INSUSCEPTIBILITY OF PUPS TO CHLOROFORM POISONING DURING THE FIRST THREE WEEKS OF LIFE.*

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When pregnant dogs are severely or fatally poisoned with chloroform and show the consequent liver injury and necrosis, it has been found that the fetuses of these animals escaped liver injury altogether.[1] At first we supposed that the explanation of the phenomenon was to be sought in the placenta, but we soon found that pups are practically not subject to chloroform liver necrosis during the first week of life. A slight amount of hyaline liver necrosis and fatty degeneration may be caused by chloroform anesthesia during the second and third weeks of life, and the pups usually show the characteristic type of liver necrosis after chloroform during the fourth week of life and later.

The experiments given below establish these facts beyond doubt, so that the question arises as to how this may be explained. We may assume that the liver performs all its normal metabolic functions just as soon as the umbilical cord is severed, and so far resembles the adult liver. The diet during the period of the experiment was normal, as the pups nursed and were cared for by healthy mothers. Young animals contain relatively more glycogen than normal adults, but starvation or forced feeding of rich food in adults causes no change in susceptibility to chloroform poisoning.

There is one striking difference between the liver of the pup at birth and the liver of the adult dog, namely, the presence of nests of blood-forming cells in the hepatic venules in all parts of the liver lobule of the former. These "blood islands" or nests of cells

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[1] Whipple, G. H., *Jour. Exper. Med.*, 1912, xv, 246.

similar to those in the bone-marrow and spleen at this age, become progressively less numerous in the pup's liver and usually vanish completely during the fourth week of life, at which time the liver appears in all respects like the adult liver. There is a great temptation to explain the resistance to chloroform liver necrosis in pups by the presence of these blood-forming cell nests. But why should these nests of foreign cells have any ability to protect the liver cells? There is no possibility of their performing any of the metabolic processes peculiar to the liver cells. In attempting an explanation, we may fall back on the presence of foreign ferments which are known to be present in blood cells of various types (Opie),[2] but it is difficult to understand the action of any ferments that could exert an influence on the liver cells and protect them from this specific toxic action of chloroform. Still another possibility is that the cells may in some way neutralize the chloroform that passes through the liver lobules and thus protect the liver cells.

It is of interest at this time to note that dogs poisoned by chloroform and showing liver necrosis, are less susceptible to a second application of chloroform anesthesia given on the second to the fourth day after the first. At this time the liver lobules are full of wandering cells of all types called out by the presence of the dead liver cells. This suggests again that the presence of these white blood cells may in some way protect the liver cells. In adults during this process of repair, the liver is not completely protected against injury by chloroform, but the second necrosis, as a rule, is much less evident. It cannot be argued that the newly formed liver cells are necessarily more resistant, because after the repair is effected and the leucocytes have disappeared, the liver may be injured as usual by chloroform anesthesia.

These experiments are of interest in connection with recent work of Opie,[3] who showed that injection of leucocytes into the pleural cavity of the dog checked more or less effectually the development of a tuberculous process. He did not attempt to explain the mechanism of this process. This inhibiting effect was most marked when the injected leucocytes came into most intimate association with the tuberculous lesions.

[2] Opie, E. L., *Jour. Exper. Med.*, 1908, x, 419.
[3] Opie, E. L., *loc. cit.*

In our experiments, the liver cell columns are surrounded by the nests of blood-forming cells. This is the condition in the new-born pup; and with advancing age the cell nests become progressively less numerous, disappearing completely at the end of the fourth week. If we assume that the immunity of the liver cells to chloroform poisoning is due to the presence of these cells, we have a clear example of protection against a known poison effected in a peculiar way. If we assume that leucocytes in great numbers may inhibit the injurious effect of the tubercle bacilli upon various tissues, is it not possible that at least a part of this effect may be due to some protective action against the peculiar poison of the tubercle bacillus?

It is possible to remove most of these blood-forming cells from the liver of the pup in the first week of life by causing an infection. For example, a bronchopneumonia will clear the liver almost completely of all the blood elements except the large bone-marrow giant cells, but as the pups succumb so readily to a slight infection, there has been no opportunity to subject such a liver to the effects of chloroform anesthesia. We hope to remove most of these blood-forming nests from the liver by injections of turpentine or other irritants and then study the effect of chloroform upon it.

