7. The exclusion of the liver from the circulation diminishes the amount of sugar in the blood.

(a) Schenck¹⁸ showed that after bleeding there is an increase of sugar in the blood, but that this does not occur after exclusion of the liver by ligature, and that it is very small in starving animals, where, of course, the glycogen stored in the liver is small in amount.

(b) Tangl and Harley¹⁷ showed that, in dogs fed on flesh, ligature of the intestinal arteries diminished the amount of sugar in the blood. Here the supply of sugar from without was, from the nature of the diet, cut off before the operation, but it was only when the blood supply to the liver was interrupted that the amount of glucose in the blood fell.

Even in prolonged starvation the amount of sugar in the blood is not diminished. How, if the kidneys are constantly excreting it, and if it is not being constantly manufactured in the body, is this supply kept up?

B. EVIDENCE OF THE DISAPPEARANCE OF SUGAR IN THE TISSUES.

1. E. Cavazzani¹⁸ shows that after muscular work there is a diminution in the amount of sugar in the blood, and that this is not due to any increased action of a diastatic zym. The older experiments of Seegen and of Chauveau and Kaufmann had given similar results.

2. Vaughan Harley¹⁹ records the results of a series of experiments upon dogs which confirm the older investigation of Limpert and Falck, and of Brasol, that glucose when injected into the blood is not all excreted by the kidneys, and that, even when the ureters are ligatured and renal secretion thus stopped, the glucose rapidly disappears from the blood. This disappearance is not due to a storage as such in the tissues, or to a conversion to glycogen, and it is accompanied by a rise in the respiratory quotient, showing an increased oxidation. These experiments Dr. Pavy has not, so far as I am aware, considered, although they overthrow his most off-repeated argument in support of his theory.

3. F. Voit²⁰ records a series of experiments on the subcutaneous injection of various sugars in the human subject. Using a 10 per cent. solution, he finds that very large quantities can be administered without causing any disturbance. The simple sugars (monosaccharids) experimented with gave the following results:

		Injected.	Excreted in the Urine.
		Grammes.	Grammes.
Dextrose ...	...	100.00	2.64
" ...	...	60.60	Trace
" ...	...	11.24	None
Laevulose...	...	10.94	0.99
" ...	...	10.13	Trace
Galactose ...	...	9.23	0.16
" ...	...	9.58	Trace

These results with dextrose—ordinary blood sugar—are supported by the previous investigations of Leube,²¹ who found that in dogs the injection of 50 c.cm. of a 50 per cent. solution of dextrose caused no glycosuria. The disaccharids—cane sugar and lactose—sugars which do not normally pass as such to the circulation, but which are broken up into monosaccharids in the intestine, he found were entirely excreted by the kidneys.²²

These experiments are directly opposed to the statements made by Dr. Pavy at p. 188 of his *Physiology of the Carbohydrates*. These statements are based upon experiments in which an increase of the sugar of the urine was found to follow the injection of even small quantities of sugar into the blood. No attempt was made to ascertain whether all the sugar injected was excreted. In the face of the experiments of Harley and of Voit, the conclusion—which Dr. Pavy makes the most important proof of his theory of the physiology of the carbohydrates—cannot be considered satisfactory.

The evidence may therefore be considered as establishing:

1. That glucose is formed in the liver.
2. That glucose is used in the tissues and is not all excreted by the kidneys.

Dr. Pavy's theories, again enunciated in his supplementary Croonian Lecture, without any mention of the work of other investigators, are thus found to be

opposed by a large amount of careful work. Dr. Pavy ignores the fact that in his views he stands alone, and that he is attacking the position to which physiologists have been driven, not by the study of the investigations of one individual but by the consideration of a large amount of independent work. He must, therefore, be prepared to consider and refute the existing evidence before his views can be accepted by those who are capable of forming a judgment on the matter.

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- ¹⁰ *BRITISH MEDICAL JOURNAL*, November, 1897.
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- ¹⁷ *Journal of Physiology*, vol. xv, p. 130, 1893.
- ¹⁸ *Münch. med. Woch.*, 1896, p. 887.
- ¹⁹ *Verh. d. Cong. f. inn. Med.*, 1895, p. 418.
- ²⁰ See also Biedl and K. Kraus, *Wien. klin. Woch.*, 1896, No. 4, p. 55.

PIGMENTED CELLS IN MOSQUITOS:

By SURGEON-MAJOR RONALD ROSS, I.M.S.

IN the *BRITISH MEDICAL JOURNAL* of December 18th, 1897, you did me the honour to publish an article by me on this subject, together with notes by Surgeon-Major Smyth, Dr. Manson, Mr. Bland Sutton, and Dr. Thin, on the original preparations. My sincere thanks are due to these gentlemen for the interest they have taken in the matter, and for the courtesy of their remarks, and I hope that the existence of the cells as attested by them may now be considered as established. As to the nature of the cells, however, doubt still remains, and I should therefore like to give two more instances in which they have been found, both having an important bearing on this point.

