

TABLE III.

Date.	R.C.	R.P.	W.C.	L.	M.	N.	E.	Remarks.
(14739) 2.9.26...	8	24	7,900	33	7	60	—	Slight anisocytosis; erythrocytes stain well. Died 2.9.26
(14795) 3.9.26...	2.7	10	9,700	24	2	71	3	Normoblasts, ghost cells, some of which are fragmented. Anisocytosis. Note absence of polychromasia. Died 3.9.26
(15160) 27.9.26..	5.7	18	16,200	12	4	83	1	Normoblasts. Few ghost cells; free haemoglobin. Died 27.9.26.
(15196) 27.9.26..	4.6	17	18,100	15	3	79	3	Slight anisocytosis. Ghost cells frequent, but smaller than erythrocytes, some of them irregularly fragmented. Normoblasts: poikilocytosis. Died 27.9.26.
(15193) 29.9.26..	11.2	44	12,900	23	6	70	1	Red cells stain well. Died.
(15533) 20.10.26.	4.3	14	7,600	22	5	72	1	Indistinct ghost cells; slight anisocytosis; normoblasts. Died.
(14814) 7.9.26...	13	50	4,400	60	4	36	—	Blood stains well. Very slight anisocytosis. Died 7.9.26.
(14922) 8.9.26...	11.1	46	10,000	15	3	79	3	Slight anisocytosis. Died 9.9.26.

R.C. = Red count.
R.P. = Red precipitate.
W.C. = White count.

L. = Lymphocyte.
M. = Monocyte.
N. = Neutrophile.
E. = Eosinophile.

It will be seen that the number of red corpuscles varied in the case in which jaundice was already present, from what apparently is the normal count for sheep, viz., 12-13 millions to 2.7 millions. That means that jaundice made its appearance before extensive destruction of the erythrocytes had actually taken place (*vide* the blood picture of sheep Nos. 14814 and 15193. In these two cases the red cells show practically no changes. In the other sheep there were signs of an oligocythaemia, and in one case this was fairly marked, viz., 2.7 millions. In these cases anisocytosis was evident,

with the appearance of normoblasts. One characteristic feature of the blood was the inextensive occurrence of polychromasia and punctate degeneration, e.g., as compared with the blood of the splenectomy and Anaplasmosis cases. Very characteristic in the blood of those sheep, which showed extensive oligocythaemia, was the appearance of "ghost" erythrocytes, i.e., red cells which had lost the greater portion of the haemoglobin. Some of these ghost-cells showed a fragmented appearance. In the majority of the cases haemoglobinaemia was present. The amount of haemoglobin varied from case to case. The colour of the serum collected varied from light reddish brown to claret. In some of the early cases bile (?) pigment was present, the serum being clear yellowish brown instead of straw coloured.

Pathological Anatomy of Enzootic Icterus.

The most characteristic change in cases of Enzootic Icterus was the general jaundiced appearance of the carcass. This was most evident in the adipose tissue which was stained a deep bright canary yellow colour. This colour gradually changed to a somewhat dirty brownish yellow as the post-mortem was proceeded with, or if the post-mortem had been delayed for some time. This icterus manifested itself on the visible mucous membranes especially in connection with the conjunctival mucous membrane. Besides icterus, anaemia was present in some of the cases. This abnormal pigmentation also occurred in connection with all the other organs and tissues of the body. The blood in advanced cases was watery, and revealed the presence of haemoglobin. Instead of being a bright red, it was a dirty brownish red and stained badly. The next most obvious change was found in the *kidneys*. These were enlarged, in some cases markedly so and showed extensive pigmentation, viz., an intense dark reddish purple colour. This colour was diffuse over the whole substance, and for that reason the zones could not be identified.

The cut surface was inclined to bulge somewhat, and presented a glassy-looking appearance. In some cases this pigmentation was not so extensive, being more of a dark reddish grey appearance. The consistence was usually slightly more friable than normal. The fibrous capsula was easily detached.

The *liver* was enlarged and in some cases markedly so, with the edges rounded. The colour varied from yellow-brown to reddish-brown. On section the cut edges were somewhat everted, the lobulation distinct, the central veins prominent, and associated with them there was a greyish-yellow zone. The consistence was soft and friable. The colour of the cut surface varied from a light greenish brown to a dark reddish-brown.

The *spleen* in the majority of cases was markedly swollen. On section the cut surface was dark reddish-brown, the pulpa somewhat protruded, and the cut edges somewhat everted. The substance had a glassy appearance. The Malpighian bodies and trabeculae were not distinct.

The *lymphatic glands* were mostly swollen, and their cut surface moist. In some instances the glands were of a light reddish colour. The substance was always transparent and brownish in colour.

The *lungs* in the majority of cases of enzootic icterus showed evidences of oedema, and in some cases hyperaemia was also present.

The Urinary bladder in the majority of cases showed the presence of pigmented urine. This varied from light claret colour to a turbid coffee colour. In some cases only a few drops were present, and in other instances there was a fair quantity. The mucous membrane of the bladder was usually pale-yellowish in colour. In a few cases patches of slight hyperaemia were present.

In practically all the cases the faeces in the *caecum and ansa proximalis of the colon*, and especially in the case of the latter, revealed interesting alterations. The faeces were much firmer and drier in consistence, and occurred in balls or masses which varied in size from that of a pigeon's egg to that of an orange. These did not completely fill the lumen of the intestine, but were usually present in isolated lumps. Sometimes they were covered with a good deal of mucus, and partly adherent to the mucous membrane itself. The colour of these faecal masses varied from a dark brown to a reddish chocolate. Oesophagostomum nodules were present in the majority of the cases, and in some instances were frequent. The mucous membrane of these portions of the large intestine were usually swollen, and from the surface a thick turbid mucous material could be scraped. The colour varied from pale yellow to dark reddish. In some cases clotted blood masses were actually present in the lumen of the intestine.

In some instances there was a slight hydrothorax, and in others hydropericardium, but this was not a common occurrence. These transudates were often of a dark greenish brown colour. Extravasations of blood in connection with the epicardium and endocardia were also noted.

The most important changes observed at post-mortem may therefore, be summarized as follows: General icterus, general anaemia, haemoglobinaemia, haemoglobinuria, extensive pigmentation and slight degeneration kidneys and liver. Swelling and pigmentation, and sometimes hyperaemia of lymphatic glands, tumour splenis, constipation in the caecum and colon (*ansa proximalis*), hyperaemia of the intestines, sometimes enterorrhagia; hyperaemia and oedema of the lungs.

Microscopical changes.—The most important changes were observed in connection with the liver, kidneys, and some of the lymph glands:—

The liver showed extensive alterations mainly in the central part of the lobule. These changes were of the nature of an atrophy of the columns of liver cells as a result of the presence of the pigment cells which had accumulated there. These pigment cells were very characteristic, and they were also encountered in large numbers in Glisson's capsule. A very close study of these pigment cells was made, because these cells were not seen in any of the other pigment studies, and as far as the author could ascertain such a type of cell has not yet been described in the veterinary literature. These cells varied somewhat in size and shape, and presented a large amount of cytoplasm as compared with the small spherical nucleus. The latter was variously situated on account of the pigment matter present, usually the nucleus was found close to the periphery. These cells as a rule were spherical, and in sections of the liver they were sometimes irregularly quadrilateral. A number of these cells have been clearly depicted in the plates (see plate IV).