If it is difficult to explain the absence of liver necrosis in young pups after the administration of chloroform, it is just as difficult to explain the presence of central hyaline necrosis in adults under the same conditions. We have no good explanation for this specific toxic action of chloroform upon the liver, although various hypotheses have been advanced to account for it (Wells[4] and others). Nor can we explain the specific toxic action of phosphorus upon the liver and pulmonary tissues, and we must content ourselves for the moment by stating that these poisons have specific affinities for different tissues and organs.

These experiments and Opie's published observations, if a correct interpretation of the results has been given, invest the white blood cells with new and interesting powers, not the least of which is the neutralization of poisons by some mechanism at present obscure. We hope to report further upon some of these points in the near future.

[4] Wells, H. G., *Jour. Am. Med. Assn.*, 1906, xlvi, 341.

EXPERIMENTAL PART.

PUP NOT POISONED BY CHLOROFORM WHILE IN UTERO NOR DURING THE FIRST WEEK OF LIFE.

Pup 106-a.—Born May 13; nursed by healthy dog. It is to be noted that this pup's mother (dog 106)[5] had been subjected to chloroform anesthesia for two hours, and consequently the fetal tissues were subjected to the action of the drug for the same period (May 12).

May 19. Pup in excellent condition and nursed well. Chloroform anesthesia for 1¼ hours; ½ oz. given. Anesthetic well taken.

May 20. Pup perfectly well and nursed as usual.

May 21. Chloroform anesthesia for 1½ hours; ½ oz. given. Anesthetic well taken.

May 22. Pup appeared perfectly well and nursed vigorously.

May 23. Pup has gained weight and looks well. Chloroform anesthesia for 1½ hours; ½ oz. given.

May 24. Pup normal.

May 25. Pup strong and active. Operation, under ether anesthesia, with the usual technique for removal of a wedge-shaped piece of liver for histological examination.

Microscopical section shows normal liver tissue. No necrosis. Some increase in polymorphonuclear leucocytes about the portal structures. No operative difficulty and the blood clotted in the usual way. Nothing to suggest a lessened amount of fibrinogen, which is usually present with chloroform poisoning.

May 26–28. Pup made a rapid recovery and the wound healed normally.

June 14. Pup had grown rapidly and was in excellent condition. Chloroform anesthesia for 1¾ hours; ¼ oz. given. Recovery from the anesthetic was rather slow.

June 15. Pup did not nurse well; vomited about ½ oz. of curds and mucus, and appeared rather drowsy.

June 16. Pup did not nurse and appeared ill and rather drowsy. Ether anesthesia and bleeding from the carotid. Blood collected in oxalate. Blood clotted normally, but the clots were rather soft. Serum was canary yellow in color, indicating a good deal of jaundice.

Autopsy performed at once. Serous cavities normal. Wounds in the abdomen and liver had healed perfectly. Heart and lungs normal. The thymus showed a few tiny ecchymoses; otherwise normal. The spleen showed conspicuous Malpighian bodies and a rather soft red pulp. The stomach contained some dark fluid and mucus with a few curds. Intestines negative except for round worms. Adrenals, kidneys, and pancreas normal. Liver large and friable. Lobulation very conspicuous, each lobule having a deep red center and yellow margin.

Microscopical section shows the usual type of central hyaline liver necrosis involving about three fifths to four fifths of every liver lobule. The remaining liver cells about the portal spaces show extreme fatty degeneration, every liver cell containing several fat droplets. The picture of extreme liver necrosis and

[5] Whipple, G. H., *Jour. Exper. Med., loc. cit.*

degeneration following chloroform anesthesia. Sections from thymus, kidney, pancreas, duodenum, and lung normal. The spleen shows considerable blood-forming elements in its sinuses, and the large bone-marrow giant cells are numerous.

CHLOROFORM ANESTHESIA GIVEN TO PUPS OF THE SAME LITTER AT VARIOUS AGES.

This series of experiments upon healthy pups of the same litter is important. Two pups, one on the fifth day, the other on the eighth day after birth, were given chloroform anesthesia for two hours. At autopsy, two days later, the findings in each case were normal. Two other pups, one on the twelfth, the other on the sixteenth day after birth, were given chloroform anesthesia in exactly the same way. At autopsy, two days later, the first pup showed only an occasional hyaline necrotic liver cell, while the second showed a more marked liver necrosis estimated as involving about one seventh of each lobule.

