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The Interpretation of the Triploid Intersexes of Solenobia

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I. *Introduction*

J. SEILER[2] and his students have enriched our science with a wealth of data on triploid intersexuality in the psychid moth, *Solenobia triquetrella*, in which all individuals produced by fertilization of diploid parthenogenetic eggs and therefore of the triploid constitution $3A + XXY$ are intersexual. The simplest formal genetic explanation for these intersexes is, of course, the old one derived from the Lymantria case, namely that the balance between male determiners in the X-chromosomes and female determiners outside of them is intermediate between the normal balances for females and males respectively. The detailed study of the morphology of these triploid intersexes showed considerable differences from the facts found in the diploid intersexes of Lymantria, indicating that the explanation of the structure of the Lymantria intersexes by the so-called time law could not be simply transferred to the Solenobia intersexes. It is regrettable that it was not always realized by both parties to the discussion, i. e. SEILER[2] and myself, that the completely different genetic situation (i. e. female and male chromosomal constitution in Lymantria, intersexual chromosomal constitution in Solenobia) could hardly result in a completely identical interpretation of both cases. It is still more regrettable that some of the workers in the field and also some in related fields indicated that the possible non-applicability of the laws found in Lymantria to the divergent facts in Solenobia would reflect upon the analysis of the Lymantria case, based upon greatly different genetic and morphological facts. This unfortunate and unjustifiable generalization is the more deplorable because outsiders who are not sufficiently acquainted with the facts become confused and no longer know what is proved and what is disproved. The result is plainly seen in many superficial, even distorted and unobjective quotations in some of the recent literature on sex-determination.

Since I last tried (GOLDSCHMIDT[3]) to analyse the situation and to find a solution which fitted the facts, important new facts have come to light. A still more detailed and complete description of the triploid intersexes has been supplied by the SEILER school. New genetic facts have come to light in other organisms which permit a better genetic understanding of the situation. In addition, SEILER has assembled and clarified his own views[1], and I had the great pleasure to go over all the important factual data with my friend SEILER in his laboratory. Thus, I feel that I can now present my own interpretation of the facts in what I consider to be a final form, an interpretation which on some points is not greatly different from SEILER'S, but on others does disagree with his.

II. *Review of the basic facts in Lymantria*

Before considering the important facts which must be accounted for by an explanation, I shall review in a few words the Lymantria situation with which comparisons are made. Intersexuality in *Lymantria dispar* is diploid and is based upon incongruous valencies of female and male determiners. Intersexes may be XX or XY individuals, i. e. males or females in regard to their chromosomal constitution. XY intersexes, called female intersexes for brevity, and XX or male intersexes are produced in different and specific crosses, and they are clearly distinguishable from one another[2].

The degree of intersexuality from a low type up to complete sex reversal is the same in all individuals of a given cross, i. e. genetical composition, with very little

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[2] J. SEILER, Exper. *11*, 425 (1949).

[3] R. GOLDSCHMIDT, Arch. Klausstift. *21*, 269 (1946); Roux' Arch. *124*, 92 (1931).

[1] J. SEILER, Exper. *11*, 425 (1949).

[2] I should like to use this occasion to mention and to apologize for an unfortunate error which crept into former publications and to which KOSMINSKY[3] kindly drew attention. Male intersexes always show on their wings a mosaic of female and male parts; this is not usually the case in female intersexes. But when female intersexes are derived from crosses involving the so-called Gifu race as one parent the female wings do have the mosaic character. Photographs were given in GOLDSCHMIDT[4] and other publications. When later pictures of a whole series of male, female, and Gifu type intersexes were needed for a textbook and for a review, photographs of individual moths were selected from a large number and assembled for plates. In doing this, by mistake a photograph of a high grade male intersex was pasted on to the plate of the Gifu series so that now the same individual appears once as a male intersex and once as a female intersex. (See GOLDSCHMIDT[5], 1934, p. 61, lower left, and p. 62 No. III.) The individual intended for fig. 11, p. 61, is the one pictured in the book of GOLDSCHMIDT[4], fig. 46, h. It is unfortunate that this technical error was not discovered, but there is still no doubt that male intersexes and females of the Gifu type can be readily distinguished.

[3] R. GOLDSCHMIDT, Arch. Klausstift. *21*, 269 (1946); Roux' Arch. *124*, 93 (1931). – A. M. DU BOIS, Z. Morph. Ökol. *15*, 447 (1929).

[4] R. GOLDSCHMIDT, Z. ind. Abstl. *23*, 1 (1920).

[5] R. GOLDSCHMIDT, Lymantria, Bibl. Gen. *11*, 1 (1934).

fluctuation. Crosses of races of different valencies of the sex determiners result in a completely orderly way in the production of one or the other definite grade of female or male intersexes. The determiners for maleness are located in the X chromosomes and segregate always as a unit. The main determiners for femaleness are located in the Y chromosome, again behaving as one unit. Therefore, the female determiners must exercise their determining action before fertilization, as they are absent in male eggs after fertilization but nevertheless show their effect in male intersexes. There are also modifiers for femaleness in the autosomes, as shown by male intersexuality. Different races have female and male determiners of different valency and normal sexes or intersexuality are produced respectively by the proper or wrong balance of these F and M factors. The existence of all grades of intersexes in addition to the pure sexes within this balance system requires that a minimum of the balance value in favor of M or F, called the epistatic minimum, is needed to produce the normal sexes. If e is the epistatic minimum we find: $F/M > e = ♀$, $MM/F > e = ♂$, $F/M < e =$ female intersex, $MM/F < e =$ male intersex. If the value F/M reaches the value of $1/e$ we have a male by sex reversal; if $MM/F = 1/e$, a female by sex reversal.

