A Comparative Histological Study of Haemosiderin in the Uteri of Mice of Cancerous and Non-cancerous Strains

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With 3 Text-figures and 3 Plates

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INTRODUCTION

WITHIN the uterine wall in mice large masses of a brown or yellowish-brown granular substance are often observed. This has been identified as haemosiderin—a pigment derived from the breakdown of haemoglobin. This substance contains iron and therefore gives the well-known 'Prussian blue' reaction on treating with potassium ferrocyanide and hydrochloric acid.

In the course of the comparative histological examination of uteri of mice of cancerous and non-cancerous strains, it soon became apparent that, although masses of haemosiderin occurred in the uterus of almost every mouse of the cancerous strain, such large masses were not observed in the uteri from the non-cancerous strain. Further study, however, showed that the pigment is formed in both cancerous and non-cancerous strains from the blood which is extravasated into the tissues of the uterus at parturition, but in the cancerous strain it is formed somewhat more slowly and persists much longer than in the non-cancerous strains examined. The evidence for these differences, their nature, and their possible significance form the subject-matter of the present paper.

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Material and Technique

The strains of mice employed in this investigation included cancerous and non-cancerous strains. The cancerous strain—the R III albino strain of Dobrovolskaia-Zavadskai—a—showed a very high incidence of mammary carcinoma, in females over 7 months old, at the time of investigation (1940). This strain was bred in this department as two sub-strains, both cancerous, the CB and CBB strains. Another albino strain, non-cancerous, the Wistar strain, has been inbred for over 4 years in this department without ever developing cancer. A recent non-cancerous strain, of piebald mice, the P strain, has been inbred for almost 5 years, again without showing any cancer development. The PC strain, also piebald, and the XL strain, self-fawn and self-brown, have both been entirely cancer free during the 3 years that they have been inbred in this department. All the uteri used for study have been fixed in either Bouin’s fluid or formol-saline solution (9 per cent.). In order to prevent muscular contraction of the uterine walls the whole female reproductive apparatus was dissected out and pinned, in a stretched position, on a layer of paraffin wax in a shallow dish into which the fixing fluid was then poured. After fixation, dehydration, and clearing, the right and left horns of the uteri were embedded separately.

Microscopic sections were cut 5μ in thickness, and stained, for ordinary histological study, with Ehrlich’s haematoxylin and eosin. Alternate slides of the serial sections were treated with potassium ferrocyanide and hydrochloric acid, after prolonged contact with nitric acid alcohol, and then counter-stained with eosin. The details of this method are given by Bolles Lee (1937) and are as follows: The sections, after removal of the wax, are placed in nitric acid alcohol (3 per cent. in 95 per cent. alcohol) for 36 hours at 35°C. They are then washed in 90 per cent. alcohol and in distilled water. After washing, they are placed, for not more than 5 minutes, in a freshly made solution composed of equal parts of 1.5 per cent. potassium ferrocyanide in water and 0.5 per cent. hydrochloric acid, also in water. The sections are again washed carefully in distilled water, stained for 3 minutes in eosin (1 per cent. in 30 per cent. alcohol), differentiated in 90 per cent. alcohol, cleared in cedarwood oil, and mounted in benzene balsam. By this method haemosiderin is stained a bright Prussian blue.

Data

Description of Haemosiderin and its Location in the Uterus

In transverse sections of some uteri a large mass of brown or yellowish-brown material is seen situated dorsally in the thickness of the wall just below the mesentery (Text-fig. 1). Serial sections reveal that these dorsal masses are present only at intervals.

Occasionally there are also in the uterine wall smaller scattered clumps of the material situated at the inner and outer borders of the circular muscle layer. Such scattered material has been observed in only a few of the uteri examined and has not been included in the present study. Where it occurs
at all it is present all along the uterus, not at intervals as are the dorsal masses. It has never been seen in uteri which do not contain dorsal masses, and in only a very small proportion of those that do.