In these figures the relation of the amount of the cytoplasm to nucleus, and the shape and size of these cells are clearly demonstrated. These cells not only make their appearance in connection with the intralobular capillaries, but are also met with in the connective tissue of Glisson's capsule, i.e., some distance removed from the actual liver parenchyma. It would appear that these cells originate in the reticulum cells present there. They can be seen in various stages, viz., from spherical cells with a small amount of pigmented cytoplasm (not much larger than ordinary monocytes), to cells of great dimensions, and containing a large amount of cytoplasm of a granular pigmented nature (see plate V). In unstained preparations the cytoplasm has a regular granular appearance of a light yellow colour. In the lobule the cells lie outside the walls of the capillaries. In the periphery of the lobule they occur singly, whereas near the central vein they are present in clusters. Their direction towards the central vein or centre of the lobule is more or less radially arranged. In the vicinity of the central vein where they accumulate, they cause atrophy of the columns of liver cells.

The pigment in connection with these cells was closely studied. It is not haemosiderin, nor is it of the nature of fat. With Sudan III it stains a reddish brown. It is not dissolved by the absolute alcohol employed in the haemalum-eosin stain, and in the paraffin-embedding method. With the latter stain the cytoplasm of the cells assumes a reddish pink, fairly regular, granular appearance, or presents a "foam-like" resemblance. In this cytoplasm the small spherical nucleus can be identified. With the Giemsa stain the cytoplasm of the cell assumes an intense blue granular appearance, in which the chromatin stained spherical nucleus can be made out with difficulty. As regards the nature of this pigment it may be said that it does not seem to be associated with an erythrophagocytosis (as was seen in the Anaplasmosis and splenectomy cases). Furthermore, it is not of the nature of bile or its intermediary products (yellow-brown pigment). These pigment cells of Enzootic Icterus as compared with bile pigments showed the following staining affinities, viz.: with haemalum-eosin regular reddish pink instead of yellow brown, with Sudan III reddish brown instead of yellow brown, and with Giemsa intense regular blue instead of greenish yellow-brown.

These cells seem to be of the type of reticulum cells, associated with the connective tissue of Glisson's capsule. Whether these cells in the lobule of the liver are stern cells is difficult to say when they are studied in sections. When we, however, compare these cells in the organ smears (see plate VI) stained by Giemsa then it will be seen that the stern cells as regards their contour are somewhat irregular and not so sharply defined as these pigment cells. Moreover, the nuclei of stern cells are not regularly spherical like those of the pigment cells, and are distinctly larger, more oval in shape and sometimes indented. The cytoplasm of the desquamated stern cells is large in amount, and shows the presence of phagocytosed erythrocytes, irregular pigment granules, or vacuoles as the case may be. The pigment cells of Enzootic Icterus are far more regular, and its cytoplasm with some stains assumes this "foamy" character. These cells are more of the nature of the so-called "Gaucher cells" referred to in the literature above.

Do these cells stand in the same relation to the connective tissue elements of the intralobular capillaries as to the connective tissue of Glisson's capsule? Are these cells in the lobule probably of the type of pericytes mentioned by Zimmermann (18), and not of the same value as the so-called *endocytes* (stern cells)? It will later on be seen that similar cells have been encountered in the reticulum of the lymphoid tissue in lymphatic glands. In one or two cases a few desquamated stern cells, showing erythrophagocytosis, were observed in the capillaries of the lobule. Moreover, these Enzootic Icterus pigment cells were never seen free in the capillaries, nor were they ever encountered free in the central veins, as described for stern cells in Anaplasmosis and splenectomy. They were never encountered in the circulation. Other changes observed in the liver were atrophy, fatty changes in the liver cells, a bile stasis, a localized increase of fibrillae and round cells in Glisson's capsule, and in some cases a slight pigmentation in connection with the liver cells themselves.

The atrophy was associated with these pigment cells, which had accumulated in great numbers around the central veins, and thus responsible for the pressure. The fatty changes varied considerably. In some cases these were only slight, whereas in a great number these changes were well advanced, and the majority of liver cells contained droplets of varying size. The nuclei of the remaining liver cells around the central veins showed some changes. Karyolysis was present only to a small extent, and some changes in the size of these nuclei were also noted. Many cells were encountered in which large nuclei were present, almost twice the size of an ordinary liver cell nucleus. The localized increase of fibrillae and round cells in Glisson's capsule seen in the Enzootic Icterus was also observed in the splenectomy and Anaplasmosis cases.

With the Sudan III stain *bile pigment* showed up well in the distended canaliculi and the periphery of the lobule was mainly affected. The canaliculi stood out as a prominent network across the liver cells. The pigment in the canaliculi with this stain was yellowish green in colour, and more or less homogeneous. In the organ smears this pigment could be identified in the cytoplasm of the liver cells, and with Giemsa stain stood out as homogeneous dark brown casts or cylinders. In some cases this bile pigment was extensively present and very prominent in the periphery, whereas in other cases only traces could be identified.

The lungs in the majority of cases showed extensive haemosiderosis, but apparently this was of a different type from that described in Anaplasmosis and splenectomy. Erythrophagocytosis as such was not observed, and the haemosiderosis was probably related to the haemolysis which was present.

Lephne recognizes two conditions in connection with the breaking up of erythrocytes, viz., *erythrolysis* and *erythrorhexis*. It would appear that in Enzootic Icterus erythrolysis occurred and set up the haemoglobinaemia. The haemoglobin was probably dissolved out of the erythrocytes and left the so-called "ghosts," in the blood. At present, however, it is difficult to say whether haemoglobin is transformed into haemosiderin in the lung tissue. Does the lung function in this respect or is the haemosiderin brought to the lung in the circulating blood from other parts of the body, excluding the liver because in that organ practically no haemosiderosis was noted? The

haemosiderin in the lung occurs in cells, but which cells are actually implicated is difficult to say from the sections studied. Are they reticulum cells, vascular endothelium or histiocytes? With Sudan III stain it was noted that a fair number of cells in the lung showed the presence of fatty substances. This was also observed in case of the spleen, where the usual breaking down process of erythrocytes occurs (see plate IX). From the evidence it would appear that the lung in *Enzootic Icterus* is associated with the formation of haemosiderin.

Pigmented reticulum cells described in the liver were also seen in the lung. They were also encountered in the smears made from the lung. In comparing the various figures in plate II, it will be seen that these pigment cells are more or less identical in the smears from the various organs. The exact distribution of these cells in the lung was studied, and the impression gained was that they were probably associated with the reticulum, and not the endothelium. Moreover, these cells could not have drifted in with the circulation, seeing that they were never seen in the blood.