Morphologically the Lymantria intersexes appear as definite grades between the sexes, but a medium female and a male intersex are completely different, as are a low female and high male intersex. The explanation is found by study of the morphology and development of the individual organs which follow the so-called time law of intersexuality. This means that a female intersex develops first according to its chromosomal constitution as a female; at a certain point in development, the turning point, development switches over to the male direction and is completed thus. The opposite is the situation in the male intersexuality, i. e. first maleness, afterwards femaleness. The time of the occurrence of the turning point is responsible for the grade of intersexuality, an earlier turning point giving a higher grade intersexuality, etc.

It should be emphasized that this interpretation fits the facts completely in *Lymantria dispar*. A look at the pictures of the intersexual gonads and their development or at the otherwise completely unintelligible series of figures of the genital armature will demonstrate this (see GOLDSCHMIDT[1]; DU BOIS[2]). Certain minor difficulties have been fully discussed in an earlier paper (GOLDSCHMIDT[3]), but the overwhelming body of facts should convince anybody who studies the details of the correctness of the time law for *Lymantria dispar*. It is rather unfortunate that some authors, who studied completely different materials, different genetically, morphologically, and taxonomically, and thought rightly or wrongly that the time law did not apply to their material, have made sweeping generalizations which included also Lymantria; the only conclusion should have been—provided their interpretations of their own data were correct—that there exists more than one type of intersexuality. But I am ready to admit that I might have been less dogmatic myself in interpreting other cases in the light of Lymantria.

III. *The genetic situation in Solenobia*

For analysis of the possible similarities or differences between diploid intersexuality in Lymantria and triploid intersexuality in Solenobia it is necessary to understand clearly the genetic background of both. As already pointed out, all Solenobia intersexes are alike, namely $3\,A + XXY$ and thus neither female nor male in regard to the sex chromosomes. Therefore, *a priori* we expect differences from the Lymantria intersexes. Actually we should expect that all Solenobia intersexes be of intermediate grade with very little variation. Furthermore, since there is no female or male chromosome constitution present but an intermediate one—balance midway between the respective epistatic minima for pure sexes—development should be intermediate throughout, i. e. intersexual. In actuality, these two expectations are not fulfilled. The intersexes vary from almost female to almost male structure, and the individual organs are, where they can be analysed, not intermediate but composed of female and male parts. SEILER[1] explains this from a genetical point of view by the assumption that all individuals are really genetically alike, i. e. $F/M =$ intermediate. In his view, this means that the female and male determiners both act in the same way and independently, and further that each cell in development has only the alternative femaleness or maleness and remains determined once the alternative has been decided. This decision he assumes to be purely phenogenetic, produced by unknown local conditions surrounding the cells. If we compare this assumption with the genetic situation in Lymantria, we notice the following. In Lymantria the various grades of intersexuality are determined by genetic conditions, by the different valency combinations of the sex determiners. The individual cells also have only the sexual alternative, but this is decided for the entire organ and all organs by the genetic constitution, by the superiority of F or M. (The time law relates to the sequence and time of the decision of the alternative.) In Solenobia, according to SEILER[1], it is the specific environment of each cell or of small groups of cells which gives control to the evenly matched female or male factors, whichever it be. If this were the case, the overwhelming majority

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[1] R. GOLDSCHMIDT, Z. ind. Abstl. *23*, 1 (1920); J. Morph. Œcol. *8*, 63 (1927).

[2] A. M. DU BOIS, Z. Morph. Ökol. *15*, 447 (1929).

[3] R. GOLDSCHMIDT, Genetica, *20*, 1 (1938).

[1] J. SEILER, Exper. *11*, 425 (1949).

of the intersexes should not show any correlation between the sexuality of different cells, cell groups and organs. We should expect an intricate and utterly irregular mosaic of sexual differentiation. Actually, this is not the case. Altogether the grade of intersexuality in Solenobia intersexes is highly correlated over the entire body. If the individual is more female-like, it is so in all organs; if it is more male-like, the same is true; only in the medium grade intersexes the correlation is less good. In order to explain this, SEILER[1] is forced to introduce abruptly genotypic differences for the existence of which no genetic basis is available and which had been excluded before in his analysis. His argumentation is, in short, this:—Phenotypic factors will act only when F and M factors balance each other completely; the nearer the balance is to the female or male epistatic minimum the more determination becomes genotypic. But we are not told how these genotypical differences suddenly come into the picture. I can visualize only the following possibilities:—(1) The valencies of F and M show a normal variation. No geneticist would make this assumption except when proved by experiments. It is, in this case, disproved by the absence of intersexes in the normal strains, where they should appear in a definite percentage if the assumption were true. (2) The strains contain heterozygous modifiers for femaleness and/or maleness, which recombine differently. If this were true, individual crosses should show specific features in regard to the degree of intersexuality of the offspring. Actually, all crosses show the same variation. Thus, the explanation of the correlation of the degree of intersexuality all over the individual, and, incidentally, also the extreme variation in degree within any brood, cannot have anything to do with the F/M balance, which is the same in all individuals. (We shall mention more details in the discussion on morphology.)

