. Fig. 80, × 99.

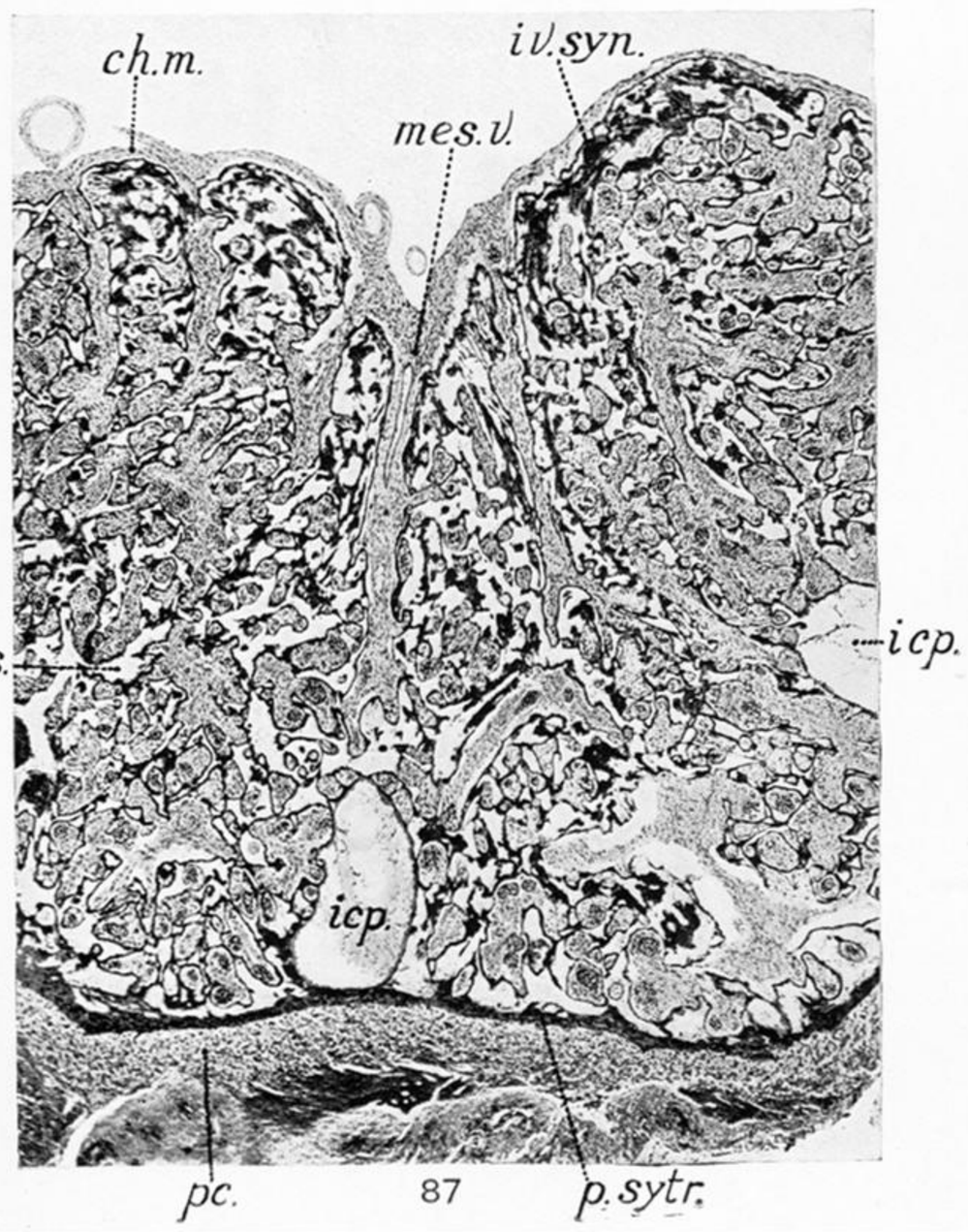
FIG. 81.—*Cebus gracilis* 475. B.C. Portion of the primary placenta illustrating the branching character of the chorionic villi (*mes.v.*). *ivs.* lacunar (later intervillous) blood-space. *u.cp.* umbilical capillary. × 78·5.

FIG. 82.—*Cebus gracilis* 475. B.C. Section of a commencing villous branch, showing its mesodermal axis (*mes.v.*) and its investing layer of cytotrophoblast (*cytr.*). *sytr.* syncytiotrophoblast. *l.* lacuna. × 356.









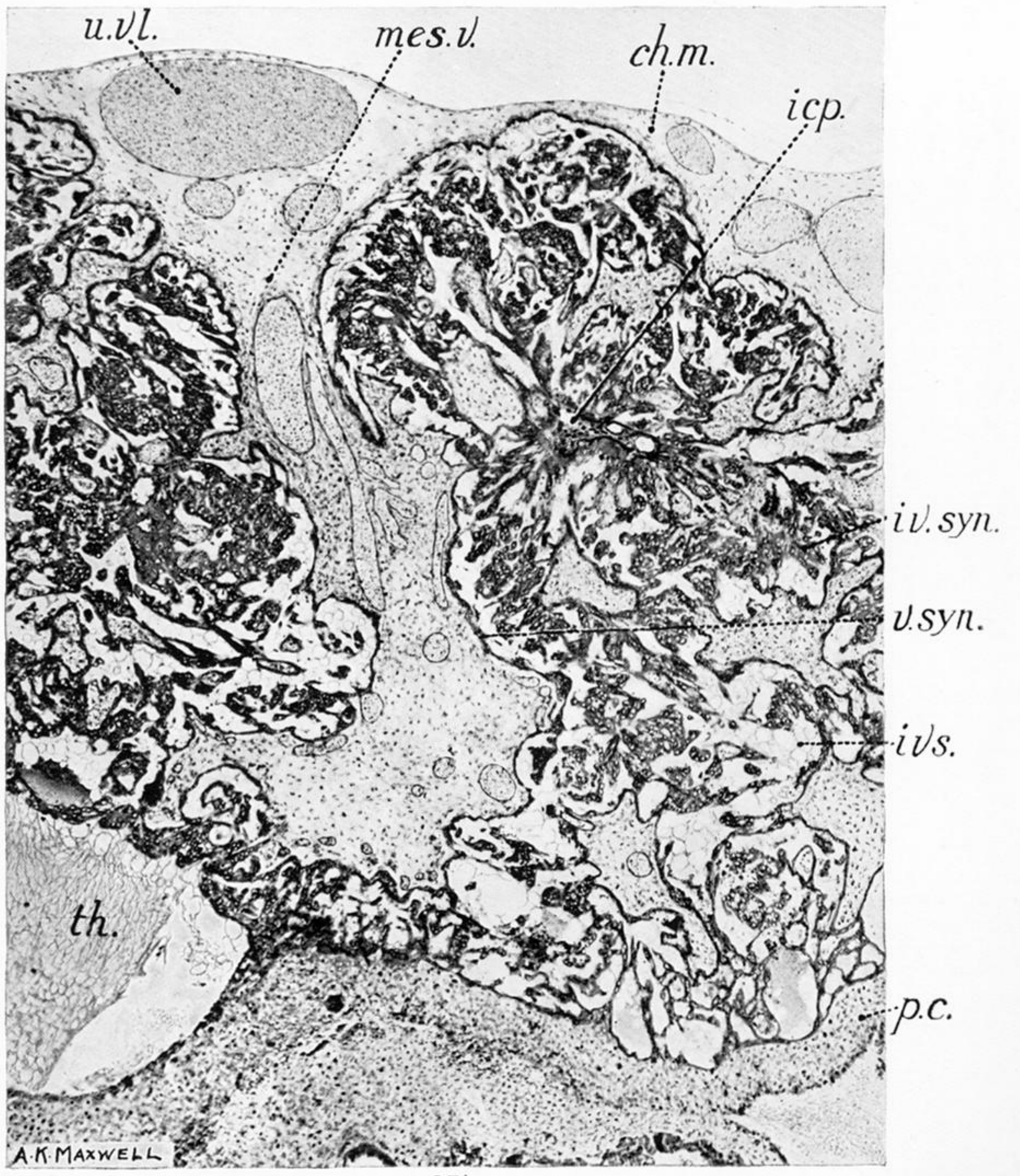


PLATE 14.

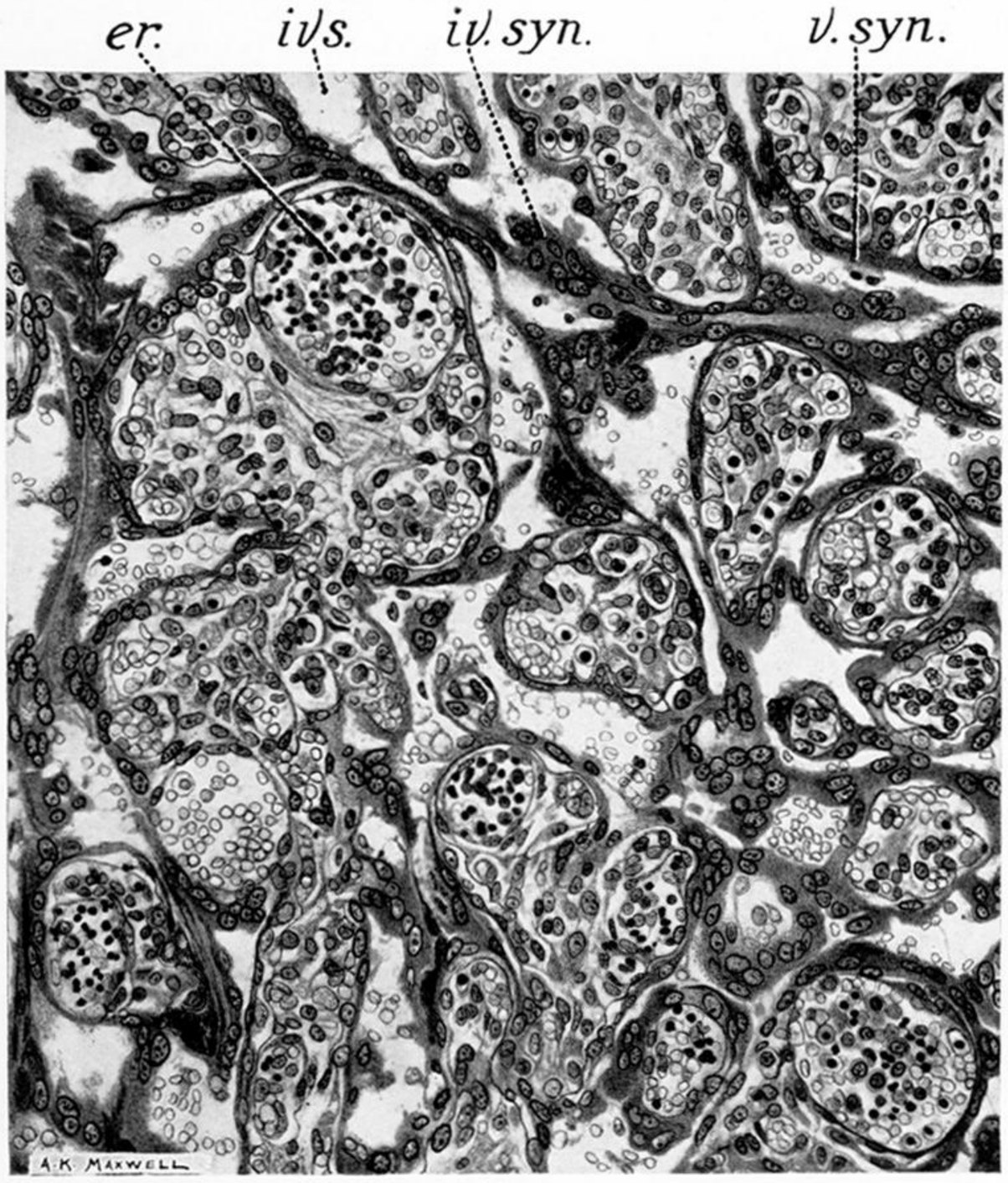
FIG. 83.—*Chrysothrix nigrivittatus* 600. B.C. Section through the primary (ventral) placenta, showing the branching chorionic villi (*mes.v.*), the intervillous syncytium (*iv.syn.*), the pars compacta (*p.c.*), with degenerating cells (*dg.c.*) specially abundant on its deep surface and the pars spongiosa (*p.sp.*). *u.vl.* umbilical vessel in the chorionic mesoderm (*ch.m.*). × 38·5.

FIG. 84.—*Chrysothrix nigrivittatus* 600. B.C. Section of a villous branch, specially to show its relations to the intervillous syncytium (*iv.syn.*). *fb.* fibrinoid. *ivs.* intervillous blood-space. *vbl.* vesicular blood corpuscle. × 220.

FIG. 85.—*Cebus macrocephalus* 528. B.C. Section through the secondary (dorsal) placenta. The intervillous syncytium (*iv.syn.*) is still strongly marked. *th.* thrombus in a large blood-space. × 51.

FIG. 86.—*Cebus macrocephalus* 528. B.C. Pregnant uterus opened, displaying the primary (ventral) placenta (*pr.pl.*) on the left and the secondary (dorsal) placenta (*sec.pl.*). The cut stems of the umbilical vessels supplying the primary placenta are seen just above the centre of the latter. Note the radiating arrangement of the vessels on the surface of the primary placenta and the interplacental vessels passing over its right margin to supply the secondary placenta.

FIG. 87.—*Chrysothrix nigrivittatus* 648. B.C. Section through the primary (ventral) placenta. Note the reduction of the intervillous syncytium (*iv.syn.*) and the increase of the villous stems (*mes.v.*) and their branches. *icp.* intraplacental capillary. *p.c.* pars compacta. *p.sytr.* peripheral (basal) syncytium. × 28.