Under the high power of the microscope the material is seen to be granular in consistency, the granules being arranged in small ovoid groups or clumps (Pl. I, figs. 1 and 2) which tend to aggregate to form larger masses (Pl. I, fig. 2). These small ovoid groups appear to be cell-bodies crowded with the granules, since each contains a nucleus (Pl. I, fig. 1). The granular material in form and natural colour agrees with the published descriptions of haemosiderin, and on staining with potassium ferrocyanide and hydrochloric acid it gives the typical Prussian blue reaction.

**Origin of the Pigment**

As haemosiderin is known to be the pigment commonly formed when there has been extravasation of blood into the tissues, it was thought that possibly the haemosiderin present in the uterine wall is derived from the blood extravasated at parturition. The large masses of haemosiderin are found only in the dorsal wall of the uterus, close to the mesentery—a location identical with that of the placentae (cf. Pl. II, figs. 3 and 4); the masses occur at intervals along the uteri, as do the placentae; these masses were never found in virgin uteri, and when the breeding records were examined for the animals under investigation it was found that in every case where these masses of haemosiderin occurred the animal had borne young. Finally, by examining a

![Diagram of a transverse section of mouse uterus showing distribution of haemosiderin](image)

**Text-fig. 1.** Diagram of a transverse section of mouse uterus a few months after parturition, to show distribution of haemosiderin.

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**Plate I**

Fig. 1. T.S. of uterus of mouse (of cancerous strain) showing haemosiderin within phagocytes. Ehrlich's haematoxylin and eosin. Oil immersion. $\times 900$.

Fig. 2. T.S. of uterus of mouse (of cancerous strain) showing massing together of pigment-carrying phagocytes. Fe and eosin. High power. $\times 600$. 
complete series of sections the number of masses of haemosiderin could be counted, and on referring to the breeding records it was found that, where only one litter had been produced, the number of masses of haemosiderin corresponded in every case with the number of young in the litter. It was then found that these dorsal masses of pigment could be seen with the naked eye as dark spots situated close to the mesentery when the whole uterus was cleared in cedarwood oil (Pl. II, fig. 5). (Uteri to be examined in this way should be fixed in formol-saline or formaldehyde as these clear much more perfectly than Bouin material.) The number of these dark spots in every case corresponded exactly to the number of young born, when the mouse had had only one litter. Uteri taken immediately or very shortly after parturition also show similar dark spots when cleared. Pl. II, fig. 7, shows a uterus, from the non-cancerous strain, taken 2 days after parturition, and Pl. II, fig. 8, a cancerous strain uterus also 2 days after parturition. When sectioned, however, these spots are found to contain very little haemosiderin, if any. Each is composed of a mass of extravasated blood and torn tissue which marks the former site of the placenta. These spots are very large, but by 25 days they are much smaller, as can be seen in Pl. II, fig. 5, which shows a cancerous strain uterus taken 25 days after parturition. This decrease in size is caused by a healing of the torn tissues. Sections then show that it is chiefly a quantity of haemosiderin which marks the site of the placentae. Later, uteri from mice which had been pregnant more than once were examined, and it was often found that the sites of the placentae of successive pregnancies could be distinguished from one another by the different size of the dark spots, since the placentae of one pregnancy did not overlap with those of another. The dorsal masses, when present, from two successive litters could always be distinguished when only a few days had elapsed since the last pregnancy, as seen in Pl. II, fig. 6. This is a photograph of the cleared uterus of a mouse of the cancerous strain, 3 days after parturition, which has had two litters with seven young in each. In the photograph, seven small dark spots and seven larger ones are to be seen situated close to the mesentery. Here the seven large spots