In all cases *the kidneys* revealed extensive pigmentation, and only slight alteration in the parenchyma itself. The main changes in the latter were of a fatty nature, and these varied from a few droplets here and there in the epithelium, mainly of the convoluted tubules, to numerous droplets affecting the epithelium of the tubules in various situations. In no instance, however, were the fatty changes extensive. In some cases the changes in the epithelium of the tubules were of the nature of hyaline-droplet formation. This, however, was in no instance extensively present.

The pigmentation of the kidney was mainly associated with the presence of haemoglobin in the lumen of the tubules and in Bowman's capsule. This pigment was present as a homogeneous material, and with haemalum-eosin was stained an intense diffuse pink. In the mass of this pigment there was evidence of haemosiderin, which, with the haemalum-eosin stain, revealed itself as a light reddish-brown homogeneous material. Haemoglobin pigment was present in the lumen of the tubules from the cortex to the medulla, and was also identified in the blood vessels.

With the Berlin blue reaction haemoglobin stains greenish yellow, and the haemosiderin in the lumen a diffuse blue. Besides the presence of haemosiderin in the lumen of the tubules haemosiderosis was also present in the form of minute granules in the epithelium, mainly of the convoluted tubules, giving these a very characteristic bluish appearance. In some sections the blue colour was prominent even to the naked eye, so much so that the cortex of the kidney in contrast with the light pink of the medulla stood out as a distinct bluish zone.

The spleen in practically all the cases showed extensive haemosiderosis, much more so than was observed in connection with clinically healthy sheep. The venous sinuses contained a large amount of blood, and in some instances the lymphoid tissue was less prominent. It would, therefore, appear, that the spleen was associated with a more extensive destruction of haemoglobin in *Enzootic Icterus*, than was usually observed in clinically healthy sheep, i.e., some of the extra haemoglobin freed by the process of erythrolysis was con-

verted by the spleen into haemosiderin. The bulk of the pigment metabolism in the spleen also seems to be associated with the formation of fatty substances.

The picture in the *lymphatic glands* varied. The great majority of the glands collected showed fairly well marked haemosiderosis in the sinus cells (see plate V). In some instances this was extensive, whereas in other cases haemosiderin occurred as scattered granules in the sinus cells. Such cells also showed the yellow-brown pigment granules, and in some cases the fat droplets described above were also seen. In some glands no haemosiderin was seen, but a yellow-brown pigment was present in the sinus cells. Such pigment granules were easily identified in unstained preparations. In the majority of lymphatic glands examined in the different cases of Enzootic Icterus, the peculiar pigment cells encountered in the liver were also seen in the reticulum of the lymphoid tissue of the gland. In some of them these cells were present in clusters, and gave the same staining reactions as described for the cells observed in the liver (see plate V).

In the smears made from the same glands and stained with Giemsa these cells could be easily identified (see plate VI).

In comparing these reticulum cells in the smears from the liver, lung, and lymphatic gland, it will be seen that they present a very close resemblance to one another.

SUMMARY.

- (i) Enzootic Icterus of sheep, first observed at the Laboratory in July, 1924, and characterized by a marked general icterus and extensive pigmentation of the liver and kidneys, presents a most remarkable occurrence and distribution. The disease peculiar to merinos, at present seems to stand in some relation to the environment of the Karroo. It has so far, with the exception of a few cases at Ermelo, Transvaal, only been observed in sheep brought from the Karroo.
- (ii) All attempts made to unravel the aetiology of this disease have proved fruitless. Unfortunately no cases presented themselves for investigation in the Karroo, whereas numerous cases occurred in Karroo sheep brought to the Laboratory for vaccine purposes.
- (iii) From July, 1924 to December, 1926, 50 cases occurred amongst the 4,000 sheep brought from the Karroo to Onderstepoort for vaccine purposes.
- (iv) From the evidence on hand it is impossible to say at what time of the year the disease was most prevalent. The majority of the cases occurred from 10-30 days after the arrival of the sheep at Onderstepoort.
- (v) The disease was in no way associated with the preparation of the Blue Tongue vaccine, nor could the disease be produced artificially in healthy sheep by the inoculation of blood, organ extracts, etc., etc., and all cultural methods tried to reveal the presence of bacterial, as well as protozoal organisms, failed.
- (vi) The most characteristic symptoms were prostration, increased respiration, a general icterus associated with the visible mucous membranes, haemoglobinaemia, haemoglobinuria

- (in the majority of the cases), oligocythaemia (in the majority of the cases), with the presence of "ghost cells" in the blood.
- (vii) At post-mortem the following changes were observed: General Icterus, general anaemia, haemoglobinaemia, haemoglobinuria, extensive pigmentation and slight degeneration of the kidneys and liver, swelling, pigmentation and sometimes hyperaemia of the lymphatic glands, tumour splenis, constipation in the caecum and colon (ansa proximalis), hyperaemia, and sometimes haemorrhage of the intestines, hyperaemia and oedema of the lungs.
 - (viii) Microscopically the most important changes were observed in the liver, viz.: accumulations of "*pigment cells*" in Glisson's capsule and in the lobule, with atrophy of liver cells and other degenerative changes in the parenchyma.
 - (ix) These characteristic "*pigment cells*" are of the nature of reticulum cells. The pigmented appearance of the cytoplasm of these cells is not of the nature of haemosiderin, nor of known fatty substances (not soluble in alcohol). With some stains (haemalum-eosin) the cytoplasm of these cells assumes a sort of "foamy" appearance, whereas with others, e.g., Giemsa, it was granular. There seems to be a certain resemblance between these cells and the so-called "*Gaucher-cells*" of Gaucher's disease in man.
 - (x) Extensive haemosiderosis, partly associated with fat formation was observed in the lung. The pigment cells described in the liver, were also identified in the lung and there probably reticulum cells were also involved.
 - (xi) The kidneys showed extensive haemoglobin pigmentation, and to a less extent haemosiderosis in the epithelium of the tubules. There was also free haemosiderin in the lumen. Slight degenerative changes were present.
 - (xii) Extensive haemosiderosis occurred in the spleen, and in the majority of cases in the sinus cells of lymphatic glands. Yellow-brown pigment and fatty substances were also encountered in these.
 - (xiii) Pigment cells described in the liver were also seen associated with the reticulum of the lymphoid tissue of lymphatic glands.

3. *Bacterial Icterus.*

The etiology of this condition is fully discussed in the paper by Robinson in this report. The pathology of these cases will be considered here. Bacterial Icterus and Enzootic Icterus resemble each other so closely that at one time it was thought that they were one and the same condition. In fact, at post-mortem the differences between these two conditions are so slight, that a differential diagnosis can often not be made. Bacterial Icterus resembles Enzootic Icterus as regards the anaemia, general icterus, haemoglobinuria (not present in all cases), haemoglobinaemia; pigmentation and degeneration of kidneys and liver, constipation, hyperaemia and oedema of the lungs (not present in all cases), swelling and pigmentation of lymphatic glands, tumour splenis, etc., etc. (see full description under Enzootic Icterus).