This leads to the question whether the intermediate F/M balance is the only genetic feature available for the analysis of the Solenobia intersexes. SEILER[1] has recently found that female intersexuality can be produced by crossing two different species of Solenobia in one direction, the reciprocal cross being normal. This is a complete parallel to the Lymantria case: A female of a "weak" species crossed to a male of a "strong" species produces diploid intersexual females. (In Lymantria "races", not species, are involved. The next step, production of intersexual males in the F_2 of the reciprocal cross, cannot be taken in Solenobia because the hybrids are sterile.) This is sufficient proof that the sex determining mechanism in Solenobia is the same as in Lymantria. In the latter, be it recalled, the female factors (F) are located in the Y chromosome and must exercise their function before the meiotic divisions. This does not include additional female factors in the autosomes; modifiers for femaleness were found in the autosomes. An analogous genetic situation seems to be more widespread than one could formerly assume. Both STURTEVANT[1] and GOLDSCHMIDT[2] have shown that in Drosophila autosomal sex factors act in the egg before meiosis. Therefore, since there is now every reason to assume the same mechanism of sex-determination in Lymantria and Solenobia, the interpretation that the Y chromosome in Lymantria conditions the egg for femaleness before meiosis (this action, it should be added, does not exclude later action in the female, since she retains the Y chromosome) can also be applied to the Solenobia case. This means that all eggs of the diploid female have already advanced to a certain degree of female determination at the time of fertilization. In other words, the intermediate F/M balance of the triploid, established by fertilization of the diploid egg, is not the only genetic condition of these eggs. It is superimposed upon an already existing female determination which has advanced to whatever extent permitted by the predetermination of the cytoplasmic components of the insect egg. Lepidoptera are known to have a highly predetermined type of embryonic determination.

It is obvious that this genetic situation allows the triploid intersexes to follow the time law insofar as differentiation is first female and is superseded, after fertilization, by whatever action the balanced F/M factors will have. A study of the morphology and variation of these intersexes will bear out this conclusion.

IV. *The morphological facts which must be accounted for by the interpretation*

The following major facts, discovered by the SEILER[3] school, must agree with whatever interpretation is adopted.

(1) The intersexual individuals of all progenies vary from preponderant femaleness through all intermediate stages to preponderant maleness.

(2) There is a high correlation between the degrees of femaleness, viz. maleness for all organs studied. This means, e. g. that an individual which as a whole is very much male shows the same degree of preponderant maleness in all organs. This correlation is best at the extreme ends of the intersexual series, not so good in medium-grade intersexes.

There are certain additional features which, in my opinion, are not relevant for the explanation but are expressions of general characteristics of insect development. Among these is the right-left correlation, which is frequently poor or completely absent. The same is

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[1] J. SEILER, Exper. *11*, 425 (1949).

[1] A. H. STURTEVANT, Proc. Nat. Acad. *32*, 84 (1946).

[2] R. GOLDSCHMIDT, Proc. Nat. Acad. *34*, 245 (1948).

[3] J. SEILER, Exper. *11*, 425 (1949).

true for many mutants of Drosophila and is clearly an embryological feature based upon threshold conditions and the like and not an expression of locally different determination. It is clear that the sexual correlation requires either a genetic or a phenotypic cause which affects the individual as a whole, but is variable (point 1) between individuals of a sibship.

(3) The component parts of organs, tissues, and individual cells are either completely female or male. Their different mixture into a kind of mosaic (see details below) determines the degree of femaleness or maleness, i. e. of intersexuality. This means that the individual cells have only the alternative reaction, female or male. In some organs the alternative is decided for one or a few cells independently so that an intricate mosaic of female and male parts can appear, e. g. in the epithelium of the oviduct. In other organs the whole or major parts may show the sexual alternative. This is the case for the gonads. In both cases we see that with the increase of the overall sexual determination, say increasing overall maleness, the male determination of the constituents of a single organ spreads correspondingly. In an organ like the gonoducts small patches of male epithelium first appear between the female cells, the patches increase in number, become confluent and, in high-grade intersexuality, leave only small patches of female epithelium. This shows, first, that there is no intersexual differentiation, as BALTZER[1] and KOSMINSKY[2] claim (Bibliography in: GOLDSCHMIDT[3]), but only female and male, as shown in Lymantria. Moreover, it shows that in such organs of mosaicistic behavior the threshold for the alternative male/female differentiation is of such a nature that it is passed more and more easily with the increase of whatever it is that produces more female or male determination; and further, that the threshold zone is so narrow that small local features, local for a few cells, influence the result.

To these general features which must be covered by an explanation of the entire phenomenon have to be added the specific features found in the individual organs. These can best be analysed in connection with the interpretation.

V. *The general interpretation*

We have already pointed out that these facts cannot be explained by a constant F/M balance and phenotypic factors which control local differentiations, and we showed that SEILER[4], who favors this explanation, was forced to add genotypic differences of unknown origin. Also, we have already discussed the genetical facts upon which, in our opinion, a consistent explanation accounting for all the facts ought to be based. The decisive fact is that the female determiners in the Y chromosome act before the meiotic divisions, so that the XY egg has already started its determinative segregation (to use LILLIE's[1] term) or predetermination (in BALTZER's[2] language) in a female direction at the time of fertilization. Only then the intersexual F/M or $3\,A/2\,X$ balance is established which makes for increased, though incomplete, male determination. If this is the genetic situation, as I am convinced it is, it follows that the developmental situation parallels in many respects that in Lymantria female intersexes, namely, first female differentiation, afterwards male, and the turning point in Lymantria is represented by the time of fertilization in Solenobia or the beginning of the action of the chromosomes in the synkaryon. This explains completely the major stumbling block to SEILER's interpretation, the correlation of the degree of intersexuality in all organs. It agrees further with the facts of triploid intersexuality in Drosophila. Here we know now that male determiners act before fertilization. DOBZHANSKY and BRIDGES[3] and DOBZHANSKY[4] have shown that these intersexes are male intersexes in the Lymantria sense and are developed with a turning point.