A fifth pup, twenty days old, was killed accidentally at the end of anesthesia and served as a control. The sixth pup (twenty-four days old) was given chloroform anesthesia for two hours, and autopsy after two days showed the familiar type of central hyaline necrosis involving two fifths to one half of each lobule. These pups with advancing age showed progressively fewer numbers of blood-forming islands in the liver sections.

Dog B-22.—Large, active, brindle bull dog, weight 50 lbs.

January 1. Gave birth to six healthy, active pups.

January 3–5. Mother and pups in the best of health.

January 12. One of the litter had its eyes partly open, and all were doing well.

January 15. All three pups had their eyes partly open and were strong and fat.

Pup B-22-a.—January 5. Pup five days old and quite healthy. Chloroform anesthesia for two hours; ½ oz. given. Anesthetic well taken, and recovery fairly rapid.

January 6. Pup quite well.

January 7, 3 P. M. Pup nursing vigorously and apparently in the same condition as the rest of the litter. Ether anesthesia and bleeding from carotid. Blood clotted rapidly in a test tube, and the clot was tough and normal in every respect.

Autopsy at once. Heart, lungs, spleen, pancreas, stomach, and intestines normal. The stomach and intestines contained large amounts of curds and

milky fluid and the lacteals were all engorged. Liver pale reddish brown in color, with normal lobulation; apparently normal in every way.

Liver sections show no necrosis of any of the parenchyma. Polymorphonuclear leucocytes present in considerable numbers in the portal tissues. Blood-forming islands in the liver capillaries also present in considerable numbers. Fat stains show fat droplets in all parts of the liver lobules. Some of the droplets are of considerable size, perhaps as large as the cell nucleus, but the majority are very fine. The distribution is quite uniform. Sections from the kidney, pancreas, and duodenum are normal. The spleen shows active blood formation in its sinuses.

Pup B-22-b.—January 8. Healthy pup eight days old. Chloroform anesthesia for two hours; about ½ oz. given. Anesthetic well taken; no muscular tremors noted.

January 9. Pup perfectly well, and nursed vigorously.

January 10. Pup nursing vigorously. 3 P. M. Ether anesthesia and bleeding from carotid. Blood collected in a test tube clotted in the usual way, forming a tough clot which retracted squeezing out milky serum.

Autopsy at once. Heart, lungs, thymus, spleen, and pancreas normal. Stomach and intestines full of curds and milky fluid with conspicuous lacteals. Liver pale brownish red in color, with tiny red specks here and there, as is the case in normal livers at this stage of development. The microscopical findings in the liver and all other organs are exactly similar to those described above (Pup B-22-a). The blood-forming islands in the liver were about as numerous as in the preceding case.

Pup B-22-c.—January 12. Pup twelve days old, quite healthy and eyes not yet open. Chloroform anesthesia for two hours; ½ oz. given. Pup recovered slowly, was cold, and suffering from shock. Thirty minutes after anesthesia, pup still somewhat intoxicated, and had not completely recovered.

January 13. Pup seemed quite well.

January 14. Pup nursing vigorously; eyes about half open. Ether anesthesia and bleeding from carotid. Blood clotted in the normal way, giving a tough clot and milky serum.

Autopsy at once. Heart, lungs, thymus, spleen, pancreas, and kidneys normal. Subcutaneous fat very abundant. Stomach full of milk, and lacteals greatly engorged. Liver pale reddish brown in color; quite normal in every way.

Sections show no characteristic liver necrosis, but here and there in the center of a lobule is seen an occasional hyaline liver cell associated with a few wandering cells. Such necrotic cells are usually in the immediate vicinity of the central venule. The fat stains show less conspicuous fat deposits than in the preceding cases, but a few larger fat droplets are found in the center of the lobule, which are absent in the peripheral portion. The nests of blood-forming cells are less conspicuous than in the previous cases, but are still to be seen in every lobule.

Pup B-22-d.—January 16. Normal pup sixteen days old. Chloroform anesthesia for two hours; ⅓ oz. given. Anesthetic well taken, and recovery fairly rapid.

January 17. Pup quite well; very active and nursing; eyes well opened.

January 18. Active and nursing. Ether anesthesia and bleeding from carotid.