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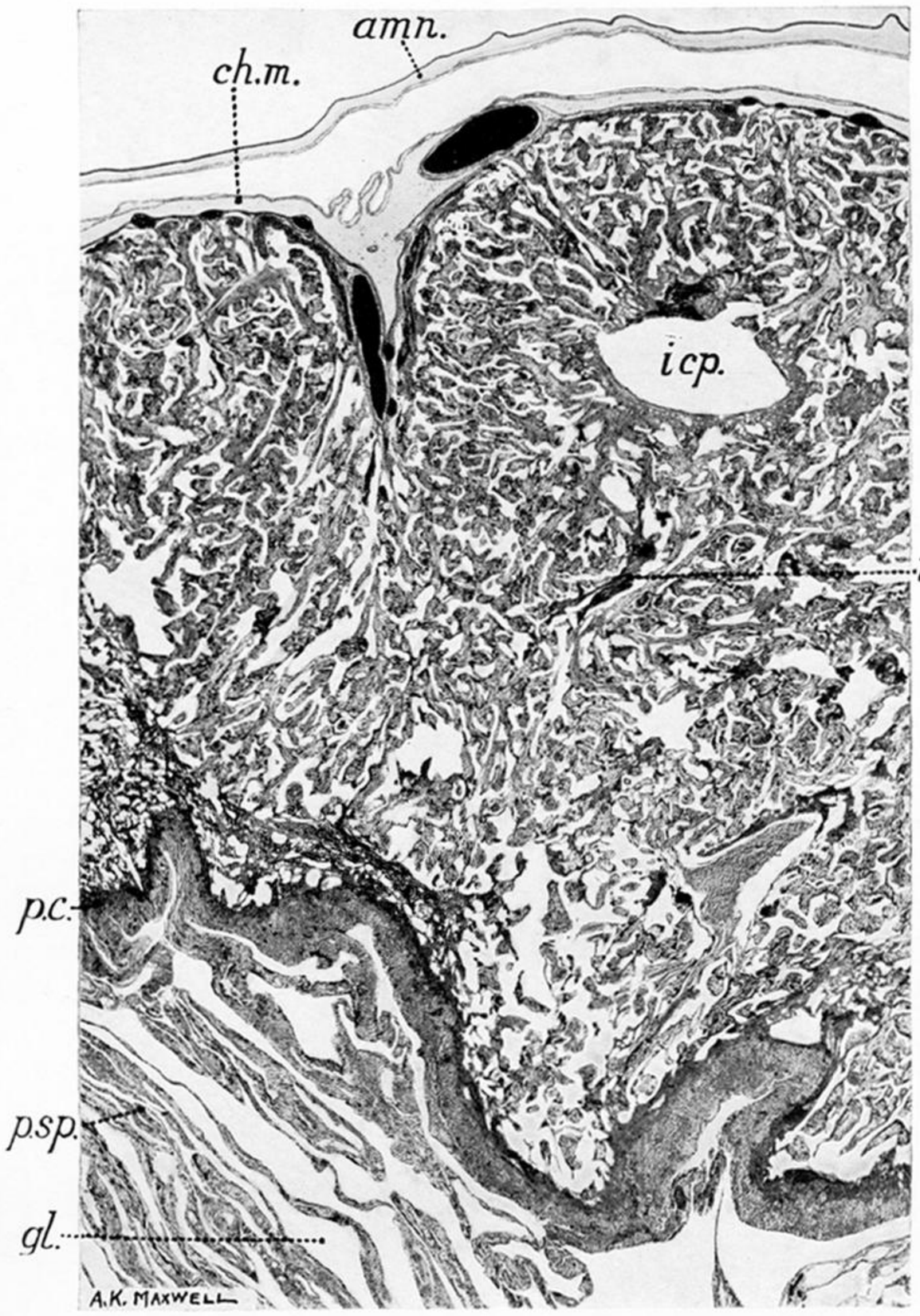

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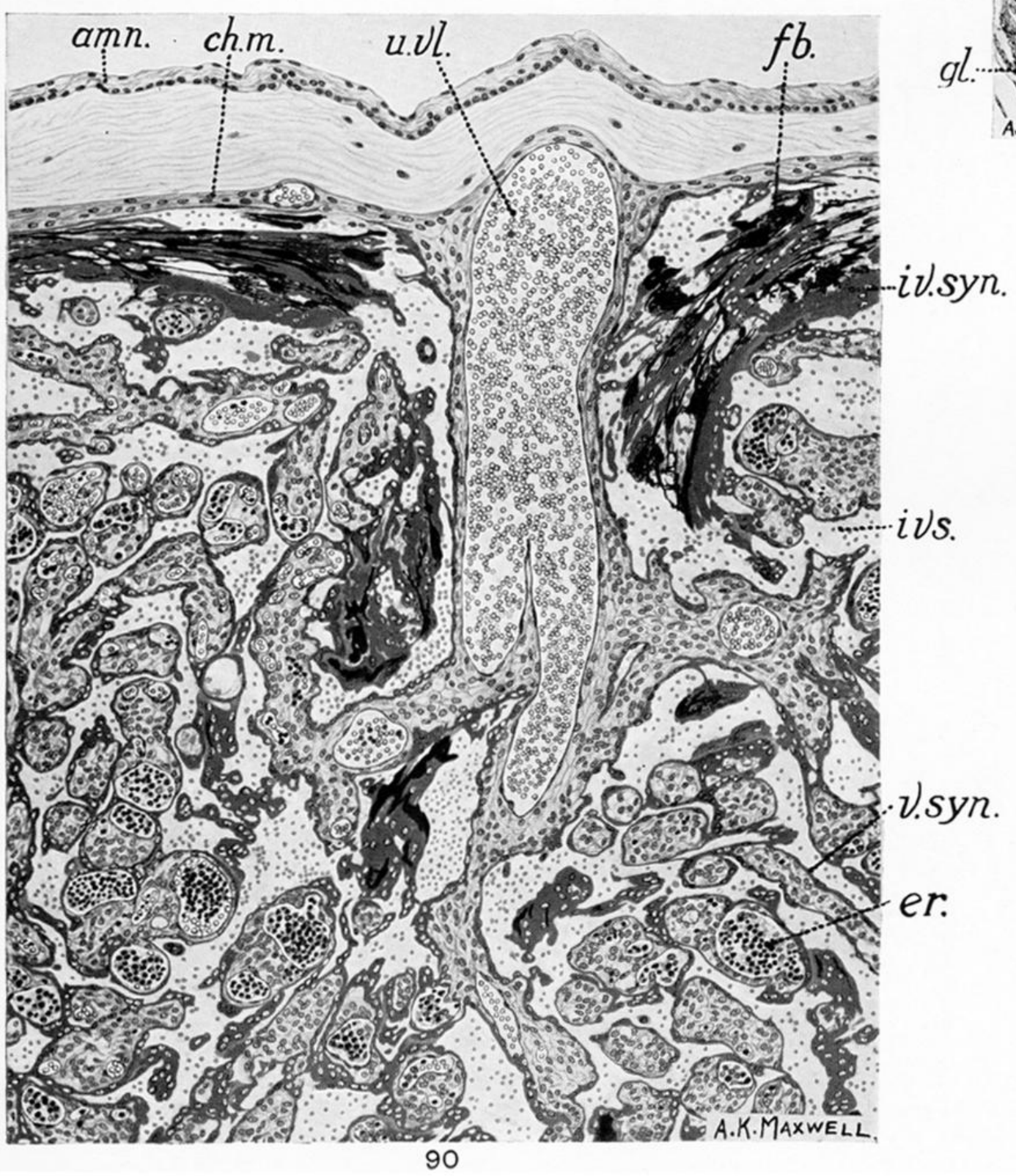

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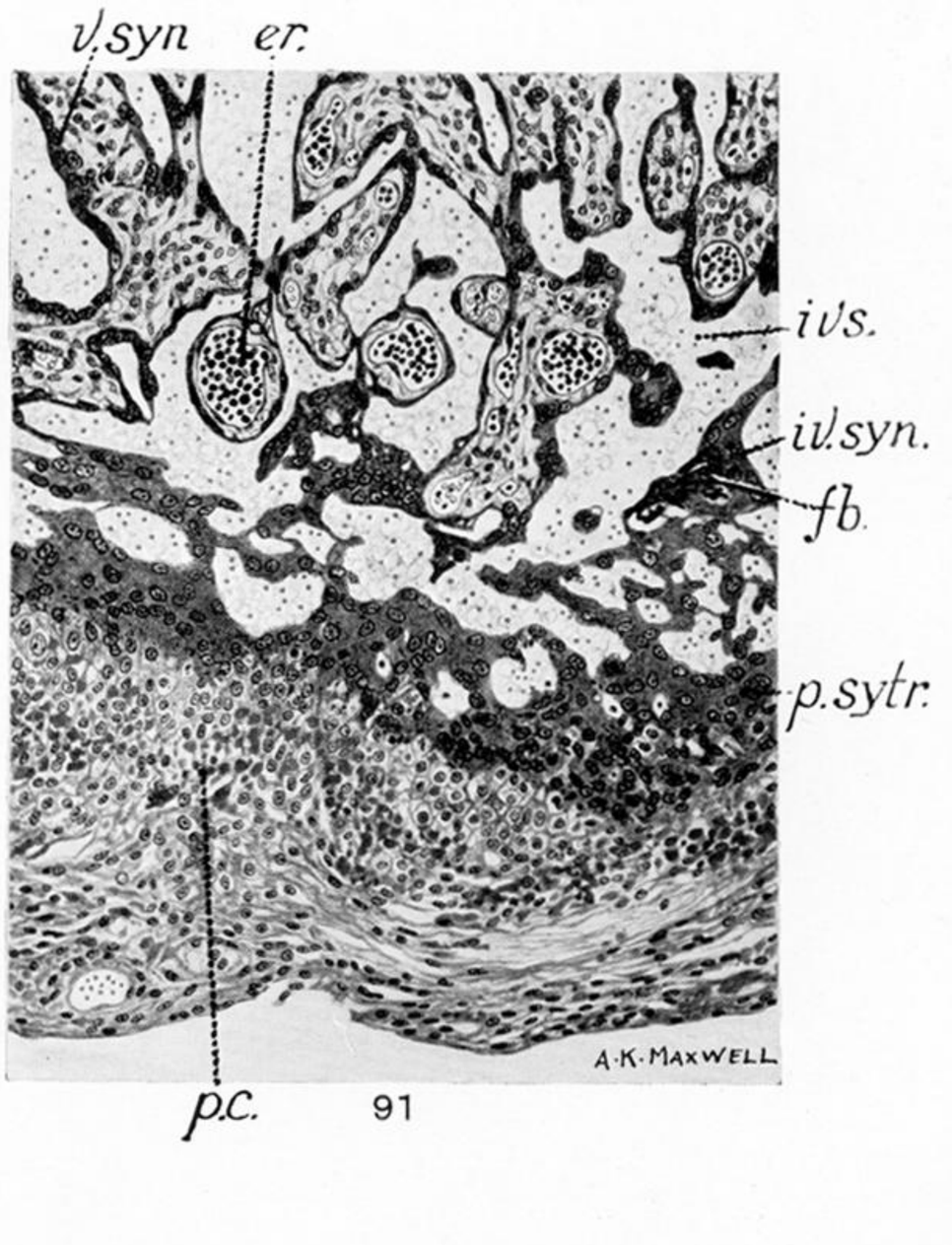

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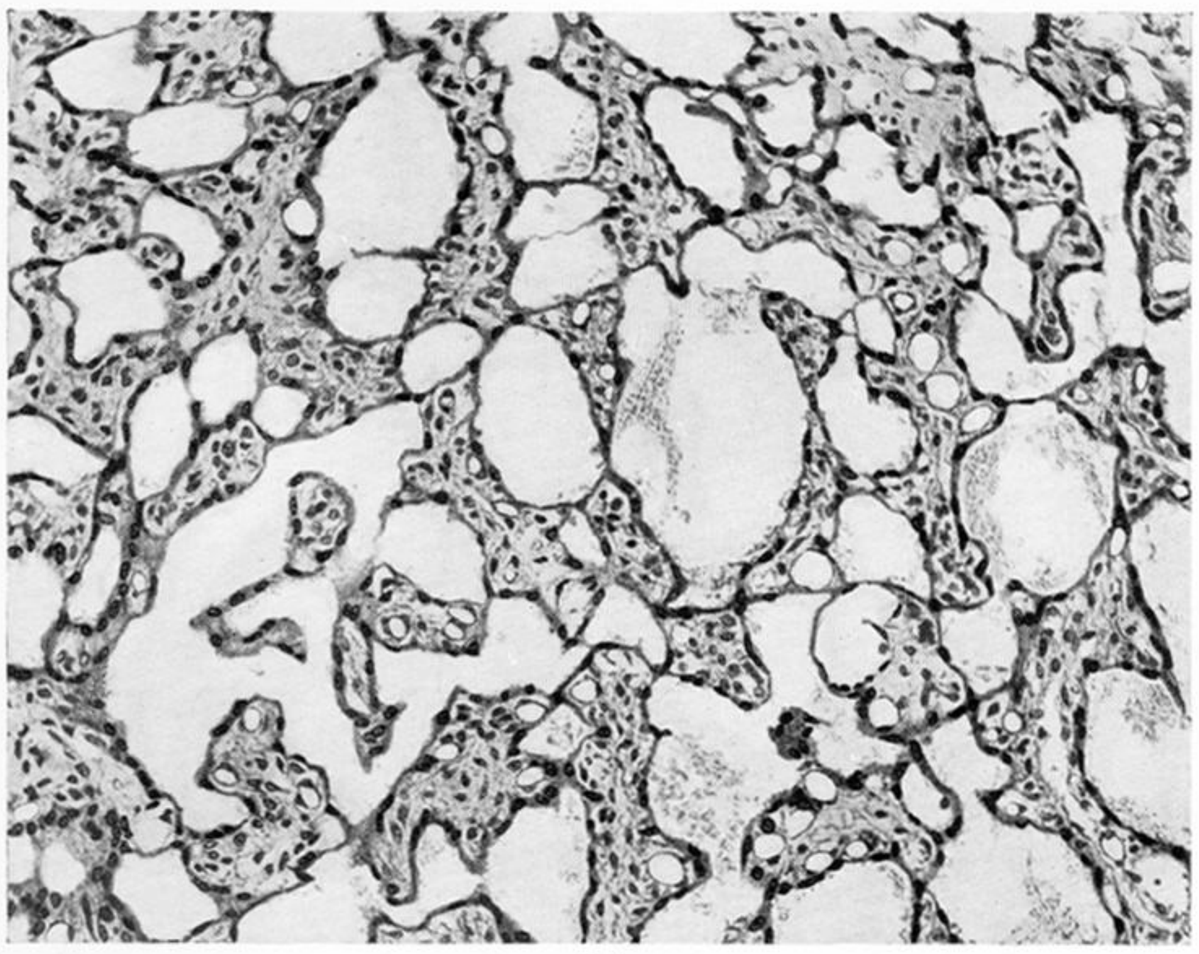
PLATE 15.

FIG. 88.—*Chrysothrix nigrivittatus* 648. B.C. Villous branches of the primary placenta seen in section. They are invested by a thin layer of villous syncytium (*v.syn.*) and are connected up into an irregular network partly by direct anastomosis but mainly by strands of intervillous syncytium (*iv.syn.*). *er.* erythropoiesis in an enlarged umbilical capillary. × 230.

FIG. 89.—*Cebus gracilis* 474. B.C. Placenta as seen in section under low magnification. Note the compactly arranged villous branches and the large intraplacental capillaries (*icp.*). ×17·5.

FIG. 90.—*Cebus gracilis* 474. B.C. Superficial portion of the placenta, showing the amnion (*amn.*), chorion (*ch.*), a villous stem, occupied by a large umbilical vessel (*u.vl.*) and the villous branches, many of them containing enlarged capillaries (*er.*) in which erythropoiesis is in active progress. *iv.syn.* intervillous syncytium, frequently transformed into fibrinoid (*fb.*). × 98.

FIG. 91.—*Cebus gracilis* 474. B.C. Deep zone of the placenta. *p.sytr.* peripheral syncytium, here quite thick. *p.c.* pars compacta. × 98.