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**PLATE II**

- Fig. 3. T.S. of uterus of mouse (of cancerous strain) containing a large amount of haemosiderin. Fe (K ferrocyanide + HCL) and eosin. Low power. $\times 74$.
- Fig. 4. T.S. of uterus of mouse almost immediately after parturition, showing extravasated blood at site of placenta. Ehrlich's haematoxylin and eosin. Low power. $\times 21$.
- Fig. 5. Whole uterus of mouse (of cancerous strain) which had had only one litter. Cleared in cedarwood oil. $\times 3\frac{1}{4}$.
- Fig. 6. Whole uterus of mouse (of cancerous strain), 3 days after parturition, which has had two litters. Cleared in cedarwood oil. $\times 3\frac{1}{4}$.
- Fig. 7. Whole uterus of mouse of a non-cancerous strain 2 days after its first parturition. Cleared in cedarwood oil. $\times 3\frac{1}{4}$.
- Fig. 8. Whole uterus of mouse of the cancerous strain 2 days after its first parturition. Cleared in cedarwood oil. $\times 3\frac{1}{4}$.
- Fig. 9. Whole uterus of mouse of a non-cancerous strain 10 months 7 days after its first parturition. Cleared in cedarwood oil. $\times 3\frac{1}{4}$.
- Fig. 10. Whole uterus of mouse of the cancerous strain over 10 months after its first parturition. Cleared in cedarwood oil. $\times 3\frac{1}{4}$. 
blood vessel

erythrocytes

large phagocyte containing fine granules and clumps of haemosiderin

nucleus

phagocyte containing fine granules of haemosiderin

mass of haemosiderin-containing phagocytes

isolated phagocytes containing haemosiderin

V. JONES.—PLATE I

V. JONES.—PLATE II
(which represent the placentae of the last pregnancy) are composed chiefly of blood and torn tissue, and the seven small spots (which represent the placentae of the previous pregnancy) consist of haemosiderin.

It seems abundantly clear, therefore, that the dorsal masses of haemosiderin under consideration are formed, after parturition, in the regions of former attachment of the placentae—probably from the blood extravasated into the tissues when the placentae break away at parturition.

**TEXT-FIG. 2.** Relative amounts of haemosiderin at various periods after parturition in the uteri of cancerous and non-cancerous mice.

**Incidence and Relative Amounts of Haemosiderin in Uteri of Mice from Cancerous and Non-cancerous Strains at Various Times after Parturition**

Since there was the ever-recurring suggestion that the cancerous strain shows more haemosiderin or shows it more frequently than the non-cancerous strain, a survey was made of the uteri of mice of different strains taken at various times after parturition, from 1 month to 10 months. The results of this survey are shown in Text-fig. 2. No attempt has been made to indicate the exact amounts of haemosiderin present—the estimates are very rough indeed. One unit represents the smallest amount of haemosiderin found in any one uterus, and therefore Text-fig. 2 gives *relative* amounts only. Where the haemosiderin is compact, the area of the largest section of the mass has been measured; where it is less compact, the area of the various parts have been measured. No attempt has been made to calculate the volume, so that
the figures given understate the difference in amount. In actually examining
the material the differences are very striking indeed.

From the data given in Text-fig. 2 it is evident that almost throughout the
series there is much more haemosiderin in the uteri from the cancerous strain
than in those from the non-cancerous, taken at corresponding times after
parturition. The difference is not apparent, however, till about 1½ months
after parturition. Up to that time the uteri of the cancerous strain contain
about the same amount of pigment as those of the non-cancerous strains
—possibly less. After about 1½ months the amount increases very con-
siderably in the cancerous strain, until about 6 months, but not appreciably
in the non-cancerous. After 6 months there is a very definite decrease in
amount in the non-cancerous strain but very little decrease in the cancer-
ous strain.