It will be remembered that the pigmented cells were not found in large a number of brindled and grey mosquitos, unfed or fed on healthy or crescent-bearing blood, but were seen for the first time in two large "dapple-winged" insects (Cases I and II) of a rare species, fed on crescent blood. Since then (September, 1897) I have observed them in two more insects. Case III: Some scores of small dapple-winged mosquitos, unfed or fed on healthy blood, had been examined without finding the cells. At last two of this species were persuaded to feed on a patient with crescents. One of them was killed next day; no pigmented cells could be found. The second was killed forty-eight hours after feeding; numerous pigmented cells were present. They were all small, much smaller than epithelial cells, ovoid, about 7 μ in the major axis, and each contained about 20 granules of typical pigment which were often arranged circumferentially, just as in the malaria parasite. No more insects of this species fed on malarial blood have since been examined. Case IV: A hundred or more grey or "barred-back" mosquitos (wings, legs, belly plain; back of abdomen transversely striated) unfed, or fed on healthy or crescent blood, have been dissected without finding the pigment cells. At last one was observed feeding on a patient whose blood that morning had been seen to contain numerous mild tertian parasites. I judged for many reasons that it had been feeding occasionally on the same man for several days. It was killed three days afterwards, when it must have been quite a week old (after hatching from pupa). Its stomach contained a large number of pigmented cells of all sizes, from 8 μ to 25 μ . They were very defined and distinct, especially the larger ones, and contained each from 10 to 20 granules of typical pigment. Some of the largest cells appeared to have a uniform structure without vacuoles, but with a central nucleus (?).

I thought I observed a few similar bodies without any pigment. Besides these cells the stomach cavity contained numbers of swarm spores, never before seen in any Secunderabad mosquito, but found in the mosquitos of the malarious Sigr ghat. In May a number of these swarm spores had been given to a person who volunteered to drink them, and he had been attacked with fever five days afterwards. I could trace no connection between the pigmented cells and

the clusters of swarm spores; that is, I could find no pigment in the latter; though it would have been difficult to do so even if it had been present, owing to the numbers of struggling flagellulæ. Since then I have examined no more grey mosquitos fed on tertian blood; and, indeed, have not been in a position to continue researches on malaria; but I have dissected thirty horse flies (*tabanus*), parasitic on tame pigeons, whose blood contained halteridium (Labbé). Though halteridium was found in the blood in the insects' stomach cavity, the stomach walls never contained pigmented cells; yet the histology of *tabanus* is closely like that of *culex*. It is interesting to note that in the four instances in which the cells have been found, their size is in proportion to the length of time between the feeding and death of the insects—namely, 7μ after two days, 17μ after four days, 19μ after five days, and 25μ after about a week.

I must correct an error due to the unfortunate use of formalin as a preservative in the two specimens sent to England. Pigment appears to have been found, not only in the pigmented cells, but also in the ordinary stomach cells, and elsewhere; and Dr. Thin draws the natural inference from this that the former are an altered form of the latter, induced by the absorption of malarial pigment from the stomach cavity. The effect is due to formalin, which not only blackens the green and yellow granules and globules always found in the tissues of *culex*, but converts traces of hæmoglobin in the stomach cavity into a multitude of minute acicular crystals very like pigment, and even has the same effect on the pigment of the pigmented cells. I know this to be the case from specimens in my possession, one of which now appears to contain pigment everywhere. I can say with confidence, and after special and repeated search for it, that when the specimens were fresh pigment was to be found nowhere else in them except in the pigmented cells; nor, except in the pigmented cells, have I ever found pigment in the stomach walls of mosquitos fed on malarial blood.

So long as the cells had been found only in two individuals (the only two properly examined) of a rare species of mosquito, it was quite possible to suppose them some kind of physiological cell, either pigment-producing or pigment-absorbing; the new facts show them to be too exceptional for this. If they be normal pigment-producing cells they should be found in most individuals of a species in one of which they have been observed; but Cases III and IV show that they may occur in a single individual out of many scores of the same species examined, while, except in these four instances, I have never observed them in allied diptera (*pulex*, *tabanus*, *musca*), nor even in allied species of *culex*. If, as Dr. Thin believes, they be ordinary epithelial stomach cells which have taken up the pigment of dead malarial parasites from the stomach cavity, they should, if found in one individual of a species fed on malarial blood, be found also in others of the same species similarly fed; but Case IV, in which they were observed in an insect fed on tertian blood, but not at all in many insects of the same species fed on crescent blood, is in direct opposition to this postulate—unless we can venture to assume that the stomach cells of this species are capable of taking up tertian pigment to the exclusion of crescent pigment. But there are now many reasons against Dr. Thin's theory. Thus, in Case III, the cells were much too small to be epithelial cells. Again, the pigmented cells are not like phagocytes in one important particular—they all contain roughly the same amount of pigment and an arrangement of it, which, as Dr. Manson says, forcibly recalls the arrangement of pigment in the malaria parasite. Phagocytes contain varying amounts of pigment, from one granule to several large clumps of it, according to the quantity they have been able to seize (compare phagocytes with parasites in malarial blood for example). Still further, if the pigment in the cells is due merely to phagocytosis, how comes it that they do not contain other granules from the stomach cavity besides, such as the yellow detritus of ingested blood corpuscles? Lastly, it remains to be proved that the stomach cells of *culex* are capable of taking up solid particles from the cavity. I have never seen any evidence of such, either in *culex* or in other families of diptera. Yet the stomach of the larva and imago contains multitudes of coloured vegetable and hæmoglobinous particles which could