The other major general fact which has to be explained is the immense variation within a sibship from near femaleness to near maleness. SEILER[5] considers all these types as variants of genetically intermediate intersexuality, some more male-like, some more female-like. According to the interpretation just proposed they are all comparable to female intersexes of Lymantria in so far as they start with female development and continue otherwise after the turning point, fertilization. If the female determination would stop abruptly at the time of the establishment of the intersexual genetic constitution, i. e. at fertilization, all individuals should show the same degree of intersexuality. The huge variation actually found demonstrates that the determinative processes do not take place in this schematic way but that the female predetermination fades out after fertilization with an irregularly variable speed and that the not-female determination takes over at a correspondingly variable time. In agreement with SEILER[5], we may call this a phenotypical control of this transitional period different from individual to individual because of the variability of internal and external environment. We may also assume that this irregular continuation and fading out of the maternal cytoplasmic determination is characteristic of determination after the ceasing of

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[1] F. BALTZER, Rev. suisse Zool. *44*, 331 (1937); Roux' Arch. *136*, 1 (1937).

[2] R. GOLDSCHMIDT, Arch. Klausstift. *21*, 269 (1946) Roux' Arch. *124*, 93 (1931).

[3] R. GOLDSCHMIDT, Genetica *20*, 1 (1938).

[4] J. SEILER, Exper. *11*, 425 (1949).

[1] F. R. LILLIE, Arch. Entwicklungsmech. *118*, 499 (1929).

[2] F. BALTZER, Rev. suisse Zool. *44*, 331 (1937); Roux' Arch. *136*, 1 (1937).

[3] TH. DOBZHANSKY and BRIDGES, Amer. Nat. *62*, 425 (1928).

[4] TH. DOBZHANSKY, Bull. U.S.S.R. Bur. Genet. *8*, 91 (1930).

[5] J. SEILER, Exper. *11*, 425 (1949).

genic control (here from the *Y* chromosome). Certainly the overall effect is the same as a variation in the time of incidence of the turning point in Lymantria.

VI. *Application to the morphological facts*

If this interpretation is correct, it must not only explain the general features just discussed, but it must be borne out also by the details of the morphology of the intersexes, the same details which the SEILER[1] School claims to be incompatible with a turning point concept. If we want to analyse these facts, we must first see clearly the expectations derived from the genetic interpretation. (We have no experimental information on the quantitative share of predeterminative processes in the final determination of individual organs of Lepidoptera. It might, however, be a fair guess that organs formed in early development have a larger share of predetermination than those differentiating lately.) In regard to sexual differences we have mainly two types. (1) There are organs formed from a single anlage which has an alternative potency of differentiation, female or male, according to which genetic control is present. Such organs should reveal a turning point by showing the consequence of more or less prolonged female differentiation followed by a not-female development. This turning point would, however, not become visible in all cases. (2) Some characters in which the sexual differences are of a purely quantitative nature, e. g. an organ long in one sex, short in the other, will exhibit an intermediate lenght. This might be interpreted as proof of intermediate, intersexual development. But it is obvious that development with a turning point leads to exactly the same result. Therefore, all these quantitative sexual differences—and these form the majority in the long list of traits studied by the SEILER School—cannot be used for a decision, and their inclusion in lists of traits which are not supposed to agree with the time law is misleading.

Thus, the analysis can be made only with organs of alternative character, say, the gonads which are either testes or ovaries. The turning point would become visible in the form of an ovary which transforms sooner or later into a testis, as shown in full detail in Lymantria. (See GOLDSCHMIDT and SAGUCHI[2], GOLDSCHMIDT[3].) Here the difference between Lymantria and Solenobia comes into play. In a female Lymantria intersex development is male after the turning point as the male determiners are more or less preponderant or, perhaps, not suppressed. In Solenobia the valency of the sex determiners F/M is exactly in between male and female preponderance. Therefore a simple switch over to male determination is not expected. If the cells, tissues, and organs have only an alternative norm of reaction, female or male, which we know they have, it will depend upon local environmental conditions whether the male control after fertilization succeeds or not. This means that we expect within an organ of the type under discussion a great variation: purely female parts, purely male parts, and those which show the turning point. There are additional features on a purely embryological basis. For example, a primary ovarial structure may, when the ± male determination begins, stop female development without change to male differentiation; or, in other cases, be already so far advanced in female differentiation that it continues more or less normally to the end. There are examples from other organisms showing that all this is possible. In Lymantria the gonads show considerable variation of the individual tubules in the succes of transformation from one sex to the other. In intersexual males, when the uncus anlage develops into labia sometimes the tip continues uncus-like differentiation. Still more extreme is the situation in *Drosophila virilis* where LEBEDEFF[1] found that after the turning point the gonad sprouts one of the opposite sex and both continue development. The anatomy of some other types of Drosophila intersexes seems to indicate similar processes.