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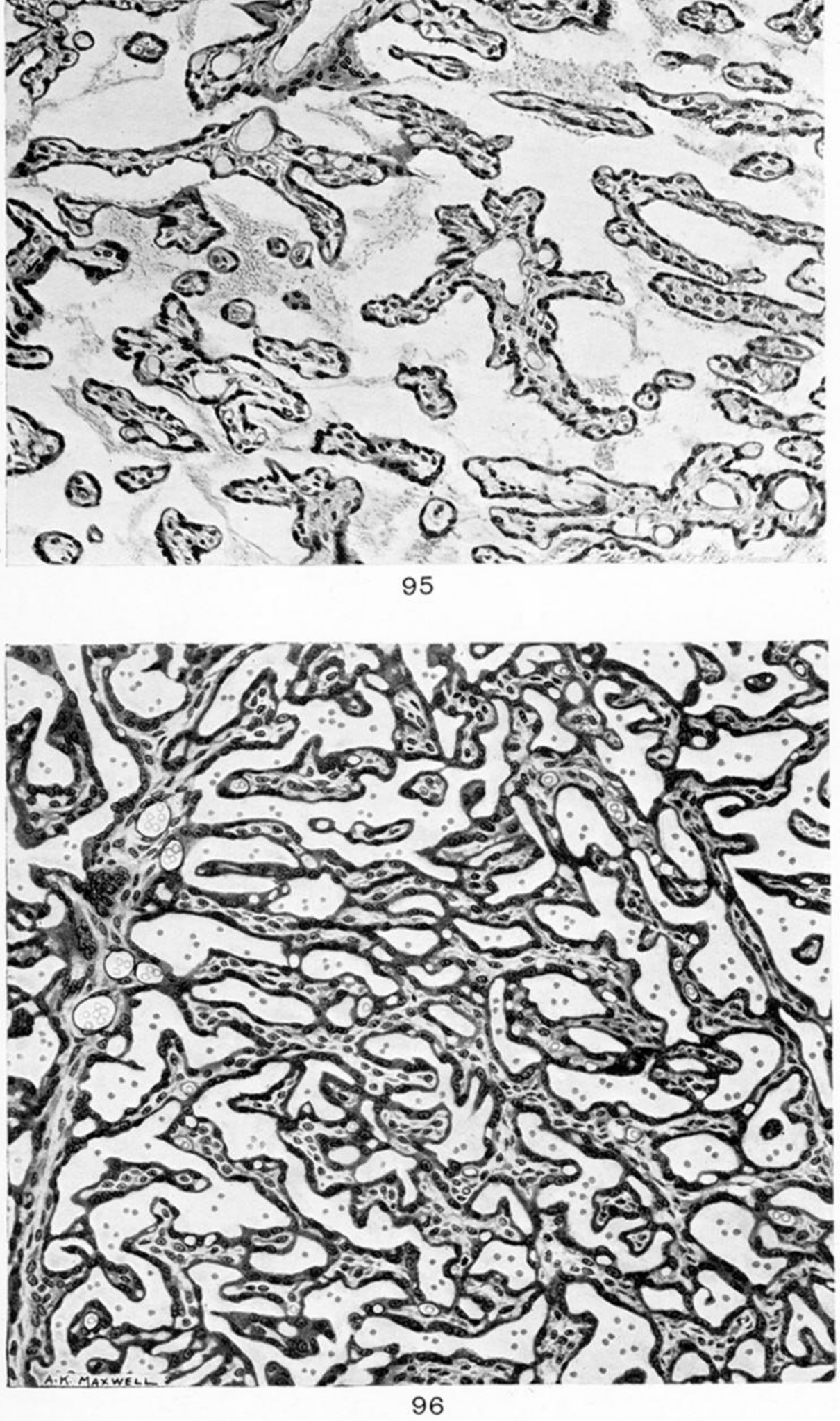

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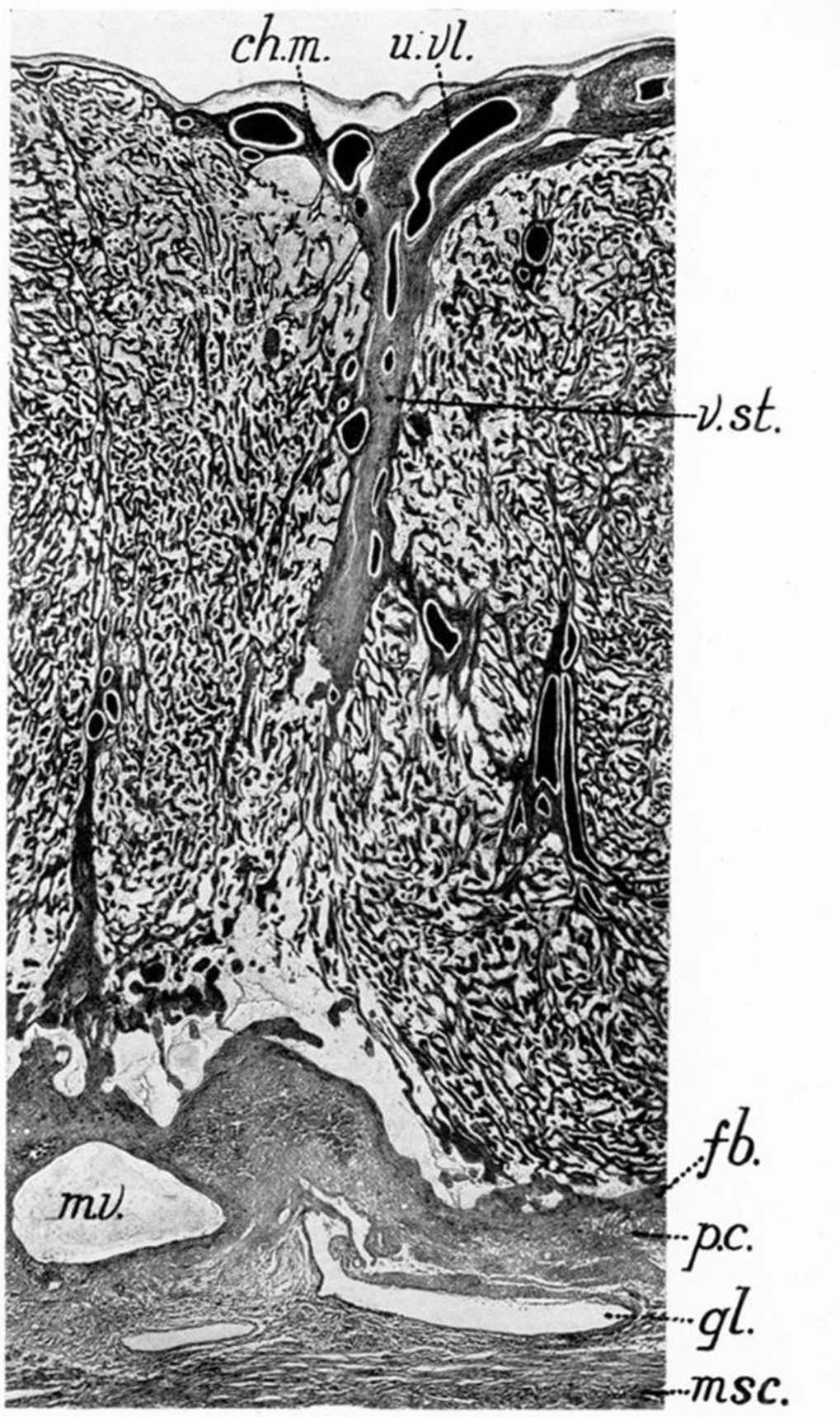

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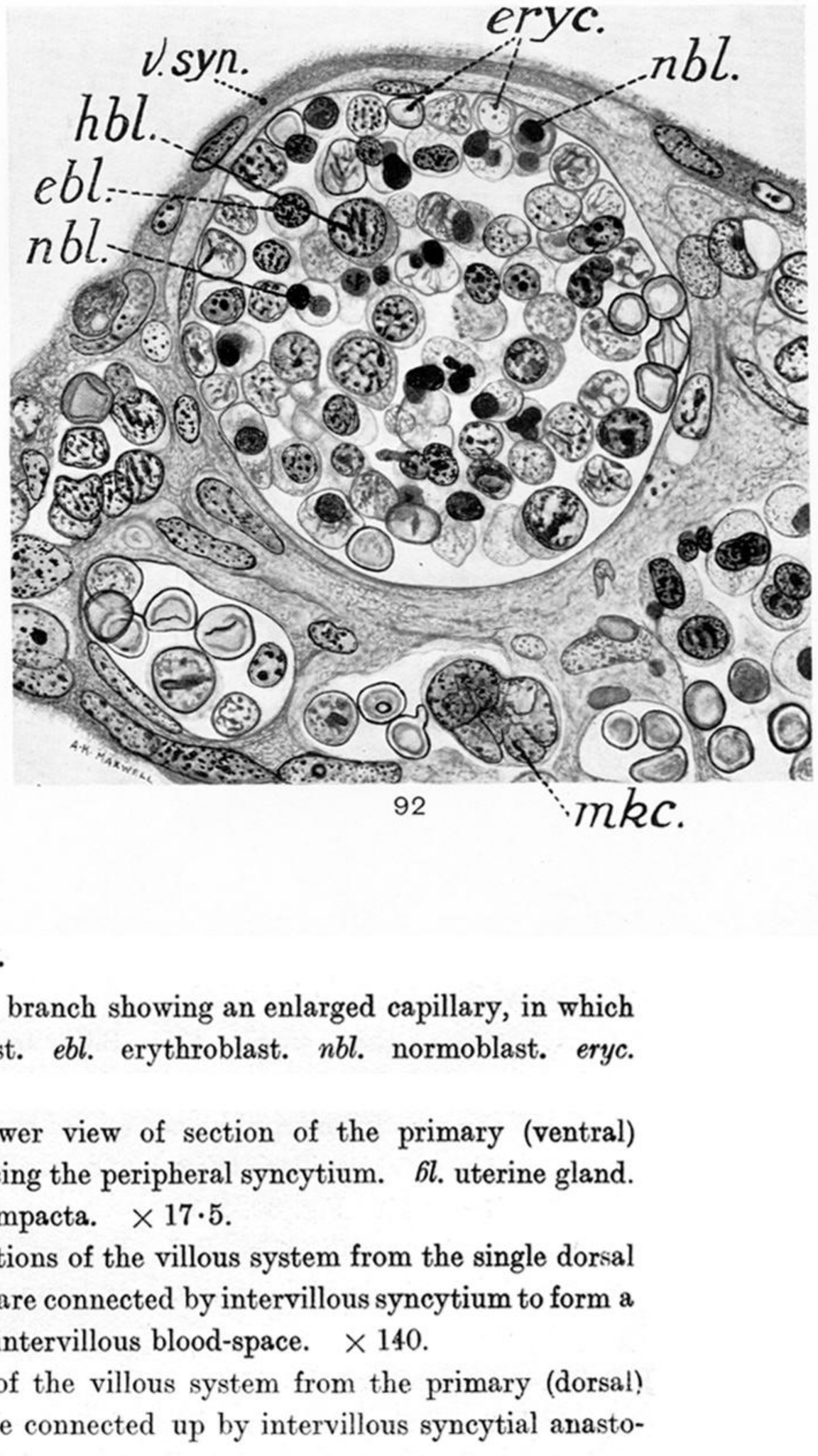

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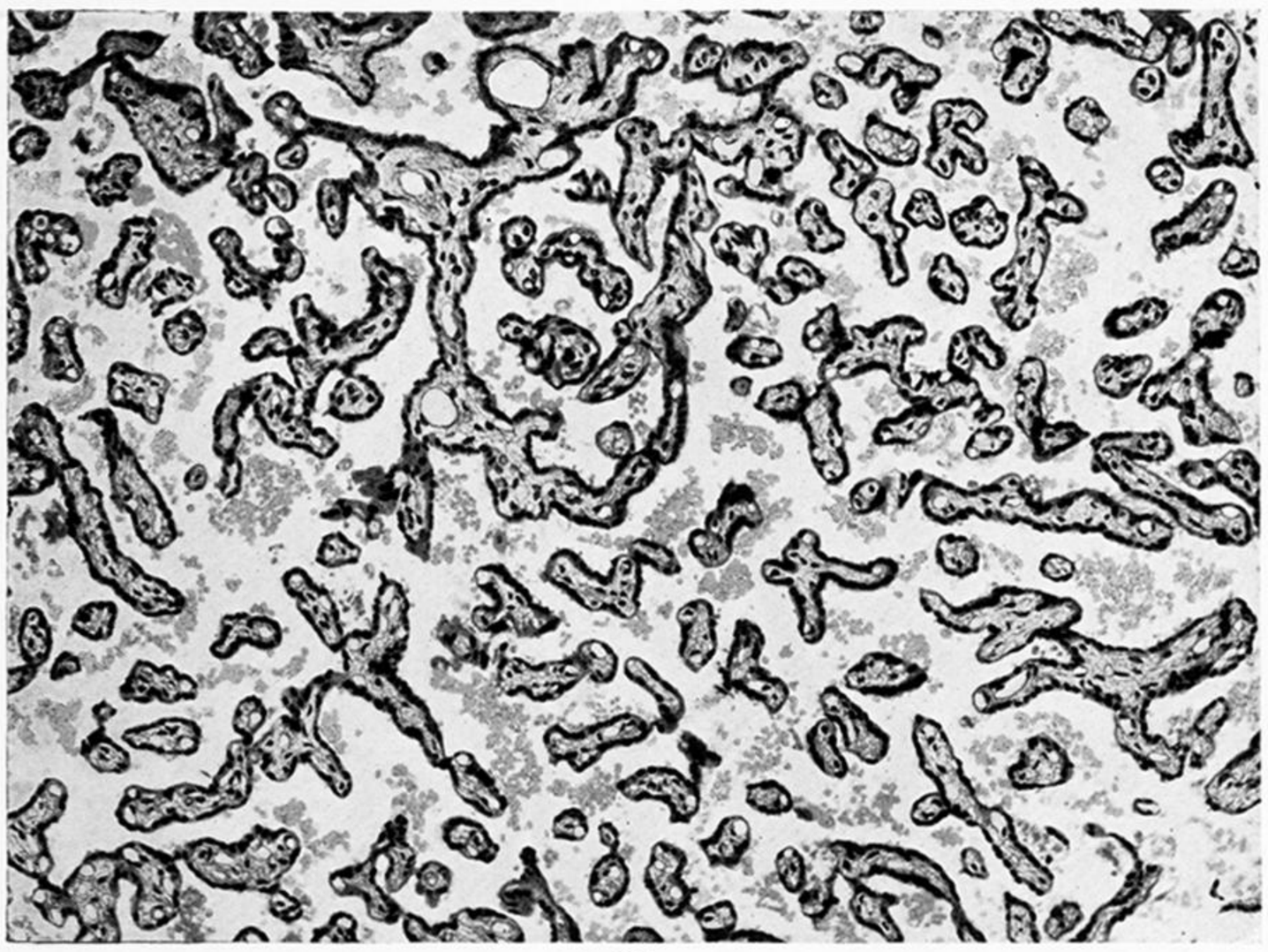
PLATE 16.

FIG. 92.—*Cebus gracilis* 474. B.C. Portion of a villous branch showing an enlarged capillary, in which erythropoiesis is in progress. *hbl.* hemocytoblast. *ebl.* erythroblast. *nbl.* normoblast. *eryc.* erythrocyte. *mkc.* megakaryocyte.