The most important difference was observed in connection with the kidneys. In no instance were the kidneys in case of Bacterial

Icterus so intensely reddish-brown in colour. They were usually less pigmented, and the zones could always be identified. The cortical zone varied from a light greenish brown to a reddish brown, and the medulla from a light greenish grey to a diffuse pink.

Some of the cases did not reveal the presence of blood pigment in the urine. The liver presented more or less the naked eye characters seen in Enzootic Icterus. In some cases evidences of regressive changes could be identified around the central vein, viz., as a light greyish brown opaque centre. It may be pointed out that in a number of the experimental cases changes were noted at the seat of inoculation, viz., on the medial aspect of the thigh, right hind limb, as a localised infiltration of the subcutis with a yellowish gelatinous-like material, over an area of about four centimetres in diameter. The vessels were markedly injected, and the whole swelling presented a dark reddish brown appearance.

Microscopical changes in case of Bacterial Icterus.—On the microscopical changes seen in connection with the liver a definite differentiation could be made between these two diseases. In some instances the columns of liver cells of three-quarters of the lobule were dissociated, as it were, through the loss of the Kitt substance. The zone of dislodged liver cells is sharply marked off from the intact columns around the periphery. The cells around the central vein are much lighter in colour, and seem to be much swollen. They appear distinctly larger, and the majority of them show the nuclei affected with a slight necrobiosis, i.e. pyknosis and karyolysis (the latter to a less degree). The central part of the lobule is light pink in contrast to the reddish purple of the periphery. With Sudan III the cells around the central veins show the presence of a large number of fat droplets, and the majority of these are very minute. These fatty changes are also present in the liver cells around the periphery. These, however, vary in the different cases. In some instances the fat droplets have a linear arrangement along the periphery of the cell, whereas the central part of the cell together with its nucleus stands out clearly. In Bacterial Icterus there is a complete absence of the pigment cells described in Enzootic Icterus, whereas haemosiderin in the stern cells was fairly prominent in some of the cases, especially in that part of the lobule where the liver cells were still intact.

In a number of cases the liver cells, besides fatty changes described above, showed the presence of a few yellow brown pigment granules in the cytoplasm. This was particularly well seen with the Berlin blue stain. In some of the cases the bile canaliculi in the periphery of the lobule were distended with a yellow green homogeneous material. Glisson's capsule revealed in a number of cases a localised increase of fibrillae and round cells. In some instances there was an increase in the number of bile-ducts, and eosinophiles could also be identified.

The *lungs* in all cases revealed an intracellular haemosiderosis in the capillaries of the alveolar walls. In some instances it was very extensively present, so much so that the alveolar walls stood out as a bluish network.

The *kidneys* revealed more or less a similar picture to that described in Enzootic Icterus, except that there was much less haemoglobin present. That most probably accounted for the difference in

the macroscopical appearances referred to above. Probably the difference may be regarded as one of degree only, i.e. in Enzootic Icterus haemoglobinaemia in the kidneys was more marked.

The *spleen* and *lymphatic glands* in Bacterial Icterus revealed more or less similar pictures to that described in Enzootic Icterus, except for the complete absence of the pigmented reticulum cells.

SUMMARY.

- (i) At post-mortem Bacterial Icterus resembles Enzootic Icterus so closely that it can easily be confused with it. In Bacterial Icterus, however, the haemoglobin pigmentation of the kidneys is less extensive.
- (ii) Microscopically Bacterial Icterus could be differentiated from Enzootic Icterus. The liver was associated with: regressive changes of the central portion of the lobules, a haemosiderosis in the stern cells, and a bile stasis. There was complete absence of the pigment cells of Enzootic Icterus. The microscopical picture of the other organs was like Enzootic Icterus, except for the absence of these peculiar pigment cells.

DISCUSSION.

In the literature reviewed it was apparent that different species of animals reacted variously to the removal of the spleen. (Kiyono, Schmidt, Lepohne, Warthin.) It would appear that the reticulo-endothelial system in the sheep is so developed that it can adapt itself, after the removal of the spleen, to deal with normal blood destruction, without manifesting specific lesions in any of the haemopoietic organs. The observations of Warthin as regards the part played by the lymphoid tissue could not be confirmed *in toto*. It may be pointed out that sheep and cattle, splenectomised in 1924, and kept under stable conditions for three years, have thrived exceptionally well and have shown no abnormalities in the study of the blood at regular intervals.

The presence of brown pigments in the sinus cells of the lymphatic glands of splenectomy cases was referred to. This, however, also occurred in clinically healthy sheep. This pigment stained a light reddish brown with haemalum-eosin, yellow brown with Sudan III-haemalum, and a light brown with a slight tinge of green with Berlin blue. Some of the sinus cells showed, besides the pigment just described, the presence of fatty substances, which was readily revealed by the Sudan III-haemalum stain. In some instances fatty substances were exclusively present in these cells. The presence of haemosiderin in the sinus cells was only observed in one case, and was, therefore, not the rule. It would appear, therefore, that the sinus cells of the lymphatic glands as well as the sinus cells of the spleen of the sheep, are associated with pigment metabolism in splenectomised, as well as in clinically healthy sheep. What the nature of this pigment is, and in what relation these fatty substances stand to this pigment is at present not known. Graf (20) with the van der Bergh reaction, showed that in the sera of normal sheep no colour reaction could be obtained, and even in a few cases of distinct clinical Icterus no perceptible bilirubin was identified in the serum It may be possible that the pigment concerned in staining the tissues is not actually bilirubin, but some allied derivative not shown by the diazo-reaction in the serum.

The presence of fat droplets in these cells is interesting. Are these products of pigment metabolism within the cytoplasm of the sinus cells, or are the sinus cells associated with fat metabolism apart from pigment metabolism? Such fatty substances have, however, actually been encountered in desquamated endothelials associated with an erythrorhexis. Ribbert showed that the "macrophagen" not only hoarded carmine granules, but also iron and fat. Heitzmann frequently found in the enlarged endothelials, besides phagocytosed erythrocytes, fat droplets. It would appear, therefore, that fatty substances become "*unmasked*" in this pigment metabolism.

The slight oligocythaemia produced by Anaplasma in the blood of clinically healthy non-splenectomised sheep did not leave abnormal traces of an exaggerated blood destruction in any of the haemopoietic organs. Extensive changes were, however, observed in those cases of Anaplasmosis associated with splenectomy. Most extensive lesions were encountered in the liver and were characterised by a marked erythrophagocytosis, and desquamation of the stern cells. In these cells phagocytosed erythrocytes were found in all stages of disintegration or "digestion," from erythrocytes almost the size of normal ones to mere pigment granules. These findings correspond to those of Lauda referred to above, viz., erythrophagocytosis and desquamation of stern cells, and the presence of erythrocytes in various stages of disintegration. In some instances these desquamated cells showed the presence of "vacuoles." As soon as the erythrocytes are engulfed they lose their normal eosin-staining affinity, and become reddish-brown in colour. When stained with Berlin blue, these engulfed cells stand out as dark bluish "blotches," which means that the haemoglobin of the red cell has become transformed (and probably immediately after phagocytosis) into haemosiderin.