These facts are clearly illustrated in Pl. III, figs. 11 to 15. At 1 month
6 days after parturition (Text-fig. 2) the two uteri (of cancerous and non-
cancerous strains) contain approximately the same amount of haemosiderin,
although in the non-cancerous strain the pigment is more dispersed, but at
3 months after parturition the cancerous strain uterus (Pl. III, fig. 12) shows
a very great amount of haemosiderin as compared with that of a non-cancerous
strain (Pl. III, fig. 11). The pigment in the non-cancerous strain uterus is
spread over as great an area as that in the cancerous strain, but again is very
loosely distributed. Pl. III, fig. 13, shows a uterus of a non-cancerous strain
7 months after parturition and Pl. III, fig. 14, shows one from a cancerous
strain at 8 months. Again, the haemosiderin is very much greater in amount
in the cancerous strain, and much more compact. By 9 months after parturi-
tion the non-cancerous strain uterus shows only a very small amount of
haemosiderin (Pl. III, fig. 15) and by 10 months only the merest trace remains
—not sufficient to show satisfactorily in a photograph, whereas in the cancer-
ous strain the uteri still show a very large amount of pigment. This decrease
in the amount of haemosiderin in the non-cancerous strain and its retention
in the cancerous strain is borne out by examination of cleared whole uteri
taken at 10 months and more after parturition. In the non-cancerous-strain
uterus shown in Pl. II, fig. 9, taken 10 months after parturition, there is no
trace of the dark dorsal masses (the small trace found in sections is not visible
to the naked eye), whereas in the uterus of the cancerous strain taken after
a much longer period (exact date unknown, but at least 10 months) the
masses are still clearly visible as dark spots close to the mesentery
(Pl. II, fig. 10).

It seems to be clearly established, therefore, that at all times after parturi-
tion, apart from about the first month and a half, as long as haemosiderin is
present at all, it is present in greater quantities in the cancerous-strain uteri
than in the uteri of the non-cancerous strains. Further, it seems quite clear
that it disappears almost completely after about 10 months in the non-
cancerous strains examined, whereas in the cancerous strain it is scarcely
diminished in amount at all at that time.
These findings raise several interesting questions. Is less haemosiderin formed in the non-cancerous strains? Or is it dispersed more quickly as it is formed, so preventing the accumulation of large quantities? Is it dispersed at all in the cancerous strain or is it merely more tightly packed as time goes on? In an attempt to throw light on these questions an investigation of the method of formation of haemosiderin was undertaken.

**Mode of Formation and Fate of the Pigment in Non-cancerous Strains**

For an investigation of the method of formation of haemosiderin within the wall of the uterus, only material from non-cancerous strains was used in the first place, and it is an account of the process as observed in this 'normal' material which is given below.

Immediately after parturition the former site of the placenta shows a considerable quantity of extravasated blood and, a little later, numerous phagocytes can be distinguished ingesting the blood. Cells containing ingested red corpuscles are first observed in uteri taken 12–24 hours after parturition. Ingestion of the erythrocytes seems to be followed within 48 hours after parturition by the appearance of haemosiderin, firstly in a diffuse form and then granular. In material taken at about 48 hours after parturition and stained with hydrochloric acid and potassium ferrocyanide, the phagocytes containing ingested erythrocytes show a diffuse blue coloration of their cytoplasm (Text-fig. 3a), and in slightly later material they show minute darker blue granules in the cytoplasm (Text-fig. 3b). This suggests that after ingestion some of the haemoglobin diffuses out of the erythrocytes and is broken down into diffuse pigment which is then converted into small granules of haemosiderin. In later material again, stained in the same way, blue-staining non-granular bodies are observed within the phagocytes, similar in shape and size to the erythrocytes (Text-fig. 3c) and later still, similar bodies, but of a granular consistency, are to be seen in the same situation (Text-fig. 3d) — which seems to indicate that the haemoglobin remaining within the erythrocytes is broken down, in situ, into haemosiderin which is at first in a diffuse state and later becomes granular. Phagocytosis of the red corpuscles continues until all extravasated blood is removed from the tissues. This takes a considerable time and cells containing unaltered red corpuscles have been observed as late as 21 days after parturition. Meanwhile, deposition of granular haemosiderin increases day by day until the phagocytes are crowded with the pigment (Pl. I, fig. 1). By 21 days a considerable amount of haemosiderin can be seen in the uterine wall and this continues to increase until about a month and a half after parturition. After this time little or no increase has been observed (see Text-fig. 2, non-cancerous). Increase in quantity of haemosiderin is accompanied by a close aggregation of the pigment-forming phagocytes. These cells, at first widely dispersed, gradually come together into small groups which aggregate to form a loosely packed mass. It should be emphasized that in this non-cancerous material the pigment is never very closely packed (see Pl. III, figs. 11 and 13). No extracellular formation of
haemosiderin has been seen. All the pigment has been found within cells except in extravasations of long standing where a small amount of extracellular pigment is present, almost certainly due to disintegration of some of the phagocytes.