FIG. 93.—*Chrysothrix nigrivittatus* 31*a*. B.C. Low power view of section of the primary (ventral) placenta. *ch. m.* chorion. *fb.* fibrinoid largely replacing the peripheral syncytium. *gl.* uterine gland. *m.v.* maternal vessel. *msc.* muscularis. *p.c.* pars compacta. × 17·5.

FIGS. 94 & 95.—*Chrysothrix nigrivittatus* 816. B.C. Portions of the villous system from the single dorsal placenta. In fig. 94, the villous branches (trabeculæ) are connected by intervillous syncytium to form a network, whilst in fig. 95 they mostly lie free in the intervillous blood-space. × 140.

FIG. 96.—*Chrysothrix nigrivittatus* 31*b*. B.C. Portion of the villous system from the primary (dorsal) placenta. The villous branches are again seen to be connected up by intervillous syncytial anastomoses to form a network. × 140.



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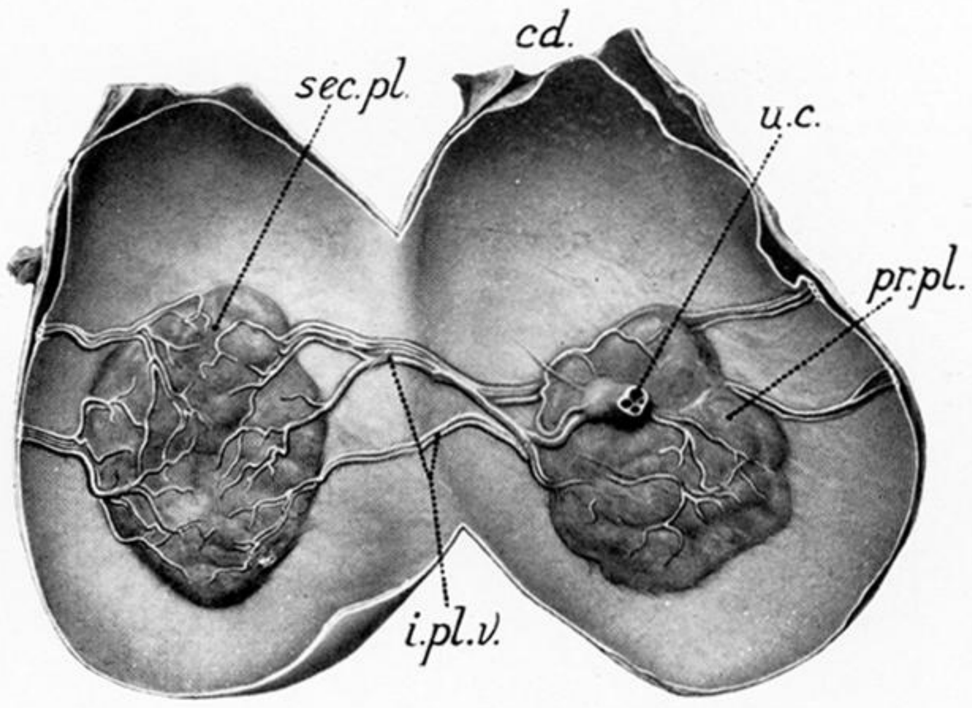

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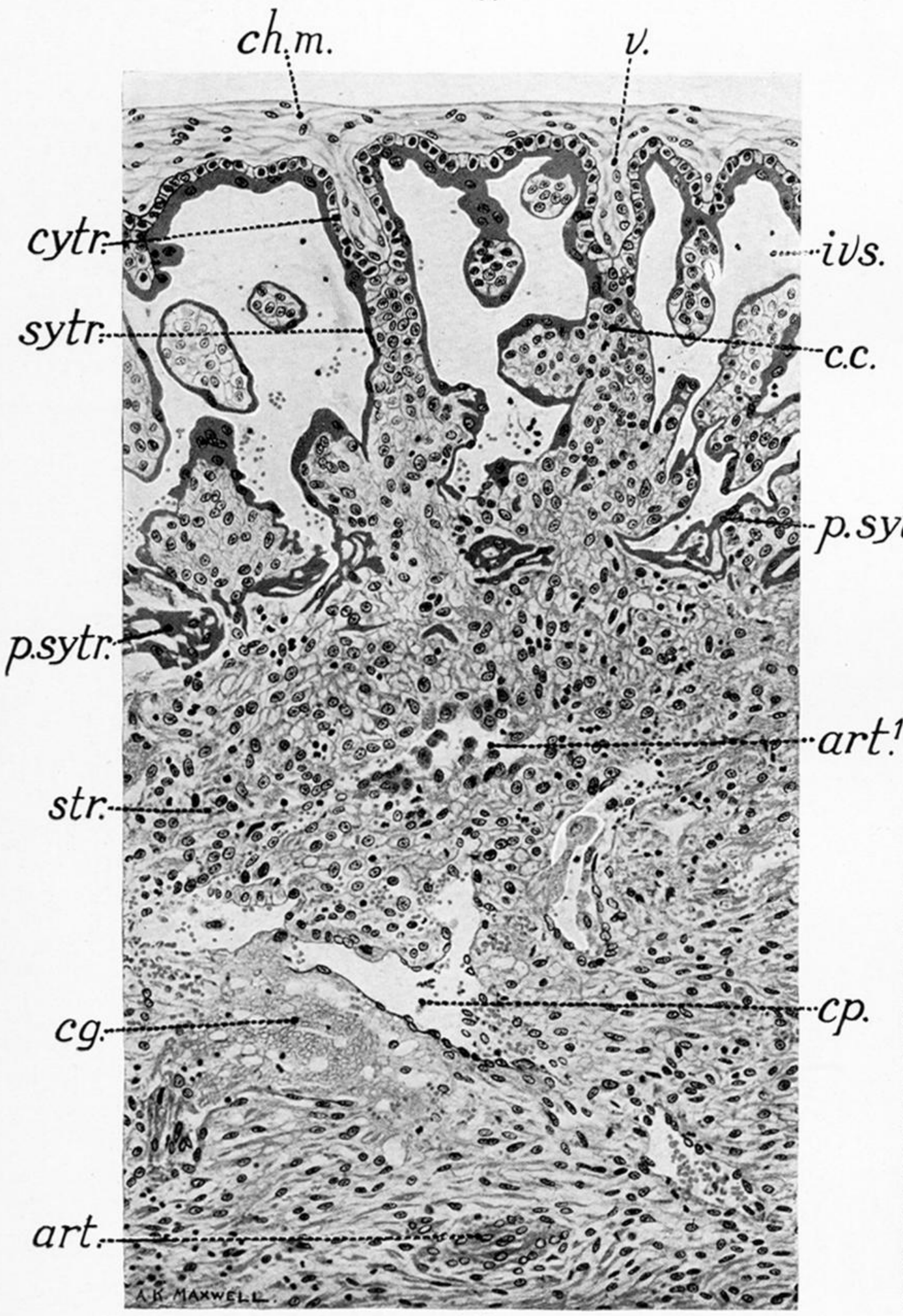

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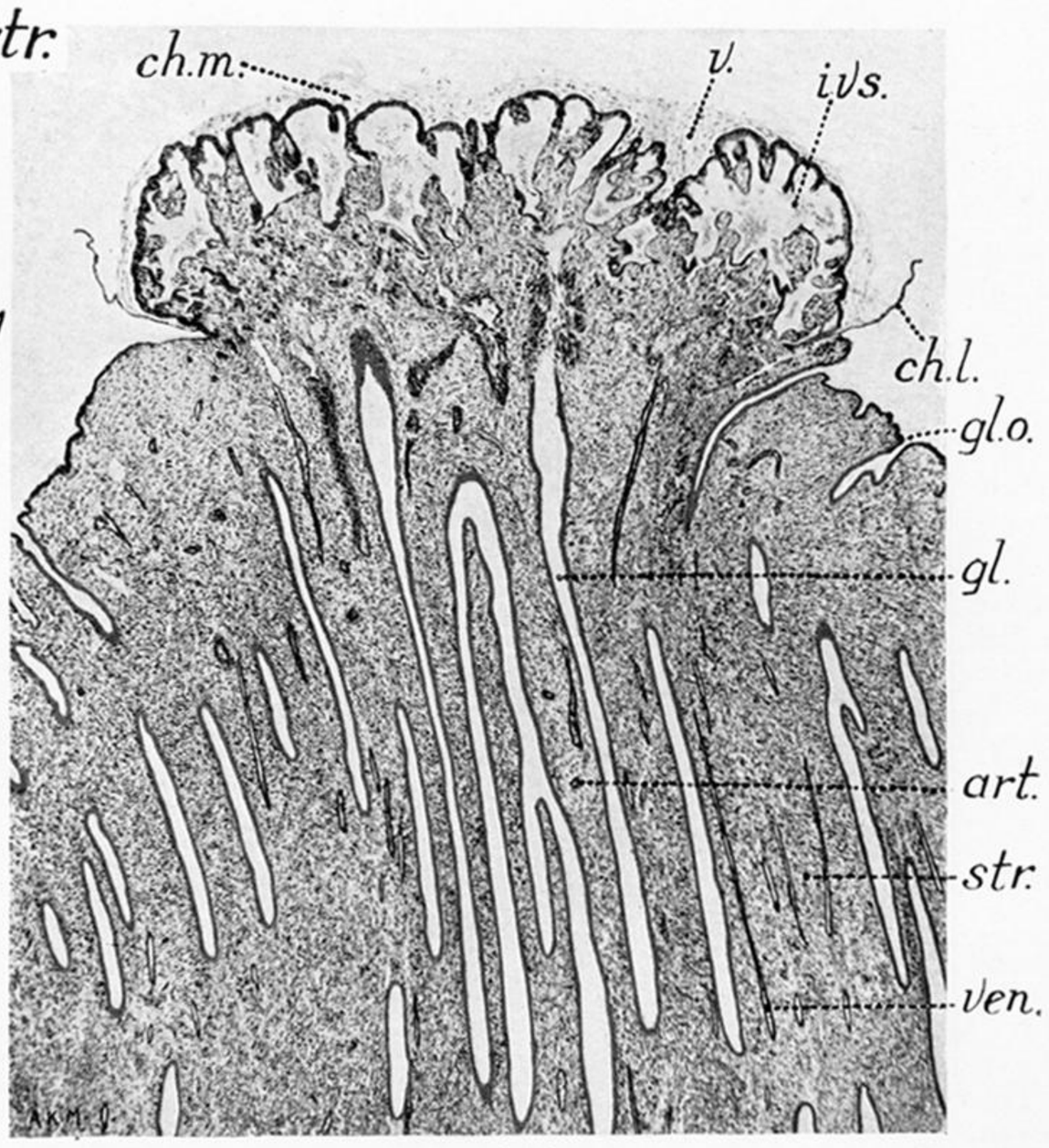

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PLATE 17.

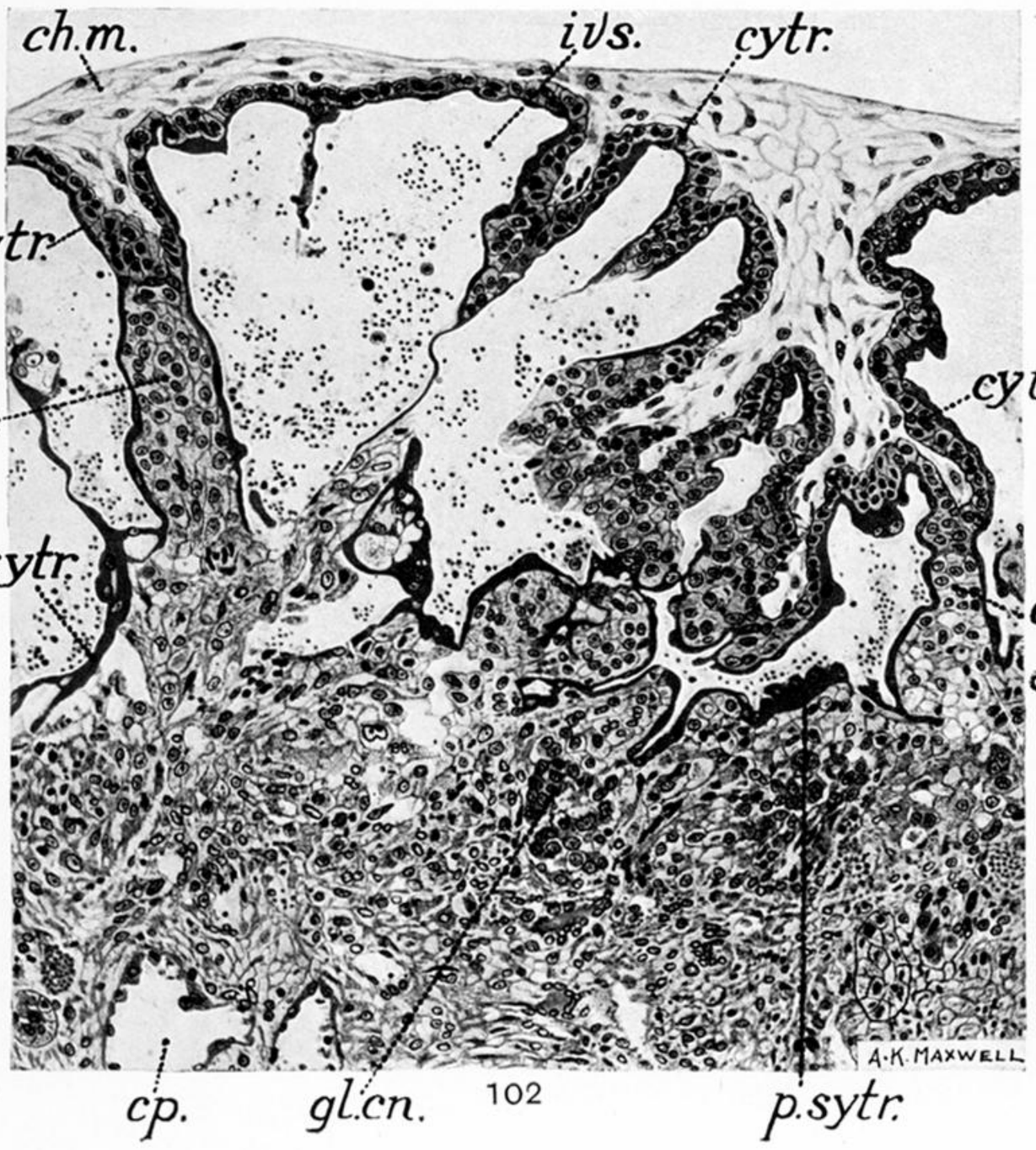
FIG. 97.—*Cebus macrocephalus* (?) 33*a*. B.C. Portion of the villous system of the placenta. The villous branches, simple and irregularly branched, are largely free of each other and lie in a continuous intervillous blood-space. × 128.

FIG. 98.—*Cebus apella* 624. The uterus opened to show the primary (dorsal) placenta (4·9 × 4·3 cm. in diameter) and the secondary (ventral) placenta (5·6 × 4·1 cm. in diameter) and the interplacental vessels (*i.pl.v.*) connecting the primary with the secondary placenta. *u.c.* umbilical cord. The caudal extremity of the uterus is directed upwards.