These desquamated cells in the liver are derived from the endothelium of the intralobular capillaries, i.e. they are the so-called stellate or stern-cells of Kupffer. The various plates in the appendix indicate the character of the cells.

The fate of these cells in the animal body forms a very interesting problem, and has not yet been solved. It presents many difficulties. Some maintain that they are carried away with the circulation to the lungs where the pigment becomes liberated (Aschoff). What happens to the cell itself is not stated. In the Anaplasmosis and splenectomy cases endothelial cells with erythrophagocytosis and pigment granules have been observed in large numbers in the capillaries of the lungs. In the lung tissue stained with Berlin blue, these cells manifested themselves as a bluish network associated with the alveolar walls. The presence of such cells in the lungs is also mentioned by Lauda. Although these cells in the lungs resemble stern cells (see plate II), it was not clear whether these cells, or some of them, at any rate, were derived from the endothelium of the capillaries of the lung, or whether they were cells of the R.E. system, which had drifted into the lung with the blood from other parts of the body. In the splenectomy and Anaplasmosis cases there is a connection between the number of desquamated stern-cells in the liver and desquamated endothelials in the capillaries of the lungs. In Enzootic Icterus on the other hand, there was very little desquamation of stern cells, yet cells with haemosiderin associated with the walls of the alveoli were as frequent.

In view of these considerations a number of important questions may be put:—

- (a) Where do these desquamated endothelials in the capillaries of the lung come from?
- (b) Do these endothelials brought to the lung in the blood break up there and so set free their metabolised pigments, or do they metabolise the “engulfed erythrocytes,” and extrude the metabolised pigments in a form in which it becomes excreted by the liver, and under certain conditions by the kidneys?
- (c) Are any of the tissue cells of the lung, i.e. alveolar epithelium, vascular endothelium, or histiocyte involved in erythrophagocytosis, or pigment metabolism?

The cells encountered in the capillaries of the lung resemble those seen in the liver. In spite of a most careful examination the point about the origin of all desquamated cells in the blood vessels of the lungs and their relation to the reticulo-endothelial system could not be settled. It may be pointed out that these cells encountered in the lung capillaries in cases of Anaplasmosis and splenectomy, were always intact. No debris of cells or their contents were observed in the lung capillaries. Moreover, phagocytosed erythrocytes in all stages of disintegration occurred to the same extent as in the liver. Free pigment demonstrable by microchemical tests was not seen. Of course, that does not exclude free pigment entirely, seeing that it may be present in a soluble form. Furthermore, blood counts made from the vena cava caudalis and aorta did not reveal any variation in the number of large mononuclears associated with an erythrophagocytosis. The following suggestion about the fate of the cells implicated in an erythrophagocytosis is put forward by the author, viz:—

“These cells are capable of digesting the erythrocyte, i.e., they are associated with pigment metabolism within their cytoplasm; part of the pigment is extruded, most probably as a soluble pigment (a type of pigment probably not yet clearly identified in the sheep), to be excreted by the liver and kidneys as the case may be; the cell passes on in the circulation as a typical monocyte, and sets up a monocytosis.”

“Differential counts from the jugular in these cases show the presence of large numbers of such cells with granules, which are most probably the remains of the phagocytosed erythrocytes [see plates in the paper of De Kock and Quinlan (1)]. Such pigment granules in the mononuclears do not occur in the blood of healthy sheep.”

The question relating to the phagocytic functions of the various tissue cells of the lung, i.e., *alveolar epithelium*, *vascular endothelium* or *histiocytes* has been referred to in the discussion of the literature. The author is inclined to agree with Sacks that the many efforts of numerous investigators to establish the source of the lung phagocyte must still be considered *sub judice*. In *Enzootic Icterus* it would appear that the transformation of haemoglobin into haemosiderin actually takes place in the lung.

Whether all the *mononuclears* (monocytes) recognized in the circulation are of the same origin and value has been questioned

sized lymphocytes in respect of their nuclei and dimensions, and showing an erythrophagocytosis. Is this the type of cell referred to by Kiyono as the "mononuclear" of lymphatic origin?

Besides these three types of cells referred to above, it may be pointed out that cells closely resembling the plasma cells described by Naegeli were also seen in the blood of sheep.

Enzootic Icterus was characterized by the sudden onset of a generalized icterus and associated in the majority of cases with an oligocythaemia, haemoglobinaemia and haemoglobinuria. The breaking up of the erythrocytes was of the nature of an erythrolysis revealed by the presence of "ghost cells" in the circulation, and large quantities of free haemoglobin in the plasma. A large proportion of this free haemoglobin was directly excreted by the kidneys, and could be recognized as such in Bowman's capsule, in the lumen of the tubules, and in the urine of the bladder. At present it is not known what exactly brings about this haemolysis. Haemosiderosis also occurs, as shown by the presence of haemosiderin in the sinus-cells of the lymph glands, an increased haemosiderosis in the spleen, the marked presence of haemosiderosis in the lungs, and in the epithelium of the convoluted tubules of the kidneys. It is not known how much of this freed haemoglobin is directly transformed into haemosiderin, i.e., without the distinct evidence of a preliminary erythrorhexis (so evident in case of Anaplasmosis and splenectomy). Shimura holds that haemoglobin as such split in the circulation can be transformed into haemosiderin. In Enzootic Icterus the stellate cells of the liver were unassociated with haemosiderosis, yet the lungs revealed a large amount of haemosiderin. The question arises: does the lung tissue play a part in the transformation of freed haemoglobin into haemosiderin? Are other tissues besides the reticulo-endothelial system associated with this function under abnormal conditions? Does the presence of haemosiderin in the epithelial cells of the convoluted tubules in cases of Enzootic Icterus indicate a metabolic function in these cells, or is this epithelium only associated with the excretion of haemosiderin, which becomes freed in the circulation?

Furthermore, the reticulo-endothelial system appears to be responsible for the manufacture of excessive amounts of bile pigments, evidenced by the marked general jaundice. This is in support of Rich and others, who maintain that haemoglobin spilled into the tissues almost anywhere is transformed into bile pigment, and excess of haemoglobin in the circulation liberated during haemolysis in pathological conditions is regularly followed by increased formation of bile pigment. One important feature in Enzootic Icterus was the almost total absence of erythrophagocytosis and haemosiderosis in connection with the stern cells of the liver, and the absence of these cells from the circulation.

From the information gained in the above study it would appear that the transformation of freed haemoglobin partly into haemosiderin, and partly into bile pigments does take place without a preliminary erythrophagocytosis and erythrorhexis, and that such transformation in the cell is not necessarily associated with the desquamation of the cell into the circulation. Therefore, Enzootic Icterus is unassociated with a monocytosis, which was so characteristic in Anaplasmosis and splenectomy. In connection with

by many investigators, e.g., Doan and Sabin, De Kock (29), etc. Doan and Sabin differentiate between monocytes and endothelials in the normal circulation of humans and rabbits. Frequently great difficulty has been experienced (De Kock and Quinlan) in differentiating between the different forms of mononuclears. In the differential counts it was often impossible to say whether some of these mononuclears were monocytes or large lymphocytes. As stated above Kiyono recognizes three types of mononuclears (monocytes?):—

- (a) histiogenous monocytes (from stern cells);
- (b) cells corresponding to the "transitionals" of Ehrlich;
- (c) mononuclears of lymphatic origin.