It is of interest to compare these observations with those of Muir and Niven (1935). These workers injected fresh mouse blood into mice and studied its fate in the tissues. They observed phagocytosis of red corpuscles within 24 hours after injection and also the appearance of diffuse and granular haemosiderin within the phagocytes from 24 hours onwards. They, too, observed both small granules and large granular masses of haemosiderin and also ingested erythrocytes which gave the Prussian blue reaction. They also

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**TEXT-FIG. 3.** Four stages in the formation of haemosiderin within the normal mouse phagocyte. Drawings made from T.S.s of uteri. Fe (K ferrocyanide + HCl) and eosin. Oil immersion. × 2,700.

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**PLATE III**

Fig. 11. T.S. of uterus of mouse of a non-cancerous strain 3 months 28 days after its first parturition. Fe and eosin. Low power. × 40.

Fig. 12. T.S. of uterus of mouse of the cancerous strain 3 months 5 days after its first parturition. Fe and eosin. Low power. × 40.

Fig. 13. T.S. of uterus of mouse of a non-cancerous strain 7 months 12 days after its first parturition. Ehrlich's haematoxylin and eosin. High power. × 275.

Fig. 14. T.S. of uterus of mouse of the cancerous strain 8 months 12 days after its first parturition. Fe and eosin. High power. × 275.

Fig. 15. T.S. of uterus of mouse of a non-cancerous strain 9 months after its first parturition. Fe and eosin. High power. × 275.
state that they observed only intracellular formation of the pigment. Muir and Niven go on to say that at about the seventh day after injection of the blood haematoxidin appears in the bodies of the phagocytes and gradually replaces the haemosiderin from which they believe it to be derived. Our own findings, however, show that haemosiderin is the only pigment formed in the mouse uterus from the extravasated blood after parturition: it can still be demonstrated after 10 months in small traces and throughout that period there is no suggestion of haematoxidin or of any other pigment anywhere in the uterus. Muir and Niven state that in the period covered by their observations (24 hours to 36 days after injection) they found no haematoxidin in phagocytes situated close to blood-vessels or to nerves, haemosiderin being the only pigment found in the cells in these localities, and they add that in the rabbit there was no formation of haematoxidin up to 5 days, when their observations ended.

The fate of the haemosiderin in our own material is not known with certainty, but there is a strong suggestion that the phagocytes carry it away from the site of formation. They are never found in the tissues of the uterus surrounding the region of formation, but they are found in the mesentery (Pl. III, fig. 11). It is not certain that they have migrated there from the dorsal mass, but the appearance strongly suggests that they have done so. The dorsal mass seems to "tail off" into the mesentery and to be continuous with a "stream" of phagocytes within the mesentery. At the same time the appearance of the dorsal mass changes in a way which suggests bodily removal of some of its constituents. The actual size of the region in which the haemosiderin occurs remains about the same, but the material looks more loosely packed as time goes on until, when only a trace of the pigment remains, it is seen, in section, as tiny clumps of granules scattered over the original area as in Pl. III, fig. 15. Dark blue granules are visible but nothing is clear-cut—they seem to be slightly bordered by a pale blue diffuse stain. On first examining sections in this condition it was thought that the method of preparation had partly dissolved the granules, but this is not the case: every section showing the haemosiderin during its late history shows this blurred appearance. It looks as though there might be a slight diffusion of the pigment immediately around the granules, but the matter is very uncertain. The whole picture of the process, as gleaned from sections, much more strongly suggests bodily removal of the phagocytes with their loads of pigment.