FIG. 99.—*Cebus apella* 624. Fœtus, C.R.L. 10·3 cm., D.C.L. 22·5 cm., H.L. 5·5 cm.

FIG. 100.—*Macacus nemestrinus* (DUCKWORTH). Low power view of the knob-shaped placental primordium. *ch.l.* unattached chorion of blastocyst wall. *ch.m.* chorionic mesoderm. *v.* villus. *ivs.* intervillous blood-space. *gl.* uterine gland. *art.* arteriole. *ven.* venule. × 36·5.

FIG. 101.—*Macacus nemestrinus* (DUCKWORTH). Section of the placenta, showing the chorion (*ch.m.* chorionic mesoderm), its villi (*v*) with their cell-columns (*c.c.*), the intervillous blood-space (*ivs.*) and the superficial zone of the endometrium. *art.* arteriole. *art.*¹ capillary (? arteriole), the endothelium of which is represented by detached oval cells. *cg.* serous coagulum. *cp.* enlarged capillary. *p.sytr.* peripheral syncytium. *str.* stroma. × 150.



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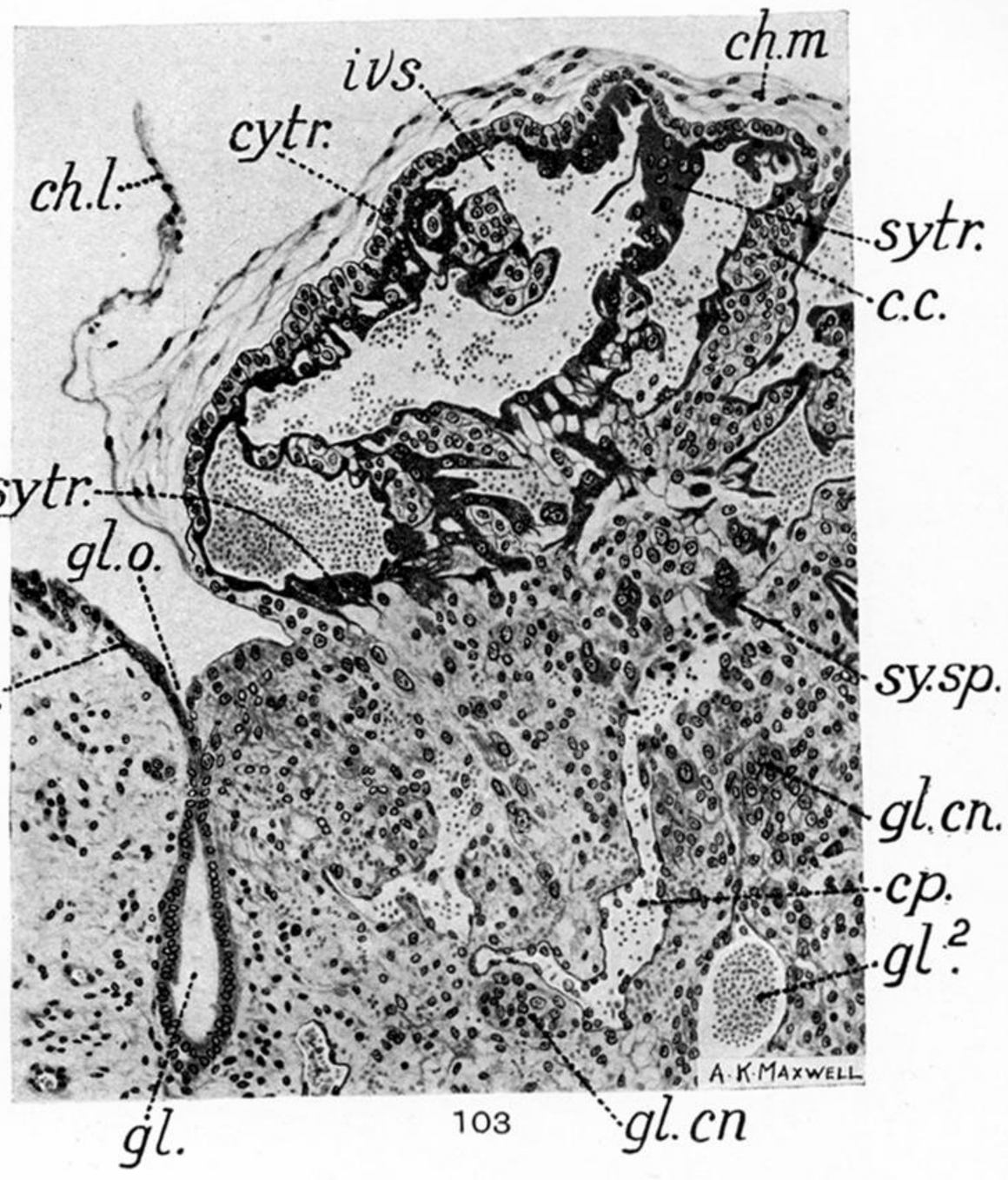

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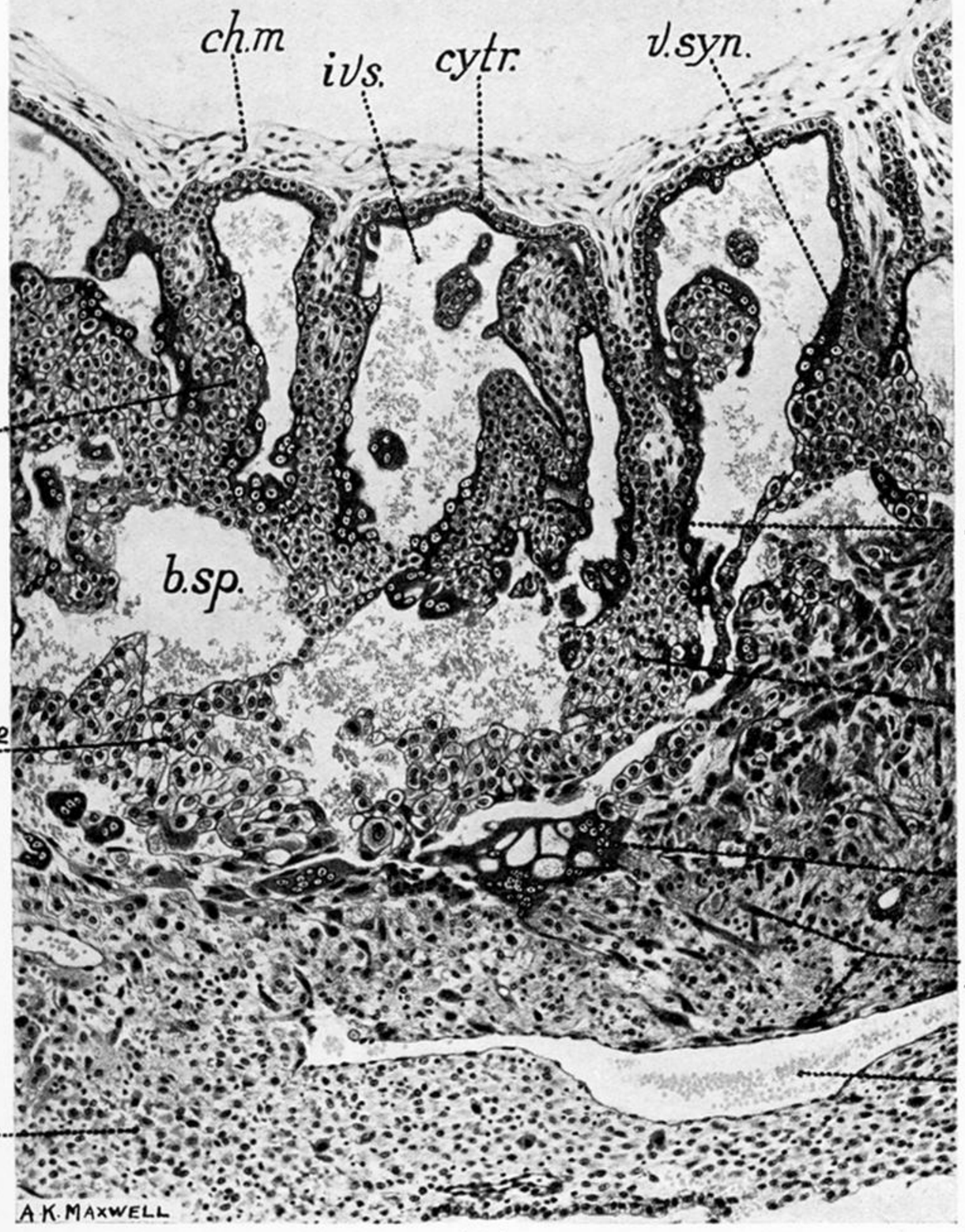

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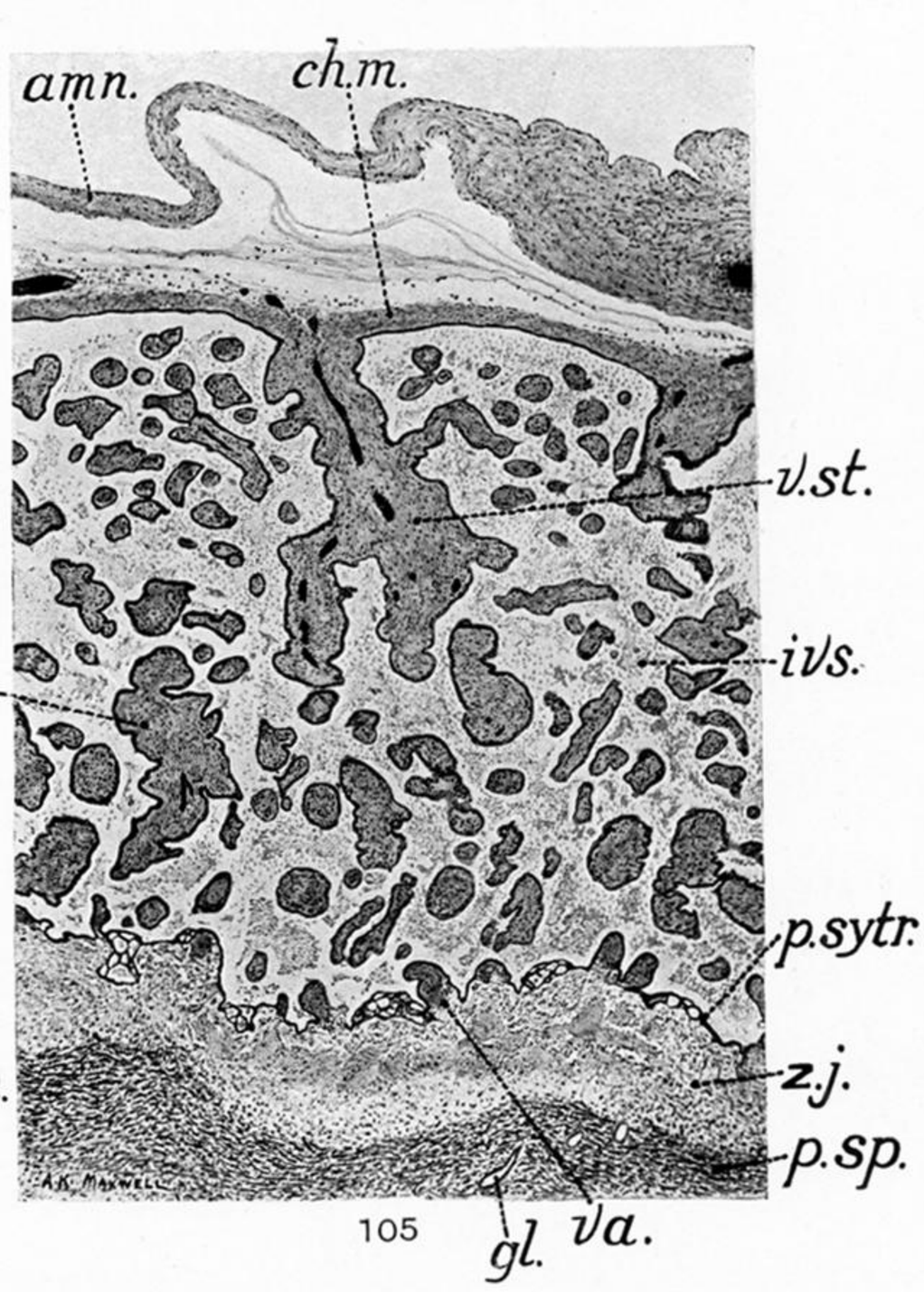

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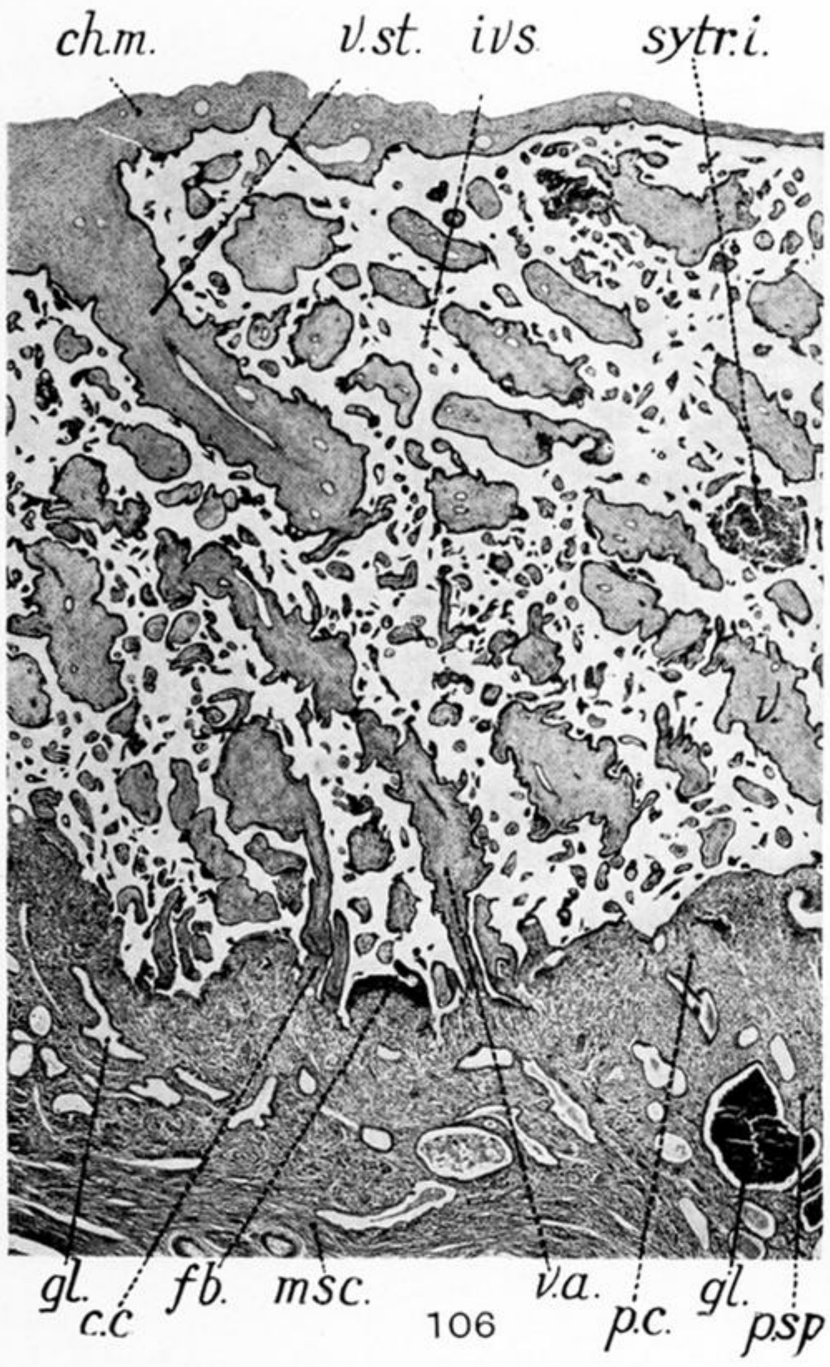
PLATE 18.