Let us now compare the facts with these expectations. The most important organs having alternative norms of reaction are the gonads, and in Lymantria they strikingly show the time law at work. In Solenobia the more female types of intersexes have ovaries which are more or less normal and the more male-like intersexes have more or less normal testes. In the intermediate group the individual tubules (4 in each gonad) may be female or male in a variable way and may contain sex cells of the other sex. In addition, many types of incompleteness, insufficient histological differentiation and rudimentation are found. But in a certain percentage of cases the typical structure of an ovary on the way to transformation into a testis is found, structurally identical with the type found in Lymantria. SEILER[2] is ready to ackmowledge that these tubules agree with the turning point concept but is much impressed with the observation that only 4% of the tubules are found in this condition. I think that the computation is not correct in this case. As the entirely female and entirely male gonads cannot show such a structure (in the male gonads it might be found in early development), they ought to be excluded from the calculation. Further the calculation in terms of individual tubules is not justifiable. If the turning point occurs for the whole gonad, small differences in the determinative condition of the individual tubules of one gonad will result in one being still female, the other already transformed into a testis compartment, the third still in the clear stage of transformation.

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[1] J. SEILER, Exper. *11*, 425 (1949).

[2] R. GOLDSCHMIDT and S. SAGUCHI, Z. ges. Anat. *65*, 226 (1922).

[3] R. GOLDSCHMIDT, Roux's Arch. *124*, 618 (1931).

[1] G. A. LEBEDEFF, Genet. *24*, 553 (1939).

[2] J. SEILER, Exper. *11*, 425 (1949).

The percentage of the gonads found in the "turning point stage" should be based only upon the cases of medium intersexuality and on gonads showing at least one such transforming tubule. If calculated thus, the percentage will be considerably higher. The variability found within tubules is actually very much greater than in Lymantria. This is expected on the basis of the different genetic constitution as discussed above. In addition, SEILER[1] himself emphasizes that there is order within this variation. The more an individual approaches the type of one or the other sex, the fewer are the parts having the structure of the opposite sex. The facts thus agree completely with our interpretation.

Another organ with alternative norm of reaction is the proximal gonoducts. Their structure is very interesting. There are cell groups of flat female epithelium and others of high cylindrical epithelium typical of the male organ. There is no intersexual structure, but the quantity of these mosaic patches is—within a variation similar to that of the gonad—strictly proportional to the grade of intersexuality. A largely female intersex has only a few male epithelial spots, which increase with intersexuality towards the reciprocal condition. According to SEILER, this requires the interpretation that from the beginning of development both female and male determiners act simultaneously and that phenotypic conditions control the result *in loco*. We have already pointed out that this explanation does not work because it fails to explain the correlation of the quantity of the mosaic spots with the general grade of intersexuality. This correlation requires an explanation of the turning point type for the phenomenon as a whole, plus an explanation of the special feature of mosaicism versus sexual shift for all cells simultaneously. As a matter of fact, certain features of the Lymantria intersexes point to an interpretation for the latter facts. While in female intersexes in Lymantria the wing color as a whole turns male, in male intersexes the wing color (and structure of the scales) shows exactly the same mosaicism as just described for the gonoducts of Solenobia. Now in Lymantria a certain cross exists (the so-called Gifu type) in which female intersexual wing color also shows mosaicism, for which some genetic factor introduced by the Gifu race is responsible. It is obvious that mosaicism in the Lymantria intersexual males is due to features of the determination system in the wing which are characteristic of the male genotype, but which can be introduced also into the female genotype by appropriate genetic factors. (A theory of how this determination system works to produce the mosaicism has been developed [see GOLDSCHMIDT[2]] but is irrelevant for the present discussion.) From all this I conclude that mosaicism in the Solenobia gonoducts has nothing to do as such with the F and M action but is the result of the type of determination in the organ. This means that in the case of the more female type of intersex female determination has spread in the organ in such a pattern that some spots are still undetermined when the turning point (i. e. the action of the chromosomal factors after fertilization) arrives. The undetermined patches will be male as there is no intersexual differentiation possible. Correspondingly the situation changes with earlier and earlier occurrence of the turning point.

SEILER[1] mentions some other organs with exactly the same behavior, including intersegmental membranes, abdominal sternites. The same discussion, criticism, and interpretation apply to all these organs as to those just discussed.

The second group of organs, most important for the interpretation, are those occurring in only one of the sexes. These are those parts of the sexual organs which develop from imaginal discs formed only in one sex. In the female there are a pair of imaginal discs in the 8th and 9th segments from which the bursa and distal gonoducts are developed. In the male the 9th segment has a disc which transforms into Herold's organ and differentiates into the main parts of the genital armature, valvæ and penis. If the time law controls intersexual development in the way discussed above we expect that low grade (i. e. preponderantly female) intersexes will have the female discs and their derivatives but no Herold's organ; further, that high-grade intersexes will have Herold's organ and derivatives but no female discs. According to SEILER'S work, both expectations are fulfilled. In the intermediate grades of intersexuality the female disks are already formed (or determined, which means that the decision for their formation is reached before they become actually visible, as is a general rule in embryonic. determination) when the turning point sets in. This may mean that their further differentiation is slowed up or stopped entirely. But it might also mean (see discussion above) that they continue with a more or less normal development. The male Herold's organ will develop only after the turning point and therefore reach, at the end of development, a more or less advanced state of the formation of its derivatives, as is so beautifully demonstrated in the Lymantria series. What are the actual facts in Solenobia? There are more or less complete female distal gonoducts present in intermediate intersexes (together with the male ones); also, more or less of the female genital armature beside the male apparatus. Herold's organ and its derivatives, valvæ and penis, are present in a series of conditions of growth from a simple bladder to a bladder with rudiments of valvæ and penis to in-

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[1] J. SEILER, Exper. *11*, 425 (1949).