Comparison of the Cancerous and Non-cancerous Strains, with regard to the Mode of Formation and Subsequent History of Haemosiderin in the Uteri

In the present study, after the process of formation of haemosiderin and its subsequent disappearance had been followed in the uteri of non-cancerous strains of mice, attention was turned to the process in the cancerous strain. The basic procedure was found to be the same in both, but certain differences stand out very clearly. In the first place, ingestion of red corpuscles by the phagocytes seems to be slower in the cancerous than in the non-cancerous
strains. In the former, it does not begin at the earliest until after 24 hours after parturition—in some not until after 48 hours; whereas in the non-cancerous strains it is clearly marked between 12 and 24 hours. Further, in the cancerous strains phagocytosis can be observed to be still taking place a month or so after parturition, whereas in the non-cancerous strains no trace of it is found after 21 days. The appearance of haemosiderin is also delayed in the cancerous strain until nearly 3 days, sometimes until 4 days, after parturition, whereas in the non-cancerous strains it is unmistakably present at 48 hours. The amount of haemosiderin gradually increases, but again very much more slowly in the cancerous strain. Comparison between a cancerous-strain uterus and a non-cancerous-strain uterus at 21 days after parturition shows very much less haemosiderin in the cancerous strain. But by 1 month 6 days the two strains show approximately the same amount of pigment, although it is more compact in the cancerous strain than in the non-cancerous.

The later history of the pigment in the two strains has already been dealt with above (see p. 483 and Text-fig. 2). In the cancerous strain the amount of haemosiderin continues to increase until 5 or 6 months after parturition and thereafter shows a very slight decrease, but is still not much below its maximum at almost 11 months. In the non-cancerous strains, on the other hand, there is very little increase after the first month, the amount remaining fairly constant until 5 to 6 months, when it begins to decrease, and by 10 months it has practically disappeared. The history of the haemosiderin in the cancerous strain is not known after 11 months. One uterus only has been obtained which was known to be more than 14 months post-partum and unfortunately the exact period is not known, but in the cleared specimen the dorsal masses of haemosiderin were still clearly visible to the naked eye.

Increase in quantity of haemosiderin is accompanied in both strains by a closer aggregation of the pigment-carrying phagocytes, but in the cancerous strain this aggregation is much more marked than in the non-cancerous strains—the packing is very much tighter. Compare Pl. III, figs. 12 and 11, and 14 and 13, showing uteri of cancerous and non-cancerous strains in pairs of comparable ages. The tightly packed masses in the cancerous strain (Pl. III, figs. 12 and 14) contrast strikingly with the loosely aggregated masses in the non-cancerous strains (Pl. III, figs. 11 and 13). This solid packing of the haemosiderin is as characteristic of the cancerous strain as is the excessive amount of the pigment and its prolonged retention.