Autopsy at once. Heart, thymus, spleen, pancreas, and kidneys normal. The lungs showed a few tiny pink specks in the posterior portions. The stomach and duodenum were full of curds. A few round worms in the duodenum. Liver fairly normal in gross; possibly somewhat increased in size. Liver sections show a slight amount of central hyaline necrosis in every lobule, involving perhaps one seventh of the parenchyma. Fat stains show conspicuous droplets in the central third of each lobule associated with the areas of necrosis. Islands of blood-forming cells present in the liver sections, but not conspicuous, indicating a liver approaching maturity. Mitotic figures in the liver cells were seen close to the areas of necrosis, indicating beginning regeneration.

Pup B-22-e.—January 20. Pup twenty days old; well and strong. Chloroform anesthesia for two hours; overdose and death at the end of the two hours.

Autopsy at once. Heart contracted. The lungs showed a few ecchymoses in the posterior portion. All organs normal in gross, except for considerable congestion.

Liver sections show very few islands of blood-forming cells. No indication of necrosis, but fat stains show the presence of a good many fat droplets in liver cells in all parts of the lobules (control sections).

Pup B-22-f.—January 24. Pup twenty-four days old; fat and in perfect condition; could walk actively. Chloroform anesthesia for two hours; ½ oz. given. Anesthetic well taken and recovery rapid. 4 P. M., pup nursing and apparently perfectly well.

January 25. Pup very quiet and does not seem normal.

January 26. Pup quite active. No vomiting, but some loss of weight. No obvious intoxication. 4 P. M. Ether anesthesia and bleeding from carotid. Thorax, heart, lungs, thymus, spleen, and pancreas normal. Stomach full of curds and contained a few ascaris worms. No hemorrhages. The kidneys showed a pale cortex; otherwise negative. Liver large and friable. Lobulation very conspicuous, the lobules having red central dots and opaque yellow edges, the invariable finding in chloroform poisoning. Obvious central necrosis in gross. Blood clotted perhaps a little more slowly than normally, but the clot was firm and abundant.

Liver sections show a familiar type of hyaline central necrosis involving about two fifths to one half of each lobule. Wandering cells numerous. Fat stains show a conspicuous fat deposit in the middle zone between the necrotic and more normal liver cells. Mitotic figures numerous in the liver cells, indicating beginning regeneration.

PUPS RESISTANT TO CHLOROFORM POISONING DURING THE FIRST THREE WEEKS OF LIFE.

Dog C-13.—Small black and tan mongrel terrier.

October 28. Normal birth of eight pups.

October 31. Three pups found dead and cold.

Pups C-1, C-2, C-3.—Autopsies similar in all. Heart, spleen, kidneys, pancreas, and adrenals normal. Liver normal in gross, and of a very dark purple color. The lungs showed small purplish patches scattered throughout all lobes.

Numerous sections from the different pups show practically the same picture in all. The liver sections show normal parenchyma. Nests of blood-

forming cells rather inconspicuous, but bone-marrow giant cells fairly numerous. Fat stains show small fat droplets in all parts of the lobules, diffusely scattered in the protoplasm. Larger fat droplets more numerous close to the portal spaces. Kidney sections negative. Lung sections show beginning inflammation in the alveolar walls, with large numbers of polymorphonuclear leucocytes and congestion, but relatively little exudate in the alveoli or bronchi,—the picture of an interstitial pneumonia.

Pup C-4.—November 2. Pup found dead and cold.

Autopsy showed little abnormality. Organs in general as in the three previous pups. Liver normal in size, but paler and a little more opaque than normally, suggesting possible fatty degeneration.

Microscopical sections are similar to the other pups in this litter. The liver shows about the same amount of fat deposit as the others. Fat droplets small, as a rule. No necroses seen.

Pup C-5.—Normal and fairly healthy.

November 4. Pup seven days old and in good condition. Chloroform anesthesia for 1¾ hours; 1 oz. given. Anesthesia deep, and animal stopped breathing at the end of the anesthesia (artificial respiration). Recovery after anesthesia slow, and the pup was cold and appeared much shocked.

November 5–6. All pups nursing and apparently perfectly well.

November 7. Pup examined carefully and found to be absolutely normal; quite fat and active; nursing vigorously; same as control pups in every respect. Eyes not yet open. Ether anesthesia, and bleeding from jugular. Blood clotted in ten minutes with the formation of very tough, elastic clots.

