edematous. When observed with UV-light the uterine wall, the placenta, the fetal membranes and the pups fluoresced blue, while the placenta from a normal rat had a red fluorescence.

Pathologic Study. There were no tumors observed in this group of rats. The 6 non-pregnant females that had been fed the chow containing benzpyrene for $3^1/_2$ months averaged 253 g, while the 3 non-pregnant controls averaged 270 g. No significant differences were observed histologically in the ovaries, adrenals or pituitary gland of the treated and the control groups of rats. Several of the rats had an acute and chronic pneumonitis. No pathologic changes were observed in the viscera of the benzpyrene-treated rats that could be associated with this hydrocarbon. No attempt was made in this study to observe fluorescence in the cells of the benzpyrene-treated rats, and no significant histologic lesions were observed.

Discussion. It may be concluded from this experiment that the feeding of benzpyrene to rats does not interfere with the ovarian cycles, ovulation, fertilization, or implantation; however, it does have a deleterious effect on embryonic development. It may interfere with lactation, although more data is needed to establish this point.

Only one pup was observed to be malformed. This abnormality may or may not be related to the presence of this hydrocarbon. In several of the pregnancies the fetuses apparently died and were absorbed. The fetuses removed at autopsy were dead in one female fed benzpyrene. These observations would support the opinion that either benzpyrene or a metabolite may be lethal for developing embryos.

The blue fluorescence as observed in the viscera of the rats fed benzpyrene is similar to that previously described in ducks, chickens, dogs, mice, and cockroaches fed benzpyrene[4–7]. It is not known at this time whether this blue fluorescence results from the presence of benzpyrene or a metabolite. In previous studies of mice fed large amounts of benzpyrene the liver and kidneys were blue and benzpyrene was demonstrated spectrophotometrically.

The fetuses from mothers fed benzpyrene had a blue fluorescence. The uterine wall, fetal membranes and the placenta likewise fluoresced blue, while similar tissues in rats fed the control rations had a red fluorescence. The agent responsible for this blue fluorescence is transmitted through the milk to the young mouse[4].

Obviously the amount of benzpyrene fed to this group of rats is excessive. We have not observed, however, any evidence of toxicity, other than in the developing embryo. WHITE and WHITE[8] in 1939 expressed the opinion that certain of the carcinogenic hydrocarbons were toxic and suggested that the growth-inhibitory substances exert their effects by the production of a specific deficiency in the sulfur-containing amino acids, probably through the requirements of the organism for organic sulfur in the form of cystine and methionine, for detoxication mechanisms.

RIGDON and GIANNUKOS[9] observed a loss of weight in mice fed methylcholanthrene, pyrene, anthracene and benzpyrene. This loss of weight was shown to be related to the amount of food consumed. Mice ate little of the food containing large amounts of these hydrocarbons. No pathologic changes were observed in the viscera of the mice fed benzpyrene and methylcholanthrene. The rats fed benzpyrene in the present experiment had no pathologic changes that we could associate with a toxic effect resulting from the benzpyrene. HADDOW and ROBINSON[10] and HADDOW et al.[11] did not observe histologic changes in the liver, spleen, kidney, bone marrow, adrenals, or thyroid of mice given benzpyrene intraperitoneally.

PAYNE[12] injected rats intraperitoneally with benzpyrene and observed cysts in the ovary, endometrial hyperplasia of the uterus, and the development of mammary adenocarcinomata. The interstitial (Leydig) cells were completely absent except in those animals where interstitial cell adenomata occurred. CRAMER and HORNING[13] found no changes in the endocrine organs of mice painted with benzpyrene. LARIONOW[14] observed changes in the endocrine organs of mice painted with benzpyrene that were similar to those occurring in old age. PEACOCK[15] did not observe any benzpyrene in the developing mouse embryo when pregnant mice were injected intravenously with benzpyrene.

Résumé. Lorsque des rats sont soumis à une diète riche en benzopyrène, leurs embryons peuvent dégénerer et être résorbés. Le placenta et les membranes fétales ont une fluorescence bleue. Normalement, ces mêmes tissus ont une fluorescence rouge.