[2] R. GOLDSCHMIDT, Arch. Mikr. Anat. *98*, 292 (1923).

[1] J. SEILER, Exper. *11*, 425 (1949).

complete valvæ and penis. This series is proportional to the general degree of intersexuality of the individual (detailed description by Nuesch[1]). In other words, Herold's organ, the most important organ for checking on the time law, behaves exactly as expected.

Why does Seiler not accept this well documented conclusion ? The reason is that he is greatly impressed with the fact that whatever parts are present are histologically completely female or male, and that therefore, in his opinion, they cannot represent developmental stages, as required by the time law. Here Seiler[2] overlooks an important point. In insect development epidermal differentiation culminating in chitinization is clearly determined for the entire body, most probably by hormones. If, e. g. a valva has grown in Herold's organ to half its size and an uncompleted form when the hormonal system produces the last stages of metamorphosis for the entire body, namely final histological differentiation and chitinization, whatever is present of the valva at that point, in our example, will undergo this final differentiation. It is therefore the stage of growth attained, not the kind of histological differentiation, which is the expression of the time law. Thus, we see that the morphology of the most important organs of the Solenobia intersexes agrees perfectly with our interpretation.

VII. *The time law of intersexuality*

In the discussion of the interpretation of the Solenobia intersexes, we find that the differences of opinion center around the time law of intersexuality. In my opinion, both parties to the discussion have committed errors in these discussions, the Seiler[2] School (especially its enthusiastic younger members) by a pessimistic and, I think, erroneous interpretation of the facts and unjustified extension of their divergent views upon other objects, and myself by being too dogmatic in the application of the time law to different materials. Therefore, it may be useful to see clearly where we stand now in regard to the time law.

Before doing this it might be appropriate to mention here the individual cases which have been discussed in the literature, other than Solenobia. (1) Kosminsky found a completely aberrant type of intersexuality in *Lymantria dispar*, produced by specific genetic modifiers. (See analysis in: Goldschmidt[3].) In explanation of this new type he accepts the time law but thinks that after the turning point development is not female but intermediate. My analysis is found in the just quoted paper. (2) Dobzhansky and Bridges[4] and especially Dobzhansky[5] studied morphology and development of the triploid intersexes of Drosophila and found them in agreement with the time law as male intersexes. (Bridges[1] later made a deprecatory remark on the time law, completely forgetting his own results substantiating it.) (3) Lebedeff[2] made a similar study for the diploid intersexes of *Drosophila virilis* and found morphology and development in agreement with the time law, though additional features unknown in Lymantria were found. (4) Goldschmidt[3] and Goldschmidt and Pariser[4] stated that the morphology of the triploid intersexes in Saturnia and Biston species hybrids parallels so much that of Lymantria intersexes that the same explanation seems appropriate. (5) Wharton[5] found Drosophila intersexes after a species cross. The short description and the illustrations are in harmony with an interpretation according to the time law, as far as I can see. (6) Newby[6] studied in detail the diploid intersexes produced by a single mutant in *Drosophila virilis*. He concludes that intersexes do not follow the time law. The morphological and developmental data which he gives are at complete variance with Dobzhansky's[7] detailed description. As errors and misinterpretations seem to be abundant, Newby's[6] analysis must be regarded with great skepticism in spite of his arrogant and aggressive assertions. This is not the place for a detailed critique. Only one typical example of his reasoning may be given. The development of the gonad is such as would be expected under the time law. These are Newby's comments:—"Therefore, this organ might be said to follow the 'time law' or turning point requirement for an intersex. These facts, however must be considered: If I had dissected the specimens and had made only a gross examination of the gonads I could not have distinguished ovaries and intersex gonads until much later in development. If, on the other hand, I had used greater care in the preparations of my sections, had tried other fixative or stains, had made more careful measurements of average cell size; in other words, if I had used better technique, I have no doubt but that I could have distinguished ovaries and intersex gonads much earlier than I did. If, as is true, the time of the turning point depends entirely upon the technique used in its determination its significance as a 'law' becomes greatly reduced and its actual existence is subject to doubt." (7) Dobzhansky and Spassky[8] found diploid intersexes in *Drosophila virilis* which are completely

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[1] H. Nuesch, Arch. Klaus Stiftg. *22*, 221 (1947).

[2] J. Seiler, Exper. *11*, 425 (1949).

[3] R. Goldschmidt, Genetica *20*, 1 (1938).

[4] Th. Dobzhansky and C. B. Bridges Amer. Nat. *62*, 425 (1928).

[5] Th. Dobzhansky, Bull. U.S.S.R. Bur. Genet. *8*, 91 (1930).

[1] C. B. Bridges, in: Allen, *Sex and Internal Secretion*, p. 15 (1939).

[2] G. A. Lebedeff, Genet. *24*, 553 (1939).

[3] R. Goldschmidt, Biol. Cbl. *45*, 536 (1925); *Die sexuellen Zwischenstufen*, Monogr. Gesamtgeb. (Springer, Berlin) p. 554 (1929).

[4] R. Goldschmidt and K. Pariser, Biol. Cbl. *43*, 446 (1923).