There is not the same suggestion of migration of pigment-carrying phagocytes from the dorsal mass into the mesentery in the cancerous strain as there is in the non-cancerous strain. In the cancerous strain the dorsal mass does not 'tail off' into the mesentery; neither are pigment-carrying phagocytes found within the mesentery (cf. Pl. III, figs. 12 and 11). The occurrence of migration in the non-cancerous strains and its absence in the cancerous strain would account for the closer packing of the haemosiderin in the cancerous strain and for the greater amount, and for its prolonged retention.
scattered clumps of haemosiderin-carrying phagocytes forming dorsal mass

large clump of haemosiderin-containing phagocytes forming dorsal mass

stream of pigment carrying phagocytes in mesentery

mesentery

lumen 11

large mass of haemosiderin-containing phagocytes

mesenteric wall of uterus

clumps of haemosiderin-containing phagocytes

mesentery

mesenteric wall of uterus

phagocytes containing haemosiderin

mesenteric wall of uterus

V. JONES.—PLATE III
The whole question of migration requires further investigation and the material available is not what is necessary for the purpose. In most cases the uteri used in this study were dissected out fairly cleanly and only a little mesentery remained attached: no mesenteric lymph glands have been preserved, and the other organs of the body are not available.

**Conclusions and Discussion**

From the foregoing account certain facts emerge clearly. In the first place it is shown that haemosiderin is formed, in all the strains of mice examined, from the blood which is extravasated into the wall of the uterus when the placenta tears away at parturition. In this connexion the most striking facts which emerge, and which are established beyond question, are that in the cancerous strain this haemosiderin is found in much greater quantities than in the non-cancerous strains, and that it is formed somewhat later and persists very much longer. It is by no means certain that these differences are significant with reference to susceptibility to cancer, but they raise some interesting questions and encourage speculation.

In the first place it is not perfectly clear why there is such an excessive amount of haemosiderin in the cancerous strain. Is it that more blood is extravasated into the tissues? Or is it that the breakdown product is disposed of more slowly and so accumulated? The latter alternative seems to be the more probable. There is no evidence whatever of greater haemorrhage at parturition in the cancerous strain, whereas there is abundant evidence of delay in dealing with the extravasated blood. Ingesting of the erythrocytes starts later and goes on for a longer period and the breakdown pigment appears later and persists much longer on the site of formation, as though the phagocytes either fail to carry it away or are extremely slow in the process. It is as though the scavenging is in some way inefficient—as though the phagocytes are either fewer in number or less effective in action. There is no evidence that they are fewer. Histological study shows no scarcity of phagocytes on the scene of action; neither do blood counts suggest any paucity of leucocytes in general, though this latter would, of course, be difficult to demonstrate because of the wide range of variation in normal healthy material. The whole picture, however, suggests slowness or inefficiency of action on the part of the phagocytes rather than paucity in numbers.

An interesting speculation presents itself with regard to susceptibility to cancer. The hypothesis of cellular resistance to cancer put forward by J. B. Murphy (1912, 1913, 1914, 1915, and 1918) and discussed by many later workers, suggests a connexion between the activities of the lymphocytes and susceptibility to cancer. He states that infiltration by lymphocytes accompanies the appearance of a malignant growth. He also says that there is a relationship between the amount of lymphocytic infiltration and the success of a tumour graft—lymphocytosis reducing the susceptibility to tumour transplantation, and lymphocytic leucopenia producing increasing susceptibility. Murphy also found that pieces of spleen introduced into tissue cultures
or implanted in a developing hen's egg interfered with the growth of a tumour.

If the phagocytes, or even the reticulo-endothelial system in general, are indeed responsible for resisting the development and growth of cancerous tissue, and if (as the results of the present investigation suggest) this mechanism exhibits inefficiency in the cancerous strain of mice, this might conceivably be the basis of their susceptibility to cancer.

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SUMMARY

1. In mice, haemosiderin is formed in the wall of the uterus from the blood extravasated into the tissues when the placenta breaks away at parturition.
2. The pigment is formed, probably exclusively, within the phagocytes, and forms a mass in the mesenteric wall of the uterus.
3. In mice of the cancerous strain used in this study (R III strain of Dobrovolskaia-Lavadskaia) the haemosiderin is formed more slowly and is disposed of much more slowly than in the non-cancerous strains examined.
4. Phagocytic inefficiency in the cancerous strain is suggested and its possible connexion with susceptibility to cancer is discussed.

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