Autopsy performed at once. All viscera perfectly normal. Serous surfaces smooth. Stomach and intestines full of milky fluid and curds. Liver pale, reddish brown, and translucent. No gross evidence of injury.

Liver sections show more conspicuous blood-forming elements than in the controls, probably explained by the absence of pneumonia. No evidence of liver necrosis. Fat droplets present in all parts of the liver lobule, as in the controls, possibly less conspicuous than in the control sections noted in the preceding cases. Kidneys, duodenum, and pancreas normal.

Pup C-6.—Healthy and strong.

November 9. Pup thirteen days old and in excellent health. Chloroform anesthesia for 1¾ hours; ¼ oz. given. Anesthesia well taken and recovery after anesthesia rapid.

November 10–11. Pup strong and apparently perfectly well. Nursed vigorously.

November 12. Eyes partly opened. Ether anesthesia and bleeding from jugular. Blood clotted normally with tough clot formation and a milky serum.

Autopsy at once. All the viscera appeared normal. Stomach and intestines full of milk, and lymphatics engorged with milky fluid. Liver pale brown and translucent. The centers of the lobules showed tiny yellow specks, indicating some degeneration.

Liver sections show relatively few blood-forming elements, with an occasional bone-marrow giant cell. In the centers of the lobules are found occasional hyaline liver cells, and fat stains show considerable fatty degeneration in the central fourth of the lobule. Small fat droplets present in all parts of the

lobule, but more striking in the central portions. Kidney, pancreas, and duodenum normal.

Pup C-7.—November 15. Pup eighteen days old; strong and active; gained weight steadily and nursed vigorously. Eyes fully opened. Chloroform anesthesia for 1½ hours; ½ oz. given. Pup seemed badly poisoned and nearly died at the end of the anesthesia, being restored with difficulty after vigorous cardiac massage and artificial respiration.

November 16–17. Pup nursing and appeared normal.

November 18. Apparently quite well, but not very active. Ether anesthesia and bleeding from jugular. Blood clotted in the normal time with the formation of fairly firm, elastic clots.

Autopsy at once. Serous cavities, heart, spleen, kidneys, and pancreas normal. The lungs showed a few ecchymotic patches. The stomach and duodenum contained milky fluid. The liver showed conspicuous lobulation with rather sunken centers, but no opaque specks in the centers of the lobules.

On microscopical section, the liver shows more blood-forming elements and bone-marrow giant cells than in the preceding case (pup C-6). Careful search was required to find a few hyaline liver cells in the very centers of the liver lobules associated with a few wandering cells. Fat stains show striking deposits of rather large fat droplets in the central half of each lobule, and small fat droplets in the peripheral portion. Liver injury in this animal was no more marked than in the preceding case. Lungs, pancreas, and kidneys normal. The spleen shows striking evidence of blood formation in the spleen pulp with great numbers of bone-marrow giant cells and nucleated red cells.

This series confirms the observations in the preceding one (B-22). The first four pups died during the first week from bronchopneumonia, and serve as controls. The fifth pup, when seven days old, was given chloroform for one and three quarters hours. At autopsy, three days later, the viscera were found to be normal. The last two pups, thirteen and eighteen days old, were given chloroform anesthesia for the same length of time and killed after the same interval. The autopsy showed normal organs in each case, except for a very slight amount of central hyaline liver necrosis.

Dog 105.—Small fox terrier.

May 3. Gave birth to five pups.

May 4. Dog well and pups nursing normally.

Pup 105-a.—Strong active male. Chloroform anesthesia for 1 hour; ½ oz. given. Anesthetic well taken and recovery rapid after the anesthesia.

May 6-7. Pup nursed well and appeared exactly as the other pups.

May 8. Pup strong and healthy in every way. Ether anesthesia and bleeding from the carotid.

Autopsy, thorax, peritoneal cavity, heart, lungs, spleen, stomach, duodenum, and kidneys normal in gross. The liver was examined with the greatest care and appeared to be normal in gross.

Liver sections show no necrosis. Nests of blood-forming cells numerous in all parts of each lobule. There were a few leucocytes in the portal spaces. Fat stains showed some large fat droplets in the central portion of each lobule. One section of the lung shows a small area in which the alveoli contain a few polymorphonuclear leucocytes and red cells. The spleen shows active blood formation going on in the pulp.