[5] L. T. Wharton, University Texas Publ. *4228*, 23 (1942).

[6] W. W. Newby, University Texas Publ. *4228*, 113 (1942). See also W. Stone, University Texas Publ. *4228*, 146 (1942).

[7] Th. Dobzhansky, Bull. U.S.S.R. Bur. Genet. *8*, 91 (1930).

[8] Th. Dobzhansky and B. Spassky, Proc. Nat. Acad. *27*, 556 (1941).

different from triploid Drosophila intersexes. They resemble much more hermaphrodites in as much as they have both types of sex organs. Their origin might be on a different level as that of typical intersexes, involving duplication of genital discs[1].

The criticism of the time law was started by BALTZER who came to the conclusion that it does not apply to the intersexes of Bonellia. Assuming that this is so (see, however, my counter-criticism[2], it is not clear why a phenotypic, normal type of sex determination in a worm with all the unusual features of the Bonellia case should throw light upon a genetically controlled process in an insect with all its typical developmental features. In fact, BALTZER[3] after combing the Lymantria data for discrepancies, could not find anything to criticize but a few minor details and the already quoted completely different case of KOSMINSKY (for which this author also had to invoke the turning point concept). In view of rather superficial, uncritical, and biased mention of some of these criticisms in some recent literature, it may be pardonable to insert this short review at this point.

Let us return now to the time law and the Solenobia case. The time law, as derived from the study of the Lymantria intersexes, states that intersexes are individuals which develop first according to their gametic XX or XY sex and, after a turning point, finish development with the other sex. The degree of intersexuality is a function of the position of the turning point in time. It is obvious that this concept cannot be applied literally to triploid intersexes, which do not have a gametic female or male sex but are in this respect intermediate between the sexes. Even so, we have shown above that these intersexes behave like a series of female intersexes, i. e. demonstrate that development starts in each individual as female development. It is true that the primary female (or, in Drosophila, male) differentiation could not be predicted on the basis of the genetic constitution, but it is a fact, which was explained above by predetermination. In Lymantria development after the turning point according to the opposite sex is a fact. Theoretically, it might also have been an intermediate, intersexual development. In a triploid intersex with primary female predetermination followed by a turning point at or after fertilization one could expect the following to happen after the turning point:—

(1) Intermediate, intersexual development.

(2) Independent action of female and male determiners resulting in a mosaic development.

(3) Predominantly male control of development, as in Lymantria. Both SEILER[1] and I agree that the first is not the case. The second is SEILER's[1] choice (apart from his assuming a turning point only as a rare feature of the sex glands). There is very little *a priori* probability for this view. As far as I can see no genetic epistatic system is known to work this way and the F/M balance works, of course, like an epistatic system. In addition, I have shown above that almost all the important facts of the case cannot be explained this way. Thus, only number three remains. There is no possibility of telling *a priori* why, in an intermediate epistatic system, in this case intermediate between female and male determination, one partner should take over. But as we know that the Y-chromosomal F factors act before fertilization and that the autosomal F factors act more as modifiers we can state as a hypothetical interpretation that the action of the F factors is being exhausted at the time of the turning point, the latter actually being an indication of this. Thus, we think that the time law of intersexuality is at work also in the triploid intersexes, but that there are the above discussed additional features, like variability of the time at which the predetermined female action ceases, tendency of organs to continue their differentiation after the turning point if it does not occur very early or very late with consequent mosaicism and other similar features described above. Thus, I believe we are able to understand and to explain the triploid intersexes of Solenobia within the framework of other well-analysed facts.

Zusammenfassung

SEILER hat den jetzigen Stand seiner Studien an triploiden Intersexen von Solenobia zusammengefaßt. Es ist möglich, erneut zu seiner Interpretation der Resultate Stellung zu nehmen. Nach SEILER sind die morphologischen Tatsachen nicht mit dem Zeitgesetz der Intersexualität vereinbar. In der vorliegenden Arbeit wird versucht, nachzuweisen, daß das Gegenteil zutrifft.

Zunächst wird festgestellt, daß die alten Tatsachen bei Lymantria die zur Aufstellung des Zeitgesetzes führten, unerschüttert bleiben, welches auch die Ergebnisse an anderen Objekten sein mögen.

Für die Analyse der Intersexe von Solenobia ist die Tatsache wichtig, daß der Grad der männlichen oder weiblichen Ausbildung der intersexen Organe gleich oder doch sehr ähnlich ist. SEILERS genetische Interpretation dieser Tatsache wird diskutiert und abgelehnt. Neuere Arbeiten – wie auch schon die Untersuchungen an Lymantria – zeigen, daß das Ei bereits vor der Befruchtung weiblich bestimmt wird. Dies und die allgemeinen Determinationsverhältnisse im Insektenei machen es möglich, daß triploide Intersexe *vor* der Befruchtung weiblich determiniert werden, während *nach* der Befruchtung die genetische Determination intersexuell ist. Damit kann aber das Zeitgesetz gültig sein.

Folgende Haupttatsachen sind zu deuten: 1. die sehr große Variabilität innerhalb der Geschwisterschaften;

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[1] Since this was written I could analyse a new case of diploid male intersexuality in Drosophila which follows beautifully the time law and also furnishes the data for the proper interpretation of NEWBY's intersexes.

[2] R. GOLDSCHMIDT, Genetica *20*, 1 (1938).

[3] F. BALTZER, Rev. suisse Zool. *44*, 331 (1937); Roux's Arch. *136*, 1 (1937).