Morphologically type (a) are well defined cells and probably of the same value as the endothelials referred to by Sabin and Doan. They show in the splenectomy and Anaplasmosis cases a large amount of cytoplasm which, with Pappenheim, stain rather indistinctly and of a light greyish blue colour. The margins of these cells are not sharply defined and often present a "frayed out" appearance. This type of cell is well depicted in the plates, where it is seen associated with an erythrophagocytosis, in which erythrocytes in all stages of disintegration can be identified. The nucleus of these cells is usually oval, sometimes slightly indented, and the somewhat granular chromatin is slightly leptochromatic in character.

Type (b) cell is recognized as the typical monocyte, with the indented hoof shaped or slightly looped nucleus. In the cytoplasm the presence of well defined granules, especially when overstained with Pappenheim, can be recognised. These cells are smaller than type (a). They are well defined at their margins, and there is in comparison with type (a) cell less cytoplasm. With reference to type (a) and type (b) cells De Kock (29) drew attention to the fact that in equine infectious anaemia morphologically two types of cells could be identified, viz.: those derived from stern cells, i.e., the endothelial type (a) and the usual type (b). It was pointed out in that paper that it could not be settled whether the latter cells were actually derived from myelogenous tissue. Such cells were, however, never seen in the myelogenous tissue, certainly never in the proportion in which they occurred in the blood. The question is put by the author: "does not type (b) cell perhaps represent a further stage in the life-cycle of type (a) cell, i.e., does not this type (b) cell perhaps stand in the same relation to type (a) cell, as the 'ripe' polymorphous neutrophile stand to the met-myelocytic neutrophile?" Further studies and observations will have to be undertaken to ascertain how far (a) and (b) type cells are therefore actually related.

Type (c) cell.—Great difficulty was experienced in differentiating between a type of mononuclear and certain lymphocytes in the blood of sheep. The type of cell implicated closely resembled a very large lymphocyte, except that the nucleus was more leptochromatic in character and the cytoplasm assumed a light iron grey colour more than a blue. The shape of the nucleus varied but slightly from that of the lymphocyte. These cells frequently showed the presence of large chromatin-stained masses, often triangular in shape. Then there were actually cells encountered in the blood resembling medium-

this point the observations of Cowdry (19) are interesting, viz.: while *Rickettsia* of Heartwater may apparently live and multiply within the endothelial cells, there is no evidence to indicate that their action stimulates the endothelial cells to divide and increase in number in a fashion comparable with the influence exercised by ingested foreign material, such as tubercle bacilli upon the monocyte.

The question whether *reticulum-cells* and *cells of the reticulo-endothelial system* are the same or distinct can now be considered. Enzootic Icterus referred to in the text presents many interesting features in this connection, and was introduced for that purpose. Various important points in connection with that disease were referred to: e.g., the occurrence of peculiar pigmented cells in Enzootic Icterus in sheep, their relationship to "Gaucher cells" in man, the obscure aetiology of Enzootic Icterus and Gaucher's disease, etc. Is there a relationship in the pathogenesis of the two diseases? As will be seen from the summary in the text these pigmented cells in Enzootic Icterus showed a peculiar distribution in the organs in which they occurred, and presented characteristic staining features. The substance in the cytoplasm of these cells was not of the nature of known fatty substances (not soluble in absolute alcohol and chloroform), nor was it of the nature of the known pigments (e.g., bilirubin, etc.). With certain stains the cytoplasm assumed a "foamy appearance." With Giemsa the cytoplasm was greenish blue and studded with dark greenish blue granules. The nearest approach to these cells were the so-called "Gaucher cells," perhaps not so much as regards the chemical nature of the substance in the cytoplasm as their distribution in the tissues. It is evident from the above review of the literature dealing with "Gaucher cells" that no one has succeeded in obtaining definite proof as regards the nature of the substance involved, nor for the reticular or endothelial origin of these cells. With reference to the first point raised, Mandlebaum and Downey maintain that Gaucher cells do not contain fats or lipoids which are demonstrable by the usual microchemical methods. Schittenhelm holds that Gaucher's disease is of the nature of a system disease of the *reticular apparatus*, characterized by large cells filled with a peculiar substance about which there is no uniform opinion. Epstein and Lich say that the chief constituent of these cells is a complex substance of the nature of a cerebroside and that phosphatids are also present. The cells observed in Enzootic Icterus tally in many respects with the description of the Gaucher cells given by Epstein, viz.: with haemalum-eosin they acquire a reddish soft tone, are large oval cells with a "foam-like" cytoplasm, and a small round or oval nucleus situated in the centre or periphery of the cell. In Enzootic Icterus these cells were best studied in organ smears, especially as regards the relationship of nucleus and cytoplasm. The peculiar staining characteristics obtained with Giemsa bear a resemblance to similar staining peculiarities observed in cells of the central nervous system, i.e., is the substance involved in these cells in Enzootic Icterus, of the nature of some of the cells of the central nervous system?

As regards the distribution of these cells in Enzootic Icterus the author is inclined to believe that these cells are reticulum cells, and that the known endothelials of the reticulo-endothelial system (e.g., stellate cells in the liver, and the sinus cells in the lymph-glands) are not involved. In case of "Gaucher cells" Mandlebaum and

Downey held that these arise in the histiocytes of Glisson's capsule, and in the adventitial and periadventitial connective tissue of the central veins of the lobules, and in the reticulum cells of the bone marrow and lymph nodes. The stellate cells always appeared normal, even in those cases where there were numerous Gaucher cells. Schittenhelm speaks of a system disease of the reticular apparatus without the implication of the endothelials. According to Pick Morbus Gaucher is not a disease of the R.E. system. It is better to place it in the general group of histiocytes or macrophagi.

The following points raised by the author (c.f. findings of Mandelbaum and Downey) will show why the cells in Enzootic Icterus are to be regarded as reticulum cells and not endothelials of the R.E. system :

- (a) the appearance of such cells in the vicinity of vessels in Glisson's capsule and around the central veins;
- (b) the non-implication of the stern cells. A large number of the latter were not affected at all, and only a few showed haemosiderosis;
- (c) these pigment cells occurred extravascularly;
- (d) the occurrence of these cells in the reticulum of the lymphoid tissue, whereas the sinus cells were not at all involved in the same process, but were associated with a totally different pigment, etc.

It would therefore appear that Enzootic Icterus is in part a disease of the reticular system (c.f. Gaucher's disease) complicated with haemolysis.