Pup 105-b.—May 10. Small male, seven days old. Chloroform anesthesia for 1 hour; ⅓ oz. given. Anesthetic poorly taken and the pup stopped breathing several times. Recovery after anesthesia rather slow.

May 11. Pup not nursing in the morning. 5 P. M. Found dead.

Autopsy at once. Heart pale and contracted. The lungs showed small purple patches, probably bronchopneumonia. Spleen, pancreas, stomach, and duodenum normal.

In the liver, no necrosis could be made out in gross. The organ seemed a little larger than normally. Kidneys swollen and pale.

Liver sections correspond exactly to the preceding case (105-a). The lungs show great congestion of the alveolar walls, with an exudate of polymorphonuclear cells (interstitial type of pneumonia).

Pup 105-c.—May 12. Pup evidently quite sick with distemper. Ether anesthesia.

Autopsy at once. Heart, spleen, pancreas, and stomach normal. The lungs showed small purple patches of bronchopneumonia. Liver and kidneys rather pale.

Liver sections show a few areas of focal necrosis involving only a few liver cells, having, however, no regular distribution. Polymorphonuclear leucocytes numerous in the portal tissues. Nests of blood-forming cells inconspicuous, but polymorphonuclear leucocytes quite numerous in the venules. Fat stains show extensive deposit in all parts of the liver lobules, both large and small fat droplets. The lungs show the picture of an interstitial pneumonia.

Pup 105-d.—May 13. Found dead. The general picture resembles that described in pup 105-c.

On section, the liver shows no focal necrosis and less fatty degeneration. Nests of blood-forming cells numerous and of the usual type. Lung sections practically identical with the preceding cases. Other tissues negative.

Pup 108-a.—Strong and active male, weight 4½ lbs., seven weeks old.

June 22. Chloroform anesthesia for two hours; ⅔ oz. given. Anesthetic well taken.

June 23. Pup did not seem badly poisoned, but was not as active as another pup of the same litter.

June 24. Definite loss of weight. Bleeding free from small ear pricks. Bleeding time about five minutes. Operation in the usual way through the right rectus, under ether anesthesia. A small wedge-shaped piece of liver was removed. There was considerable bleeding at the time of operation, but blood clots were not very soft and were sufficient to check the bleeding after some minutes.

Microscopical sections show the usual hyaline liver necrosis involving about one half of each lobule. The middle zone shows a marked deposit of fat. Wandering cells numerous. Mitotic figures present in the liver cells.

June 25. Pup rather sick and drank water only.

June 28. No gain in weight. Appetite poor.

June 30. Appetite improving. Ether anesthesia and bleeding from the carotid.

Autopsy at once. The liver incision had healed perfectly with a few adhesions. Thorax, heart, lungs normal. Thymus small, pale, and flabby. Spleen, pancreas, and stomach normal. The intestines contained numbers of round worms. Kidneys and adrenals normal. Liver very pale, but lobulation not very conspicuous. Tissue very translucent. No gross evidence of necrosis.

Liver sections show almost complete repair with only a few wandering cells in the centers of the lobules and an occasional hyaline mass surrounded by phagocytes, the remains of necrotic tissue. Fat stains show numerous droplets in all parts of the lobule, and the fat deposit is decidedly conspicuous in every liver cell. Thymus atrophic. Kidneys, heart, and pancreas normal. The spleen shows very little evidence of blood formation, with only occasional bone-marrow giant cells.

Several other pups, one to three months of age, were given anesthesia with the production of the usual central liver necrosis. These young animals were often badly poisoned by a single chloroform anesthesia and, as a rule, seemed to be less resistant than the average adult.

SUMMARY.

Employing the liver necrosis as an index, we find that pups are immune to the poisonous action of chloroform anesthesia. This immunity or resistance to late chloroform poisoning is complete in the first week, very striking during the second and third weeks, and usually disappears during the fourth week of life.

Nests of blood-forming cells (blood islands) are numerous in the sinuses of the liver during the first week and normally become progressively less numerous each week until the liver is almost free from these cells at the end of the fourth week of life.

It is considered possible that these leucocytes in the blood islands protect the liver against the specific action of a known poison (chloroform). The mechanism of this hypothetical protective action is not understood, but it may consist of a process of neutralization. Perhaps this protective action against poisons is an important part of the functions of white blood cells and may bear an important relationship to the process of inflammation.