[1] J. SEILER, Exper. *11*, 425 (1949).

2. die Übereinstimmung der Intersexualitätsgrade aller Organe; 3. die rein männliche oder rein weibliche Struktur der Organe bis zu den einzelnen Zellen. Das schließt eine intersexuelle Entwicklung aus und läßt eine alternative Ausbildung mit bestimmten Schwellenbedingungen annehmen.

Ein konstantes F/M-Gleichgewicht zusammen mit phänotypischen Faktoren kann diese Tatsachen nicht erklären (SEILER nahm hierfür unbekannte genotypische Faktoren an). Die obenerwähnte genetische Situation mit Prädetermination durch die weiblichen Faktoren im Y-Chromosom erklärt dagegen zwanglos alle drei Tatsachengruppen auf der Basis des Zeitgesetzes ohne zusätzliche Hypothesen.

Auf Grund der so gewonnenen Erklärung – weibliche Prädetermination gefolgt von intermediärer Determination und langsamem variablen Abklingen der Prädetermination – werden in einem folgenden Kapitel die Einzelheiten der Intersexemorphologie analysiert. Die Erwartungen auf der Basis des Zeitgesetzes werden abgeleitet. Dann wird gezeigt, daß nur Organe mit alternativer Determination der gleichen Anlage oder Organe, die nur in einem Geschlecht vorkommen, entscheidend Auskunft geben können. Im einzelnen werden deshalb Gonaden, proximale Gonodukte und das Heroldsche Organ analysiert, mit dem Ergebnis, daß sie alle dem Zeitgesetzt gehorchen. Der Grund für die abweichenden Schlußfolgerungen von SEILER wird aufgezeigt.

Abschließend wird das Zeitgesetz generell diskutiert.

Das Intersexualitätsphänomen

Zusammenfassende Darstellung des Beobachtungsmaterials an *Solenobia triquetrella* (Lepid. Psychidae) und Deutungsversuch

Von J. SEILER[1,2], Zürich

1. *Einleitung*

Es glückte, auf verschiedenen Wegen und an verschiedenen getrennt geschlechtlichen Objekten, durch Kreuzung Tiere zu erzeugen, die weder Männchen noch Weibchen sind. In allen Merkmalen, in welchen sich die normalen Geschlechter unterscheiden, stehen diese Tiere zwischen den reinen Geschlechtern und werden deshalb Intersexe genannt. Ihr Bau ist kompliziert; bald gleichen sie mehr den Weibchen, bald mehr den Männchen; wir sprechen von weibchenähnlichen und männchenähnlichen Intersexen; beide können sich in beschränktem Maße noch fortpflanzen. Dazwischen stehen die intermediären Intersexe, deren Geschlechtsorgane so sehr vom Normalen abweichen, daß eine Fortpflanzung nicht mehr möglich ist.

Es mag dem Außenstehenden müßig erscheinen, im Experiment solche Tiere zu erzeugen und noch müßiger, sie in langer Arbeit zu analysieren. Die Bedeutung solcher Studien wird jedoch verständlich, wenn ich daran erinnere, daß die Lösung der schwersten Frage, welche die Genetiker zu lösen hatten, die Lösung der Frage nach der Vererbung und Bestimmung des Geschlechts, sich letzten Endes aus den Intersexualitätsstudien ergab.

Dazu kommen praktische Gesichtspunkte. Auch beim Menschen treten vereinzelt intersexe Individuen auf. Man möchte wissen, welches die Ursachen dafür sind, und der Arzt wird nach Möglichkeiten suchen, diesen Unglücklichen zu helfen. Voraussetzung dafür ist, daß das Wesen der Intersexualität verstanden wird.

Dieses Phänomen ist nun an sich schon überaus kompliziert, wohl am kompliziertesten aber bei den Säugetieren und im besondern beim Menschen. Das deshalb, weil hier die Geschlechtsausprägung nicht nur von genetischen Faktoren abhängt, sondern außerdem noch von der richtigen oder nicht richtigen Funktion einer ganzen Anzahl von innersekretorischen Drüsen. Es dürfte ein fast aussichtsloses Unterfangen sein, an solchen Objekten das Phänomen der Intersexualität lösen zu wollen. Wohl mag es im Experiment glücken, den einen oder andern Faktor auszuschalten oder sonstwie zu fassen und auf seine Wirkung hin zu prüfen. Aber hinter dieser einen Unbekannten stehen Dutzende von andern, sich gegenseitig beeinflussender Unbekannten, die bestimmend in das Spiel der Entwicklungsprozesse eingreifen. Dazu kommt, daß man an solchen Objekten über die genetischen Faktoren zumeist nichts in Erfahrung bringen kann. So ist es nicht verwunderlich, daß die Untersuchungsergebnisse auch heute noch überaus widerspruchsvoll sind (vgl. die neueste Zusammenfassung über Intersexualität bei Wirbeltieren, PONSE[1]). Selbst in Grundfragen wider-

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[2] In Dankbarkeit widme ich diese Arbeit Dr. CURT B. HANIEL und Frau HEDI HANIEL, Schlederlohe/München. In ihrem Privatinstitut für Genetik durfte ich in freier Forschertätigkeit in den Jahren 1920–28 das Fundament zu den Intersexualitätsstudien an Solenobia legen.

[1] K. PONSE, *La différenciation du sexe et l'intersexualité chez les Vertébrés* (Rouge, Lausanne 1949).