FIG. 102.—*Macacus nemestrinus* (DUCKWORTH). Section of placenta, showing on the right a branched villus. *gl.cn.* gland cell-nest. × 135.

FIG. 103.—*Macacus nemestrinus* (DUCKWORTH). Section through the margin of the placenta. *ch.l.* free chorion of blastocyst wall. *ep.* uterine epithelium. *gl.* uterine gland. *gl.*² uterine gland containing maternal blood. *gl.cn.* gland cell-nest. *sy.sp.* syncytial sprout. × 130.

FIG. 104.—Human chorionic vesicle (Bi I, FLORIAN). Section of the placenta, by kind permission of Dr. FLORIAN, *v.* his photomicrograph of this same section (FLORIAN, 1928 (*a*), Tafelabb. 1), for comparison with fig. 101 of the Macacus placenta (D). *b.sp.* blood-space in trophoblast-shell, prolonged from the intervillous blood-space (*ivs.*). *c.c.* cell-columns of cytotrophoblast. *ch.m.* chorionic mesoderm. *cytr.* cytotrophoblast. *cytr.*¹ *cytr.*² cytotrophoblast of "shell." *m.v.* maternal vessel. *p.syn.* syncytial sprouts which form a network penetrating into the decidual tissue (*str.*), (Proliferationsplasmodium. FLORIAN), *sytr.*¹ syncytiotrophoblast of cell-column. *sytr.*² vacuolated mass of syncytium (degenerierendes (?) Plasmodium, FLORIAN). *v.syn.* villous syncytium (Resorptionsplasmodium, FLORIAN). × 99.

FIG. 105.—*Semnopithecus femoralis*. Low power view of section of placenta. Fœtus G.L. 35 mm. H.L. 15 mm. *amn.* amnion. *ch.m.* chorionic mesoderm. *ivs.* intervillous blood-space. *p.sp.* pars spongiosa. uterine glands (*gl.*) greatly reduced. *p.sytr.* peripheral syncytium, vacuolated. *v.* villus. *v.a.* attachment of villus to basalis. *v.st.* villous stem. *z.j.* junctional zone (chorio-basalis), here very degenerate. × 28.



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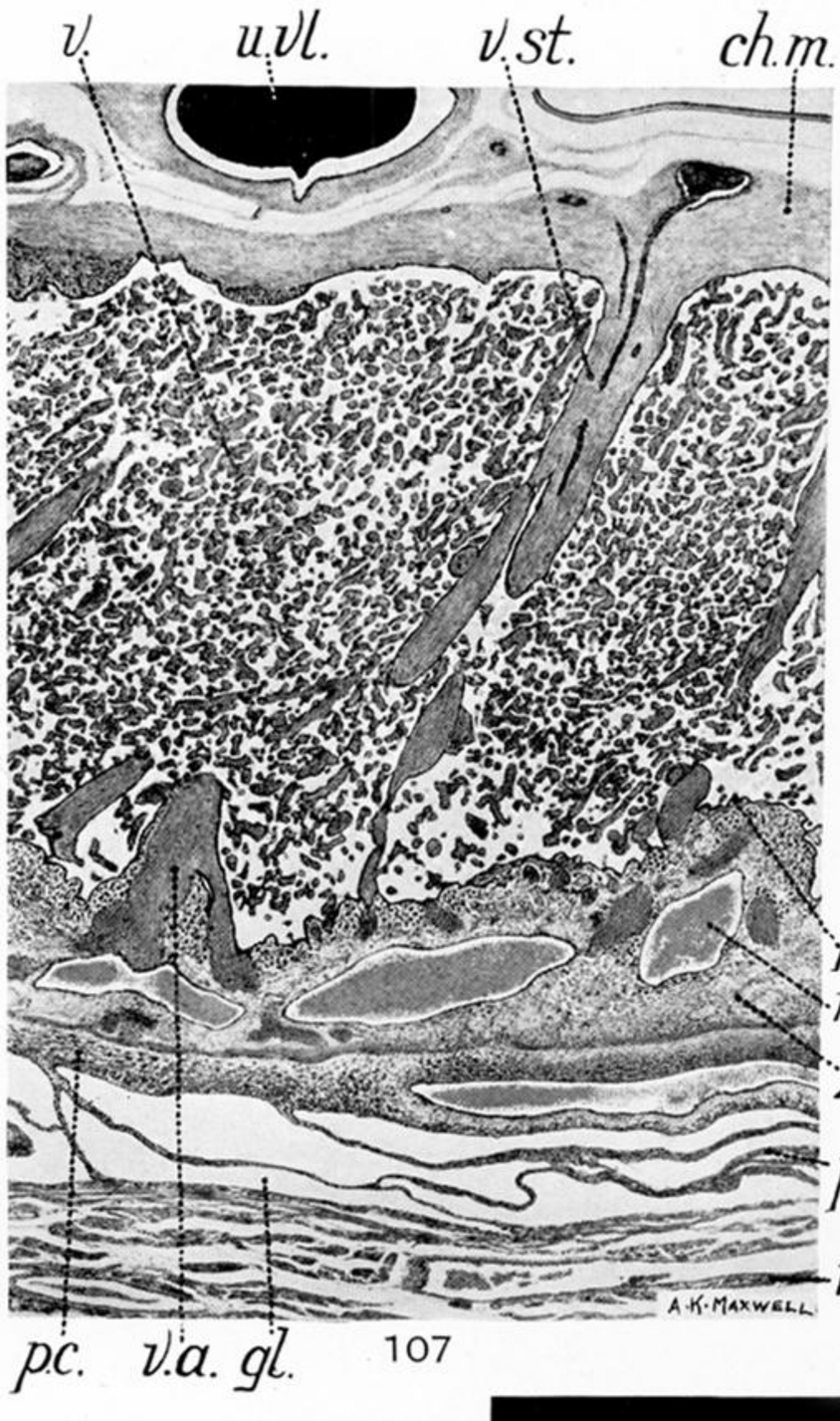

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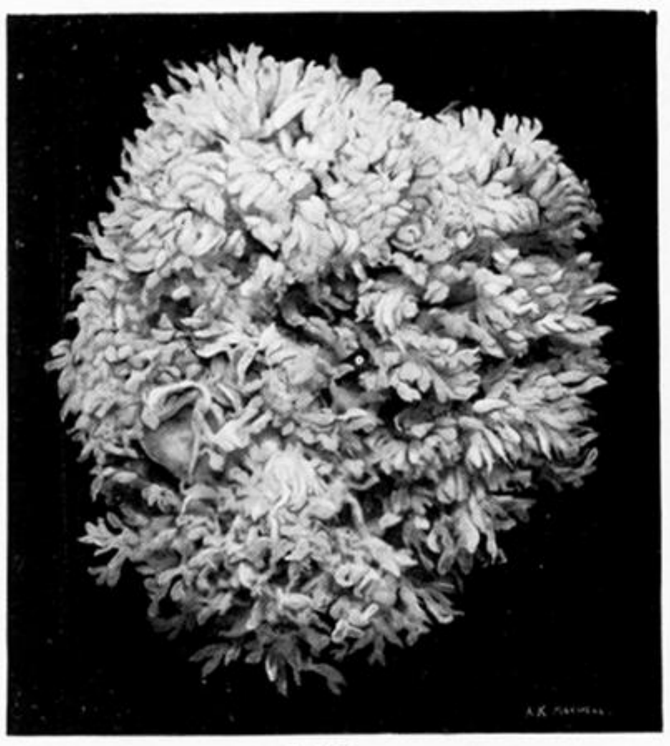

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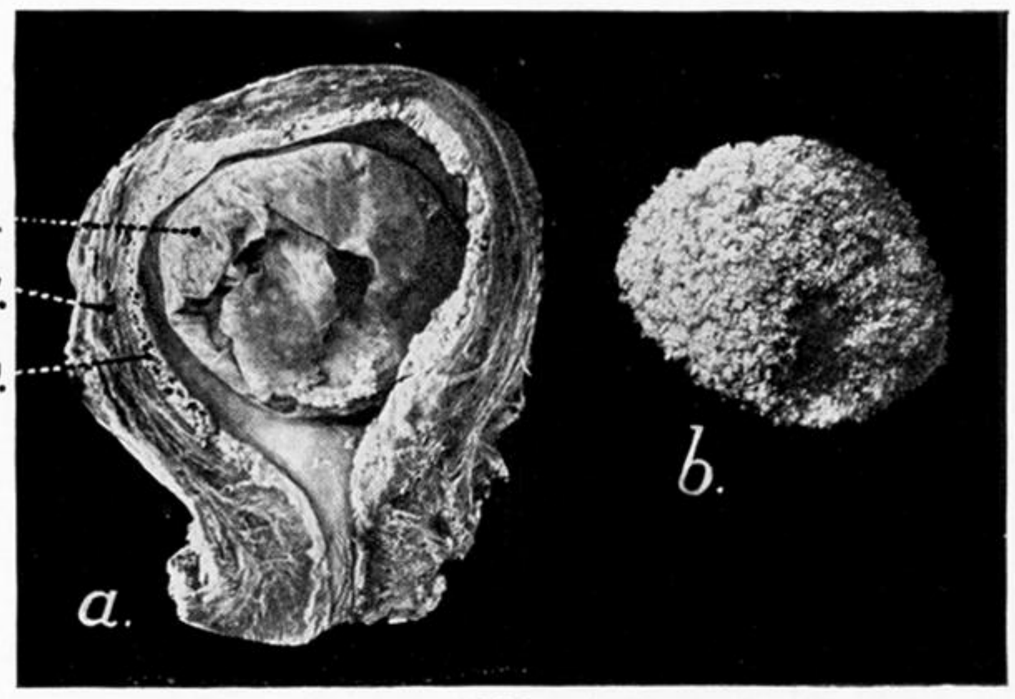

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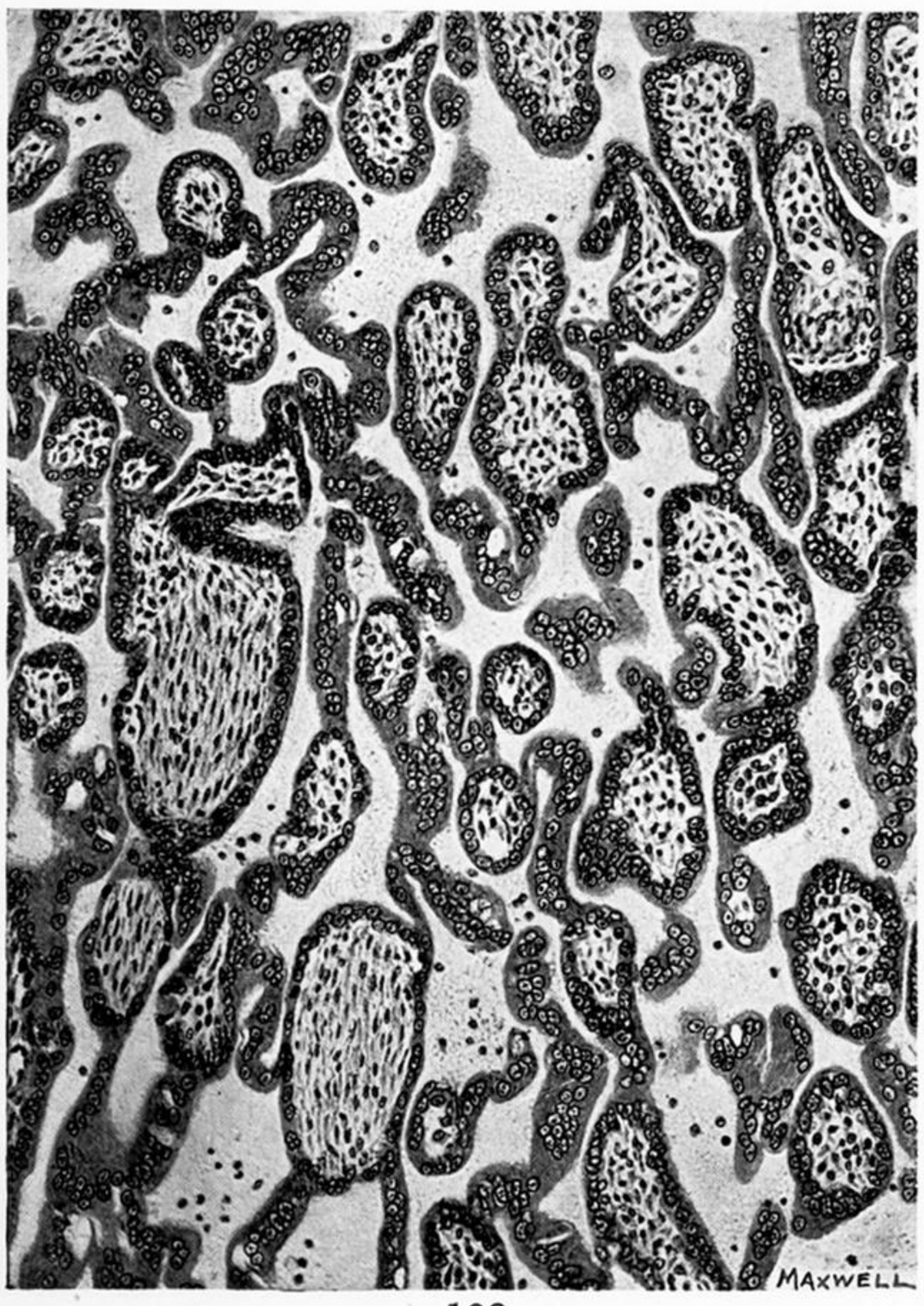

