

In support of this hypothesis, it was found³ in the case of a major sequela of iron deficiency in the pig which was characterized, among other appearances, by great destruction of liver parenchyma and a macrocytic anaemia, that the administration of liver extract produced a dramatic amelioration in which there took place a return of the circulating blood to normality and a replacement of the amitotic haemocyto-blastic blood formation in the marrow by a mitotic erythroblastic one. Recently Elvehjem and his collaborators⁴ have shown that liver extract contains nicotinamide, a substance which, as is well known, constitutes with pentose-nucleotide the coenzyme system. Further, Chick and co-workers⁵ have demonstrated that nicotinic acid brings about a rapid restoration of health in a condition of the pig termed by them "pellagra", but which, failing evidence to the contrary being forthcoming, would appear to be the iron deficiency sequela.

Caspersson and Schultz emphasize the point that in rapidly growing embryonic tissues (with frequent mitotic division, therefore) the cytoplasm of the cells stains basophile, an occurrence which they attribute to the presence of nucleotides. The characteristic feature of the haemocyto-blast is intense basophilia of the cytoplasm with marked achromasia of the nucleus. This state of affairs, on the contrary, is not associated with mitosis, rapid or otherwise, but with amitotic division, a process recognized by the competent authorities as being, in the majority of cases, a degenerative one. The degenerative aspect of the case is further added to by the fact that ripening of the erythrocyte, whether directly, as here, from the haemocyto-blast or indirectly, as in normal conditions, from the erythroblast, is essentially a degeneration.

In these circumstances it does not appear to be unreasonable to assume that, in mitotic division conditions with rapid increase in the chromatin of the dividing nuclei, nicotinic acid is a necessary adjunct to the nucleotides in the formation of coenzyme for the carrying out of important intracellular functions such as mitosis must be. Its absence would seem to furnish an explanation of the degenerative amitosis, defective chromatin formation, and premature ripening of the erythrocytes in the conditions just considered, in that coenzyme would be unable to function without it: while the return to normality in such cases after its administration could be construed as a restoration of the activity of the coenzyme by its presence.

On these lines it would seem that a tentative understanding of the pathogenesis of the anaemic conditions under discussion could be arrived at, though it is not suggested that nicotinic acid is the sole agent in liver extract which is active in such circumstances. At the same time, it is not supposed that failure of mitotic division in such cases is limited to the cells of the haemopoietic system.

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¹ Caspersson and Schultz, *NATURE*, 143, 602 (1939).

² McGowan, "Pernicious Anaemia, etc." (London: Lewis, 1926). *Proc. Roy. Soc. Med. (Sect. Compar. Med.)*, 21, 33 (1928). *Edin. Med. J.*, 37, 330 (1930); 42, 293 (1935).

³ McGowan and Sinclair, *Edin. Med. J.*, 38, 405 (1931).

⁴ Elvehjem et al., *J. Amer. Chem. Soc.*, 59, 1767 (1937).

⁵ Chick et al., *Biochem. J.*, 32, 10 (1938).

Preliminary Investigation of the Metabolism of Stilbene

EXPERIMENTS on the recovery of synthetic oestrogenic compounds related to stilbene and diphenylethane¹ from the urine of female rabbits have shown that the recoveries are very high compared with that of oestrone under the same conditions². Compounds such as 4:4'-dihydroxy- γ : δ -diphenyl-*n*-hexane and 4:4'-dihydroxy- α : β -diethylstilbene give recoveries of the order of 20 per cent compared with 1.5 per cent found for oestrone. This indicates a metabolic process for the synthetic oestrogens different from that of oestrone.

In studying the metabolism of these compounds, it was considered of importance to include stilbene, the simplest related active compound, which has been shown to produce full oestrous response in ovariectomized rats when injected in doses of 25 milligrams³.

Two grams of stilbene were injected into two female rabbits over a period of twenty days, and from the urine a crystalline phenol, melting at 283° C., was isolated. No depression in melting point was observed on mixing with an authentic specimen of 4:4'-dihydroxystilbene, melting point 284° C. No *p*-hydroxybenzoic acid was isolated from the urine, but benzoic acid was found in such quantities, more than twice that found in the control rabbit urine, as to leave little doubt that benzoic acid is a metabolic product of stilbene.

It is of particular interest to note that 4:4'-dihydroxystilbene is a more active oestrogen than stilbene, as it produces full oestrous response in doses of 10 milligrams, and 60 per cent response in doses of 5 milligrams, when injected into ovariectomized rats⁴.

Further extensive work on this subject is now in progress.

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¹ Dodds, E. C., Golberg, L., Lawson, W., and Robinson, Sir R., *Proc. Roy. Soc.*, B, 127, 140 (1939).

² Stroud, S. W., *J. Endocrin.*, 1,

³ Dodds, E. C., Fitzgerald, M. E. H., and Lawson, W., *NATURE*, 140, 772 (1937).

⁴ Dodds, E. C., and Lawson, W., *NATURE*, 139, 627 (1937).

Vaginal Smears and the Oestrous Cycle of the Cat and the Lioness

A STUDY of vaginal smears taken from ten cats during a period of a year showed that their oestrous cycle consists of the following four chief phases:

(1) *Pro-oestrus*. Characterized by the presence of very numerous nucleated epithelial cells, of fairly uniform shape.

(2) *Oestrus*. The picture obtained is variable, being apparently dependent on the individual intensity of the reaction¹. Thus in the spring large, flat, non-nucleated cornified cells predominate, together with a smaller number of nucleated cells of similar shape. The proportion of nucleated to non-nucleated cells is reversed during shorter seasons of lower temperature, such as autumn. It should be noted that these are not the only cellular elements of the oestrous smears; smaller, intensely staining round cells, with distinct nuclei, being also encountered