With reference to this *reticular system* it may, however, be stated that Mallory and Parker in a recent publication (23) doubt the existence of *reticulum* and *reticular cells*. They maintain that reticulum is collagen in separated form, rendered prominent by silver stain, and that there are *no* reticular cells other than fibrocytes. How far these observations of Mallory and Parker are correct cannot be determined at present. For the time being, the following grouping of tissue cells in the sheep, discussed in the above study, may be adopted:—

- (a) *fibrocytes*;
- (b) *reticulum cells*.
- (c) *reticulo-endothelial cells* (e.g., stern cells of Kupffer, sinus cells of lymph glands and spleen);
- (d) *endothelials* of blood and lymph vessels.
- (e) *blood cells*: Endothelials, monocytes (Endothelials and monocytes being probably stages of the same cell), neutrophiles, eosinophiles, basophiles, lymphocytes, plasma cells.
- (f) *Histiocytes*, i.e., the wandering cells of connective tissues. The present study, however, did not afford material to ascertain the true nature of these cells in the sheep.

The question of *Bacterial Icterus* is still under consideration, especially as regards its pathogenesis. Pathologically it can be distinguished from Enzootic Icterus as follows:—

- (i) The absence of the pigment cells described for Enzootic Icterus;
- (ii) the presence of regressive changes associated with the central portion of the liver lobule;

- (iii) the presence of haemosiderosis associated with the stern cells. In Bacterial Icterus erythrorhexis could be definitely identified, especially in the stern cells. To what extent erythrolysis occurs is not known;
- (iv) the kidney in Bacterial Icterus was less intensely red on account of more haemosiderin and less haemoglobin;
- (v) the presence of the specific organism of Bacterial Icterus.

Regressive changes in the liver combined with excessive destruction of blood have been recorded in case of Weil's disease (Lepohne), in experimental yellow fever, Weil's disease and Sumatra infection (Heitzmann). The author is inclined to believe that these liver lesions in case of Bacterial Icterus do not follow from the abnormal breaking up of red cells or vice-versa, but that both changes are probably due to the independent action of the bacteria isolated.

GENERAL CONCLUSIONS.

(1) The reticulo-endothelial system of the sheep is so developed that it can, after removal of the spleen, deal with normal blood destruction without manifesting specific lesions.

(2) The sinus cells of the lymphatic glands in clinically healthy sheep under stable conditions, as well as in splenectomy cases, revealed the presence of pigmentation and formation of fatty substances. What the nature of the pigment is, whether it is identical with the known bile pigments of other animals, and in what relation it stands to the formation of fatty substances, is not yet known.

(3) Fatty substances have been observed to occur in the endothelials associated with an erythrophagocytosis and erythrorhexis.

(4) The granules of the eosinophiles of the sheep seem to be in some way or other bound up with fatty substances.

(5) Extensive erythrophagocytosis and desquamation of stern cells in the liver were observed in cases of splenectomised sheep affected with anaplasmosis. The presence of these cells was reflected in the blood as a monocytosis. In them erythrocytes, in all stages of disintegration were encountered.

(6) As regards the fate of these cells with engulfed erythrocytes, the author is inclined to believe that they are capable of carrying out an intracellular pigment metabolism. Part of the metabolised pigment is extruded into the blood, and excreted, whereas the residue forms the granules so conspicuous in these cells. The cells pass on in the circulation and are responsible for the monocytosis referred to.

(7) It is clear that some of the monocytes in this study are of the nature of endothelials (c.f. Sabin and Doan), and are derived from the reticulo-endothelial system. The author is inclined to believe that the typical monocytes (i.e. the so-called "transitionals" of Ehrlich) may be regarded as a further stage in the life cycle of this desquamated endothelial (c.f. neutrophile and its myelocyte). Whether some of these cells are of lymphatic origin could not be decided.

(8) The destruction of erythrocytes in Enzootic Icterus was more of the nature of an *erythrolysis*. Haemosiderosis was manifested in the sinus cells of the lymph glands, in an exaggerated form in the spleen, extensively in the lungs, and in the epithelium of the convoluted tubules of the kidney.

(9) It appears that the lung is not associated with an erythrophagocytosis, but does play a part in the transformation of freed haemoglobin, as evidenced by the extensive haemosiderosis. Whether this conversion also takes place in the kidney could not be decided.

(10) It is believed that in Enzootic Icterus the transformation of freed haemoglobin partly into haemosiderin and partly into bile pigments occurs without a preliminary erythrophagocytosis. Moreover, such a metabolism does not seem to be associated with the desquamation of the cell, and therefore, in this disease no mononcytosis occurs.

(11) Enzootic Icterus showed the presence of peculiar pigment cells, which seem to have some resemblance to the so-called "Gaucher cells," especially as regards their distribution in the tissues. The chemical nature of the pigment has not yet been determined.

(12) As regards their distribution, these cells can, for the time being, be regarded as reticulum cells, i.e. quite distinct from the endothelial cells of the R.E. system, which cells were not involved. These pigmented reticulum cells occurred in the liver, lymph glands and lungs.

(13) Enzootic Icterus may for the present be regarded as a disease of the reticular system, complicated with a haemolysis. How these are brought about is not yet known.

(14) Pathologically Bacterial Icterus could be distinguished from Enzootic Icterus by extensive regressive changes associated with the central portion of the liver, the absence of peculiar pigmented reticulum cells, and the destruction of erythrocytes in part by erythrophagocytosis.

ADDENDUM.

Sheep No. 16836 arrived here 30/5/27 from Colesberg (Karoo). It was injected with Blue Tongue Virus on 5/6/27 and died 8/6/27 of some intercurrent disease. At post-mortem changes in the large intestine were present somewhat suspicious of Enzootic Icterus, although there was *no* sign of a general Icterus. Microscopically pigmented reticulum cells were observed in the liver (besides extensive fatty degeneration), clusters of such cells were seen in the lymphoid tissue of lymphatic gland and Malpighian bodies of the spleen. This is the first case of Enzootic Icterus observed in sheep at Onderstepoort in which there was extensive involvement of the reticular system without the presence of haemolysis and an associated icterus. This seems to support the view expressed above that Enzootic Icterus appears to be a disease of the reticular system.

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APPENDIX 1.

This deals with the macroscopical and microscopical examinations of:—

CONTROL SHEEP: 13994, 10246, 13856.

(x) Anaplasmosis in non-splenectomised sheep, viz., 8432, 8463.

(y) Healthy sheep splenectomised, of which some were killed for the collection of material, and others died as a result of the operation of splenectomy, viz., 8431, 8455, 8458, 9414, 10946.

(z) Anaplasmosis in splenectomised sheep. Some were carriers of Anaplasma and splenectomised, viz., sheep 7369, 7443, 8427, 8434, 10656, 13853. Others were splenectomised and then infected with Anaplasma, viz., sheep 8457, 8430, 8456.

SHEEP No. 8431.

History.	Particulars of P.M.	Macroscopical Changes.
1.4.24. In Expt. S. 1605. Splenectomised on 8.4.24. Died on 12.4.24	P.M. on 13.4.24. P.M. No. 3632. Spec. No. 3898. Merino. Hamel. 18 months. Condition good.	<i>Pathological Anatomical Diag.</i> —Broncho-pneumonia. Degeneration myocardium and liver. Wound left iliac region. <i>Etiology.</i> —Broncho-pneumonia and sequel splenectomy.