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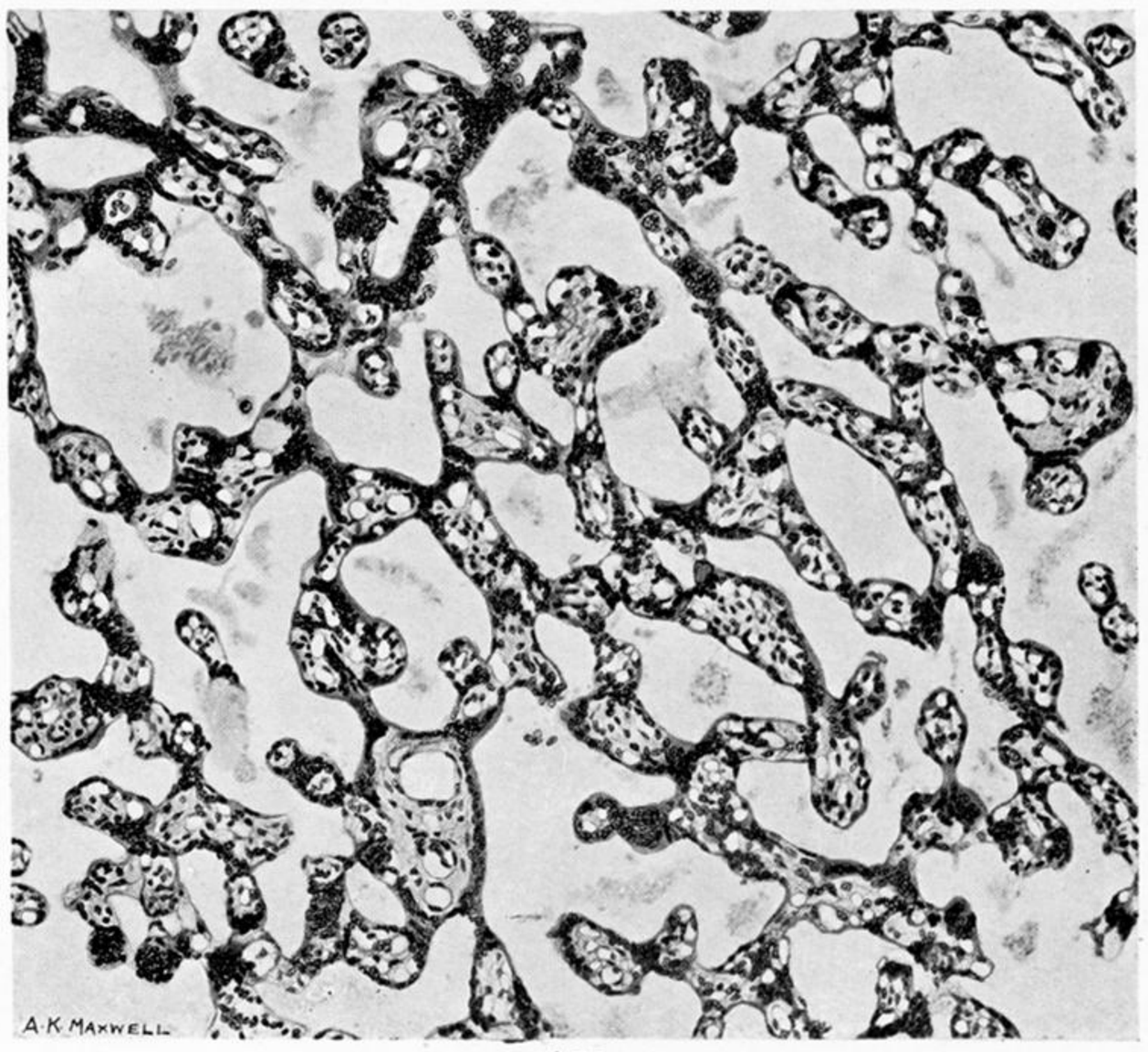

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PLATE 19.

FIG. 106.—Homo. Section of placenta. Fœtus G.L. 29 mm. *c.c.* cell-column, greatly reduced. *fb.* fibrinoid. *msc.* muscularis. *p.c.* pars compacta. *p.sp.* pars spongiosa. *sytr.i.* isolated mass of degenerate syncytium (" cell-island "). *v.* villus. *v.a.* attaching villus. *v.st.* stem of villus. × 11·5,

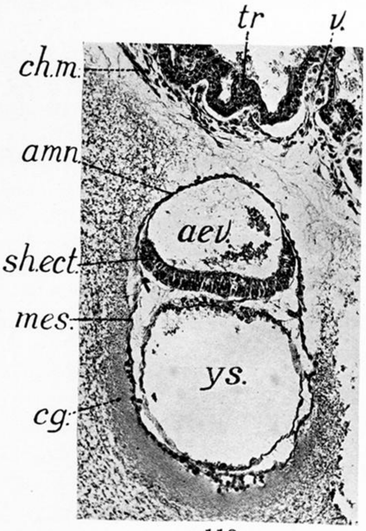
FIG. 107.—*Semnopithecus hosei* 749. R.C.S. Section of placenta. *p.sytr.* peripheral syncytium. *v.a.* base of attaching villus penetrating deeply into the junctional zone (*z.j.*). Note the sharp line of separation between the latter zone and the deep zone of the pars compacta, composed of decidual cells. × 16.

FIG. 108.—*Macacus cynomolgus* (*Macaca irus*) 737. R.C.S. Portion of the villous field of the placenta, showing the presence of irregular sprout-like outgrowths from the syncytiotrophoblast of the villi, which may end freely or may anastomose with other outgrowths or may fuse with the syncytial covering of other villi and so in the latter two events serving to connect up adjoining villi. × 154.

FIG. 109.—*Semnopithecus* sp. (R.A.). Portion of the villous field, showing the villi connected by syncytial junctions so as to form an irregular network. × 132.

FIG. 110.—Human chorionic vesicle H232 of about 15 mm. diameter. (From the collection of Professor J. T. WILSON, to whom I am indebted for the photograph of the specimen).

FIG. 111.—Orang utan 2 (after STRAHL, '03, figs. 10 and 12). *a.* uterus opened to display the decidua capsularis *d.c.* (diameter about 4·2 cm.). *b.* the chorionic vesicle of the same, isolated.



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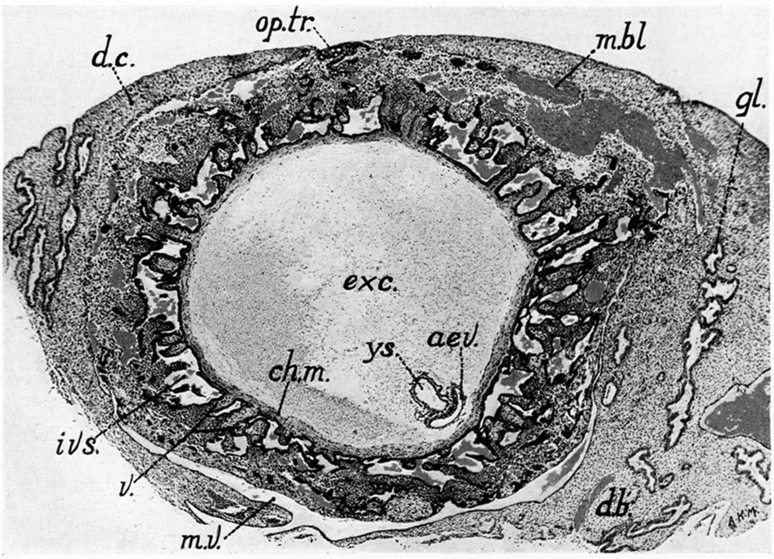

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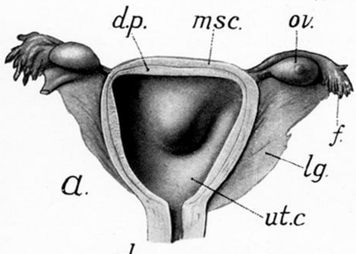

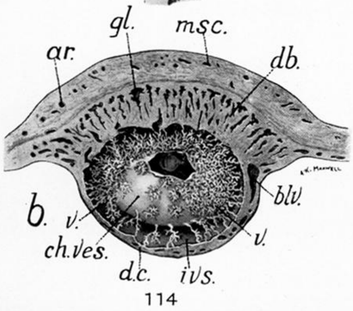

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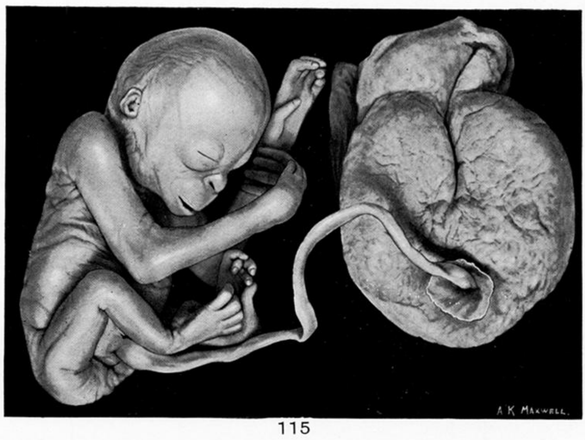

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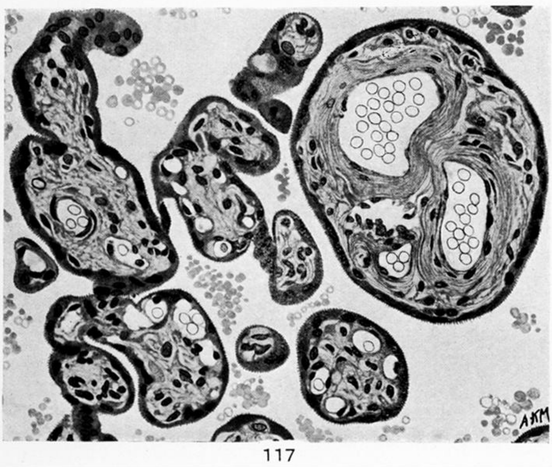

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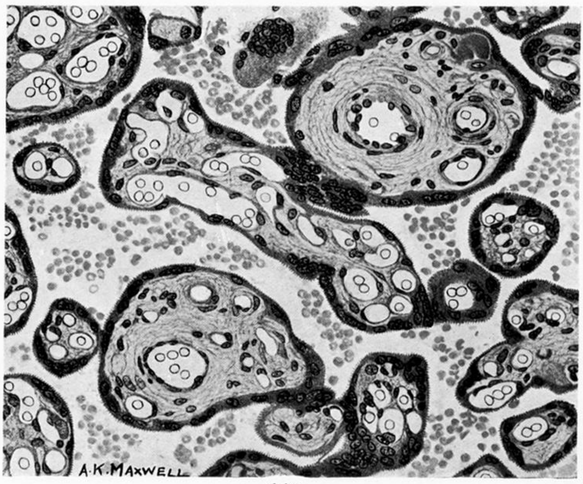

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PLATE 20.

FIG. 112.—Human chorionic vesicle (Bi I, FLORIAN, '28*b*, fig. 1). Sectional view of the vesicle *in situ* (by kind permission of Dr. FLORIAN). Measurements (FLORIAN): Internal diameter of vesicle, 2·13 × 2·12 × 2·3 mm., embryonal shield, 350μ in length × 343μ in breadth, with primordium of primitive streak and cloacal membrane. Embryo is of about the stage of the embryo Beneke (FLORIAN-BENEKE, '30/31). *aev.* amnio-embryonal vesicle. *ch.* chorion. *ch.m.* chorionic mesoderm. *d.c.* decidua capsularis. *d.b.* decidua basalis. *exc.* extra-embryonal cœlom. *gl.* uterine gland. *ivs.* intervillous blood-space. *m.bl.* maternal blood extravasation. *m.v.* maternal blood-sinus. *op.tr.* operculum deciduæ (TEACHER) marking the point of entrance of the vesicle into the endometrium. *v.* villus. *ys.* yolk-sac. × 25·5.

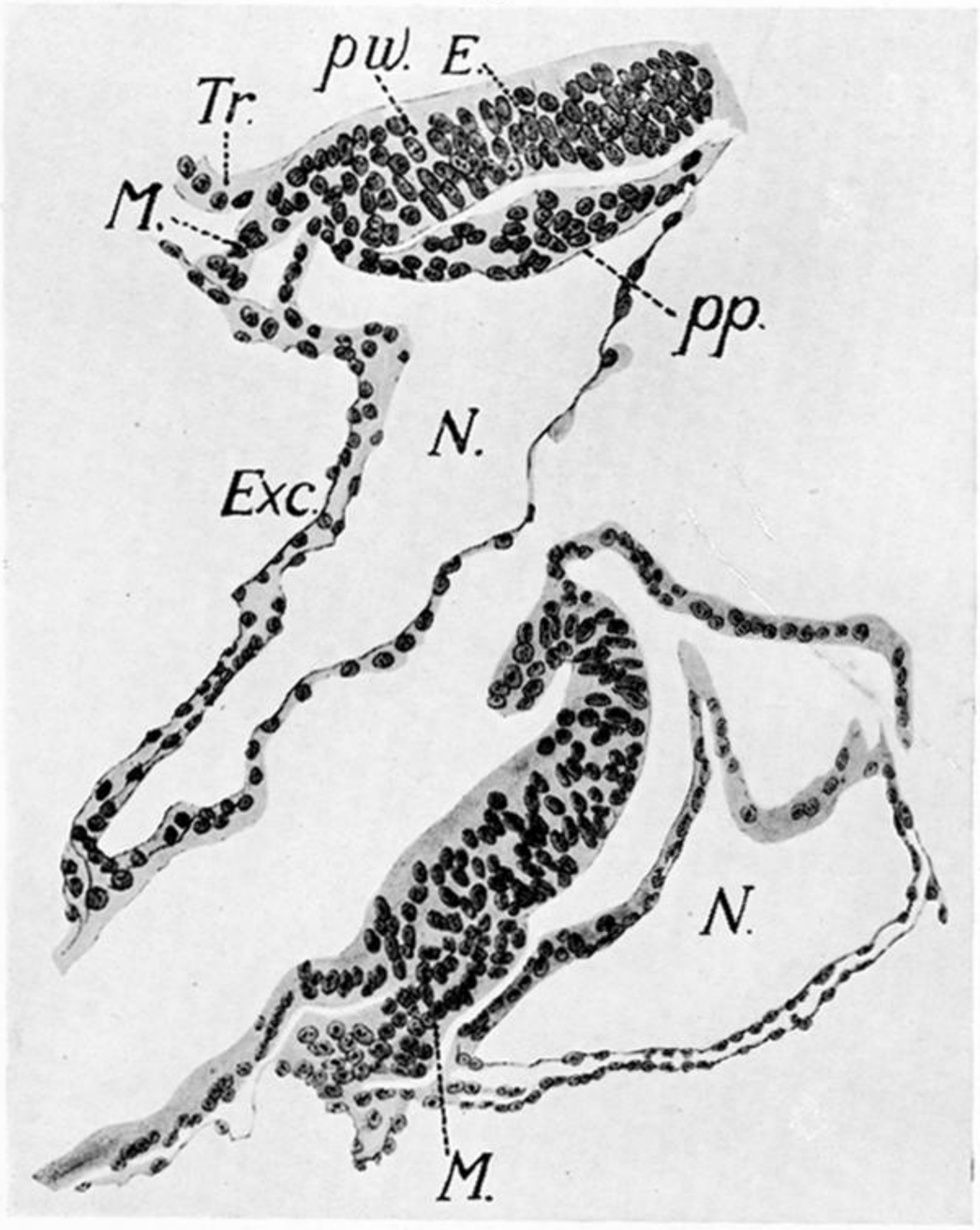
FIG. 113.—Photomicrograph of section 43 through the Beneke embryo (STRAHL-BENEKE, '10, FLORIAN-BENEKE, '30/'31), by kind permission of Dr. FLORIAN. The figure shows very clearly the amnio-embryonal (*aev.*) and the yolk-sac (*ys.*) vesicles and their investing layer of mesoderm (*mes.*). *tr.* and *ch.m.* trophoblast and mesoderm of chorion. *cg.* coagulum in exocœlom. *v.* villus. Diameter of chorionic vesicle, 2·15 × 1·2 × 2·2 mm. × 96.