R. H. RIGDON and E. G. RENNELS

Departments of Pathology and Anatomy, The University of Texas Medical Branch, Galveston (U.S.A.),
December 16, 1963.

[8] J. WHITE and A. WHITE, J. biol. Chem. *131*, 149 (1939).
[9] R. H. RIGDON and N. J. GIANNUKOS, Arch. Path., *17*, 198 (1964).
[10] A. HADDOW and A. M. ROBINSON, Proc. Roy. Soc. London, Ser. B *122*, 422 (1937).
[11] A. HADDOW, C. M. SCOTT, and J. D. SCOTT, Proc. Roy. Soc. London, Ser. B *122*, 477 (1937).
[12] S. PAYNE, Brit. J. Cancer *12*, 65 (1958).
[13] W. CRAMER and E. S. HORNING, Amer. J. Path. Bact. *44*, 633 (1937).
[14] L. LARIONOW, Amer. J. Cancer *38*, 492 (1940).
[15] P. R. PEACOCK, Amer. J. Cancer *40*, 251 (1940).

Slow Periodicity in the Dark Discharge of Retinal Units

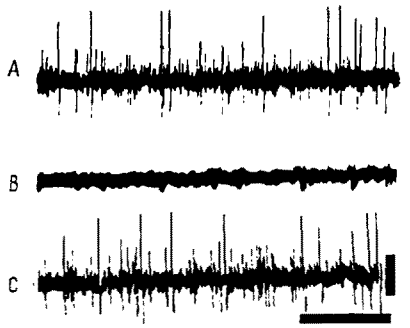
During experiments concerned with the statistical parameters of retinal discharge under conditions of complete dark adaptation, an almost regular periodic firing pattern was sometimes observed in retinal ganglion cells.

Cerveau isolé cats (postcollicular transection) were used. Eye movements were prevented by a curare-like drug (Sincurarine, Farmitalia) and the animal was maintained under artificial respiration. The cornea was excised and the lens ablated. A steel microelectrode 5–10 μ in diameter was introduced into the retina by a micromanipulator. The potentials picked up in this way were amplified and recorded on a multichannel magnetic tape, Ampex F.M. 1107 with band pass filters set from 0 to 5000 cps. In some of the preparations EEG activity and arterial blood pressure were controlled.

In a number of experiments, the firing of the dark adapted cells was observed to fluctuate, disappearing and reappearing with a certain periodicity. The time course of these fluctuations, that is the 'period' of these retinal neurons, was sometimes of a few seconds, i.e. of the order of that observed in previous experiments on conger-eels[1], frogs[2,3] and cats[4,5]. Frequently, however, we found a surprisingly slow periodicity, of the order of a few and even of several minutes.

The discharge of the three retinal units recorded in the Figure lasted from $1^1/_2$–2 min (A, C) and was interrupted by periods of silence (B) which persisted for 30–35 sec (in the Figure the horizontal bar represents 30 msec, while the voltage calibration is 100 μv). This periodic activity went on regularly throughout the time of recording (2 h). In other experiments, the 'period' of the retinal unit was still longer: up to 5–6 min and in one case up to 20 min. Obviously we considered only those experiments where this alternation of activity was regularly and repeatedly observed. By moving the microelectrode just a few microns away, this alternating activity could not be observed in neighbouring cells. It would appear, therefore, to be specific to particular points of the retinal neural net.

Future research will aim at a statistical study of samples of very long duration of retinal cell activity. The origin of this alternation, whether autochthonous, e.g. arising in the retina, or dependent upon the activity of centrifugal fibres in the optic nerve, will also be investigated[6].



Riassunto. La registrazione microelettrodica della retina del gatto «cerveau isolé» adattato completamente all'oscurità ha messo in evidenza talvolta una attività ritmica a lungo periodo, nella scarica delle cellule ganglionari.

D. Ascoli and L. Maffei

Istituto di Fisica e Istituto di Fisiologia dell'Università di Pisa e Centro di Neurofisiologia del C.N.R., Pisa (Italy), October 21, 1963.