easily be detected if contained in the interior of the cells of the stomach wall. I have never observed such a phenomenon. Why, then, should these cells absorb matter so exceptional in the ingesta as malarial pigment, and reject the numerous other granules which are much more commonly presented to them? The cells of the stomach are not scavengers like the phagocytes of the blood; what object can they possibly have in taking up the pigment of dead parasites, which otherwise will be naturally evacuated by the bowel? Or, are we to suppose that this dead pigment has the power of forcibly entering the cells? In short, I doubt whether this hypothesis will bear careful scrutiny.

Hence, the facts already collected, especially the new ones, make it difficult, if not impossible, to believe that the pigmented cells can be any kind of normal physiological cells, whether pigment-producing or pigment-absorbing cells. It would seem then that they must be some kind of pathological cells. What kind—whether new growths, or parasites peculiar to the mosquito, or a developmental form of the parasites of malaria in the mosquito—I cannot say. If not the last of these, it will always remain a curious coincidence that they should contain pigment so closely like malaria pigment, and that they should as yet have been found only in insects fed on malarial blood.

REFERENCE.

¹ No parasites found. Vide *Proceedings of South Indian Branch, British Medical Association, 1897.*

EUCHININ IN MALARIA.

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SINCE last August I have been observing the effect of euchinin on malarial fevers, and, as far as my experience goes, I find it highly satisfactory in suitable cases.

Up to now I have only employed it in undoubted cases of malaria, where I find it superior to quinine in being tasteless and requiring a smaller dose to reduce the temperature. However, I must differ *in toto* from the statement reproduced in the BRITISH MEDICAL JOURNAL of December 11th, 1897, that euchinin does not cause cinchonism, for I have seen it cause tinnitus aurium, deafness, and derangement of vision and sensation in a more marked degree than the same dose of quinine.

Contrary to the statement of Professor von Noorden, that 15 grains of quinine are equal to 25 or 30 grains of euchinin, I find that euchinin is a more powerful antipyretic than quinine, and that, in malarial fevers at least, 10 to 15 grains of euchinin are as efficacious as 20 to 25 or 30 grains of quinine sulphate, and that it nearly always, in doses of 12 to 15 grains, causes buzzing in the ears if not other symptoms of cinchonism.

The largest dose I have given has been 15 grains once or twice a day, always commencing with a good purge, which I consider essential in the treatment of all malarial fevers. This is sufficient in most cases, following the treatment with tonics and change of air if possible after the temperature has remained normal for a few days. I append notes of a few cases:

CASE I.—August 11th, 1897. A. J., a young negro woman, had had quotidian ague for eight days; temperature 104° ; severe headache, constipation. She was ordered a purge and euchinin gr. xv twice a day. August 12th, temperature 98.4° . Patient states that the fever left her one hour after the first dose of euchinin. August 15th, temperature has been normal since evening of August 11th; fever has not returned, but patient feels weak. Ordered tonics. She had buzzing in her ears while taking euchinin.

CASE II.—August 11th, 1897. J. J., husband of above, says that he also suffered from fever every day. He took one of his wife's powders, and says that the fever left him after it, and has not returned. No buzzing in ears. I did not see him during the attack of fever.

CASE III.—August 14th, 1897. F. E., European, male, aged 34. Quotidian ague for five days. Temperature 102.8° . He was ordered a purge and quinine sulph. gr. xx, acetaminilid gr. v, once a day. On August 15th he was no better. Temperature 102.8° ; weak from purge. No tinnitus. He was ordered euchinin, gr. xij, at bed time. He could not sleep from buzzing in the ears and other unpleasant sensations, but the fever was gone next morning. He felt well but weak, and the temperature was 98.2° . He was ordered tonics. He has had one attack of ague since then, but was afraid to take euchinin on account of the cinchonism, which was not caused by the large doses of quinine with which he finally got rid of the fever.

CASE IV.—October 22nd, 1897. W. B., a young negro from the goldfields of French Guiana. Quotidian ague for several weeks. He was ordered