FIG. 114.—*Hylobates Rafflesi*. Preparations of the pregnant uterus, embryo Ab (after SELENKA, '00, figs. 19 and 20, p. 183). *a.* uterus opened to show the decidual swelling. *b.* section through the uterine wall and decidual swelling showing the chorionic vesicle (*ch.ves.*) *in situ*. *ar.* artery. *blv.* blood-vessel. *d.b.* decidua basalis. *d.c.* decidua capsularis. *d.b.* decidua basalis. A window has been cut in the chorion through which the embryo is visible.

FIG. 115.—*Hylobates* sp. Advanced fœtus and placenta (from the Raffles Museum, Singapore, through the kind offices of Professor J. L. SHELLSHEAR). The placenta, single and discoidal (somewhat contracted and folded in this specimen) measures 7·5 × 5·4 cm. in diameter, and 2·55 cm. in thickness. Fœtus, G.L. 9·2 cm., H.L. 3·8 cm. The long umbilical cord is attached eccentrically, nearer to one margin. The amnion has been removed except round the attachment of the cord.

FIGS. 116 & 117.—Illustrate the structure of the placental villi as seen in section, in the full-term human placenta and in an advanced placenta of the Gorilla, respectively. Note the agreement in their structure and relations. In both, the villi are invested by a single layer of villous syncytium enclosing a mesodermal axis in which are situated the umbilical vessels and capillaries and in both syncytial connections between the villi are seen to be present (largely converted into darkly stained fibrinoid in the human placenta). The Gorilla placenta (11·7 × 10·5 cm. in diameter) was given to me some years ago by the late Professor L. BOLK. The fœtus to which it relates was described by him in 1926 ('Z. Anat. Entw.,' Bd. 81) and the genital organs in 1922 ('Anat. Anz.,' Bd. 55). × 275.

5a



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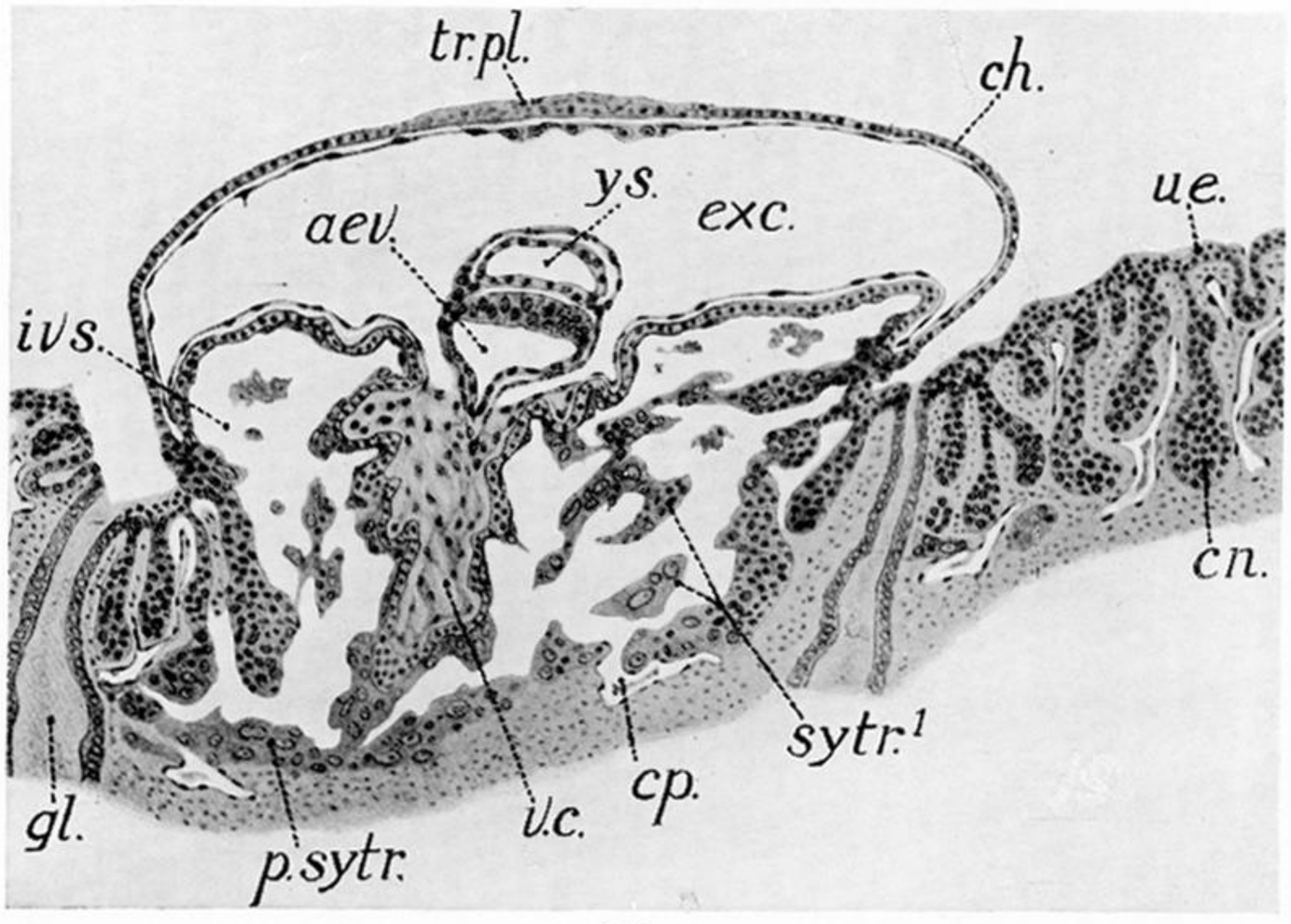

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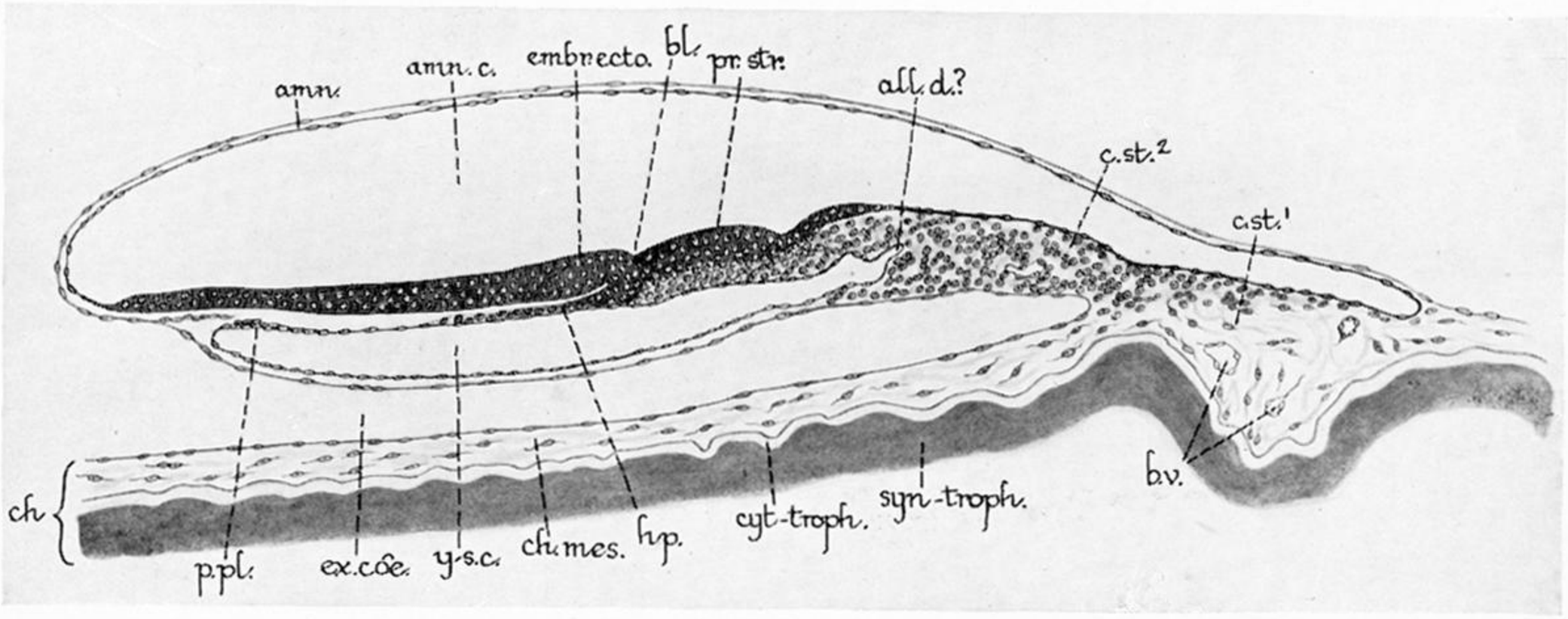
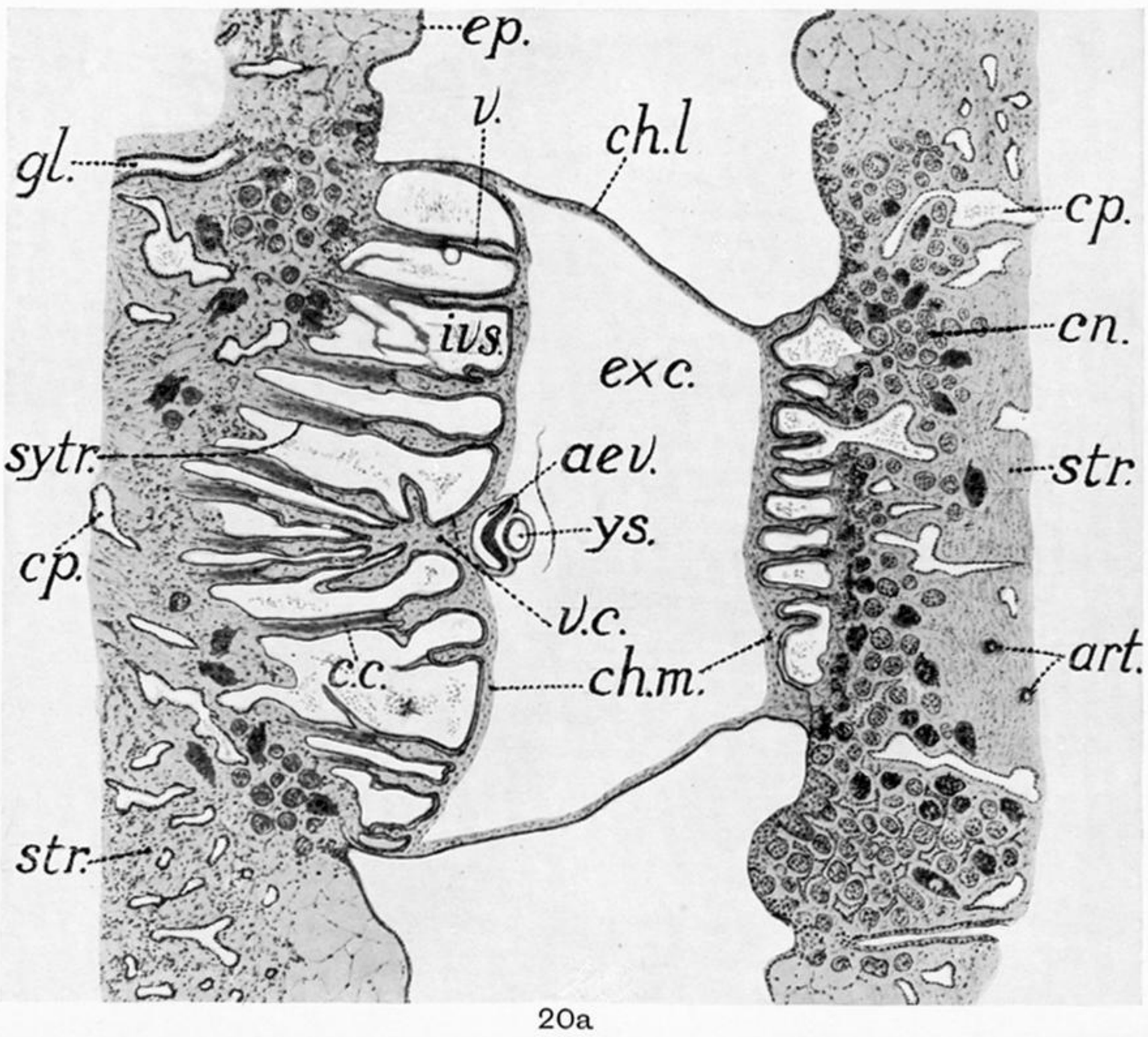


18a



20a

PLATE. 21.

FIG. 5*a*.—Longitudinal section through the embryonal area and yolk-sac of blastocyst of Tarsius 86 (after HUBRECHT, '02, fig. 47, Pl. VI).

FIG. 6*a*.—Similar section of the blastocyst of Tarsius 235 (after HUBRECHT, '02, fig. 48, Pl. VI). *E.* Shield-ectoderm. *Exc.* Exocœlom. *M.* Mesoderm. *N.* Yolk-sac. *pp.* Prochordal plate. *pw.* " Protochordal wedge " (HUBRECHT), really the primitive streak primordium. *Tr.* Trophoblast.

FIG. 18*a*.—*Chrysothrix sciureus* 467. Median section through the embryo (semidiagrammatic). *all.d.* (?) allantoic diverticulum (?). *amn.*, *amn.c.* amnion, amniotic cavity. *bl.* blastoporic depression. *bv.* capillaries forming in the mesoderm of the connecting stalk (*c.st.*[1]). *ch.* chorion. *ch.m.* chorionic mesoderm. *cyt-troph.* cytotrophoblast. *c.st.*[1], *c.st.*[2] the two regions of the connecting stalk. *embr.ect.* embryonal ectoderm. *ex.cœ.* exocœlom. *hp.* head-process. *p.pl.* prochordal plate. *pr.str.* primitive streak. *syn-troph.* syncytiotrophoblast. *y-s.c.* yolk-sac cavity.

FIG. 19*a*.—*Semnopithecus pruinosus*. Blastocyst Lk. (after SELENKA, '03, fig. 7, p. 334). For explanation of lettering see list of common reference letters. *sytr.*[1] syncytiotrophoblast in intervillous space (*ivs.*) *tr.pl.* area of thickened ectoplacental trophoblast of secondary placenta.

FIG. 20*a*.—*Macacus* (*Cercocebus*) *cynomolgus* (*Macaca irus*). Blastocyst Ca (after SELENKA, '00 fig. 28, p. 197), showing the primary placenta on the left and the secondary on the right. For explanation of lettering, see list of common reference letters.