[1] E. D. Adrian and R. Matthews, J. Physiol. *65*, 273 (1928).
[2] H. B. Barlow, J. Physiol. *119*, 69 (1953).
[3] R. Granit, Acta physiol. scand. *1*, 370 (1940).
[4] S. W. Kuffler, J. Neurophysiol. *16*, 37 (1953).
[5] A. Arduini and L. R. Pinneo, Arch. ital. Biol. *100*, 425 (1962).
[6] This research has been sponsored jointly by the office of Scientific Research, EOAR, through the European Office, Aerospace Research, United States Air Force, under Grant EOAR-62-9, and by the Rockefeller Foundation.

Über eine spontane Extrasystolie im Schrittmachersystem des Tunicatenherzens (*Ciona intestinalis* L.)[1]

Bekanntlich zeigt das schlauchförmige, klappenfreie Tunicatenherz[2] periodische Reversionen des Herzschlags. Die herrschende Vorstellung über das Zustandekommen der sogenannten Schlagumkehr nimmt zwei terminale kompetitive Schrittmacher, ein viscerales und ein hypobranchiales Automatiezentrum an, welche normalerweise alternierende Serien peristaltischer Kontraktionswellen produzieren. Der vorhandenen diffusen Automatie bzw. den basalen Schrittmachereigenschaften des ganzen Herzschlauchs wird für die spontane Reversion keine funktionelle Bedeutung beigemessen[3]. Eine extrakardiale Regulation fehlt offenbar. Das Schrittmachersystem scheint rein myogen, eine Auffassung, die auch durch die bisherigen pharmakologischen Befunde gestützt wird[4,5].

Eigene experimentelle Untersuchungen (EKG) an nichtisolierten und isolierten Herzen von *Ciona intestinalis* lassen hingegen erkennen, dass die alternierende Dominanz der Endzentren nicht die Hauptursache der Reversion des Herzschlags ist, sondern dass der zentrale Schrittmacher über eine charakteristische Spontanaktivität und Extrasystolie verfügt, die eine echte Störung der Automatie herbeiführt und die Schlagumkehr induziert. Zunächst wurde mit Ligatur- und Zerschneidungsexperimenten bewiesen, dass die diffuse Automatie über den ganzen Herzschlauch ubiquitär verteilt ist, ohne Ausbildung eines Automatiegradienten. Bei gleichzeitiger Ableitung der Aktionspotentiale aus verschiedenen Herzregionen mit Hilfe von Platin-Aspirationselektroden[6] findet man häufig an den Herzenden höhere Frequenzen, die von sehr niedrigen Potentialen herstammen. Das jeweils «dominierende Endzentrum» verfügt aber nicht über eine grössere Automatiestärke als die mittlere Herzregion. Synchronableitungen der Aktionspotentiale aus beiden Herzenden und zentralen Herzabschnitten mit Niederfrequenzverstärkung, Direktschreibung sowie gleichzeitiger photoelektrischer Registrierung der aktiven Pulswelle zeigten spontane Erregungsimpulse und Extrasystolen auf das zentrale Schrittmachergebiet beschränkt, welche der Reversion des Herzschlags unmittelbar vorausgehen (Figur 1). Führen diese Extrasystolen als echte Umkehrsystolen zur Schlagumkehr, so induzieren sie in

[1] Herrn Prof. W. v. Buddenbrock zum 80. Geburtstag.
[2] Nach bisher unveröffentlichten elektronenmikroskopischen Untersuchungen von W. Schulze, Berlin-Buch, handelt es sich beim Ciona-Herzgewebe um echte Epithelmuskelzellen (*vide* Exper. *20*, Fasc. 5 (1964), im Satz).
[3] Z. M. Bacq, P. Fischer und F. Ghiretti, Arch. int. Physiol. *59*, 165 (1951).
[4] B. J. Krijgsman und Nel. E. Krijgsman, Arch. int. Physiol. *67*, 567 (1959).
[5] B. J. Krijgsman, Biol. Rev. *31*, 288 (1956).
[6] H. Mislin, Rev. suisse Zool. *70*, 317 (1963).