MICROSCOPICAL CHANGES.

Liver: The columns of liver cells slightly disorganized around the central veins; the liver cells either lie free or occur in groups of a few cells each. The nuclei of some of these cells appear enlarged, and some cells show more than one nucleus. The intralobular capillaries are distended with blood, whereas the liver cells show vacuoles, which with Sudan III show up as droplets of a reddish brick-colour. *Note.*—No pigment could be demonstrated in the sections.

Diagnosis: Slight venous hyperaemia and fatty infiltration.

Kidney: Evidences of autolysis; slight hyperaemia and fatty changes in the loop of Henle.

Lymph Gland: Evidences of autolysis; here and there sinus cells with a yellowish granular pigment. With Sudan III it has a yellowish appearance, and is not of the nature of Haemosiderin.

Lungs: Evidences of hyperaemia and broncho-pneumonia.

Myocardium: Slight fatty infiltration.

SHEEP No. 8455.

History.	Particulars of P.M.	Macroscopical Changes.
7.11.24. In Expt. S. 1841. Showed extensive anaemia as result of treatment with pyrogallic acid and recovered 16.1.25. Splenectomised. 17.1.25. Died sequel Splenectomy, <i>vide</i> 11th and 12th Report; page 464.	P.M. on 17.1.25. P.M. No. 4301. Spec. No. 4645. Merino. Hamel. Two tooth. Condition good	<i>Pathological Anatomical Diagnosis.</i> —Healing wound in left iliac region; absence of spleen. <i>Etiology.</i> —Died from the effects of anaesthesia 18 hours after the operation.

MICROSCOPICAL CHANGES.

Liver: Good deal of blood in blood vessels. Liver cells show a good deal of vacuolation, and this with Sudan III shows up as brick-red droplets. Glisson's capsule in places seems to be widened, and contains a fair amount of round cells, chiefly of the lymphocytic series.

Kidneys: The blood vessels of the intermediate zone distended with blood. Here and there cells whose nuclei show pyknosis. With Sudan III epithelial cells show a yellowish granular pigment. With Berliner Blue stain this pigment is found to be haemosiderin.

Lungs: Blood vessels distended with blood. Here and there in the capillaries a few cells which contain a yellow-brown granular pigment. With Berliner Blue no haemosiderin could be detected.

Myocardium: With Sudan III presence of minute brick-red granules, but they are not frequent and do not interfere with the cross striations. Few sarcocysts present.

Adrenals: No lesions seen.

Lymph Gland: Shows numerous neutrophiles along the sinuses of the medulla, and this stands out as a network. With Sudan III sinus cells show a yellow-brown granular pigment.

SHEEP No. 8458.

History.	Particulars of P.M.	Macroscopical Appearances.
24. 4. 24. In Expt. 1613. Showed reaction of Anaplasmosis after inoculation of blood and recovered.	P.M. on 21.1.25. P.M. No. 4314. Spec. No. 4663. Merino. Hamel. Full mouth. Condition fair.	<p><i>Pathological Anatomical Diagnosis</i>.—Healing operation wound in left iliac region; slight localized fibroplastic peritonitis; absence of spleen; venous hyperaemia and fatty degeneration of liver; venous hyperaemia of lungs; degeneration of myocardium and kidneys. Parasitic nodules in small and large intestines.</p> <p><i>Etiology</i>.—Sequel splenectomy.</p>
10. 11. 24. In Expt. 1841. Showed extensive anaemia after treatment with pyrogallie acid and recovered. 16. 1. 25 splenectomised. 21. 1. 25 died. <i>Vide</i> 11th and 12th Report, page 465.		

MICROSCOPICAL CHANGES.

Liver: Around the central vein there is a slight venous hyperaemia with atrophy of liver cells, in the majority of the lobules. In some it is more extensive than in others. Around this hyperaemic zone the liver cells show extensive vacuolation, which with Sudan III shows up as brick-red droplets, varying from medium size to large. The nuclei in these cells are well stained. No abnormal pigmentation detected.

Kidney: Blood vessels in the medulla contain a large amount of blood. A few greenish-yellow pigment granules in the tubular epithelium, and with Berliner Blue stain appear to be haemosiderin granules, giving the tubules a bluish appearance.

Lymph Gland: Desquamation of sinus cells, and these show pigment of yellowish-brown colour. Pigment becomes very prominent with the Sudan III stain. Some of this pigment is haemosiderin, and the rest is a type of brown pigment not yet identified.

SHEEP No. 9414.

History.	Particulars of P.M.	Macroscopical Changes.
<p>3.11.25. In Expt. S. 2315. Clinically healthy sheep splenectomised to compare with those in which Anaplasmosis occurred.</p> <p>11.11.25. Killed by chloroform and bleeding for collection of specimens.</p>	<p>P.M. on 11.11.25. P.M. No. 5077. Spec. No. 5575. Interim about $\frac{1}{2}$ hour. Merino. Hamel. Full mouth. Condition good.</p>	<p><i>Skin, Left iliac Region.</i>—Presence of an operation wound about 3 inches in length in the process of healing. Stitches still present.</p> <p><i>Peritoneum.</i>—The rumen is adherent to the diaphragm over the area where spleen was attached, by newly formed connective tissue in which there are several haemorrhages.</p> <p><i>Liver.</i>—Slightly swollen; light reddish-brown appearance; on section, lobulation distinct.</p> <p><i>Spleen.</i>—Absent.</p> <p><i>Kidneys.</i>—Slightly darker in colour.</p> <p><i>Pathological Anatomical Diagnosis.</i>—Localized fibroplastic peritonitis. Healing wound in left iliac region. Slight hyperaemia of kidneys (no parasitic nodules). Absence of spleen.</p> <p><i>Etiology.</i>—Killed by chloroform and bleeding.</p>

MICROSCOPICAL CHANGES.

Liver: In the periphery are distinct alterations characterized by an increase of round cells, and between these are peculiar cells with a large amount of a granular-looking cytoplasm which stains brownish-red with Sudan III. The round cells are chiefly of the nature of lymphocytes. As will be seen in the picture, these peculiar cells contain a large amount of cytoplasm and a small nucleus situated near the periphery. These cells are probably reticulum cells. With the Berliner Blue method they stain light greenish, and with Giemsa a dark blue.

Diagnosis: Slight interstitial hepatitis with peculiar pigment cells (c.f. *Enzootic Icterus*).

N.B.—It was subsequently shown that a certain percentage of the sheep introduced from the Karroo show the presence of pigment cells.

Kidney: Here and there a few cells of the tubuli show the absence of nuclei.

Lung: No evidence of pigment cells.

Periportal Lymph Gland: Shows the presence of the peculiar cells, described in the liver, situated in the lymphoid tissue, and present the same staining features with Sudan III. Majority of the sinus cells appear to be free, spherical, and show the presence of minute granules, which with Berliner Blue stain yellow-brown.

Retropharyngeal Lymph Gland: With Sudan III sinus cells show presence of yellow granules and with Berliner Blue the granules stain yellow-brown.