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THE UNIVERSITY OF MINNESOTA

GRADUATE SCHOOL

Report

of

Committee on Thesis

The undersigned, acting as a Committee of the Graduate School, have read the accompanying thesis submitted by Emily Helen Payne for the degree of Master of Arts. They approve it as a thesis meeting the requirements of the Graduate School of the University of Minnesota, and recommend that it be accepted in partial fulfillment of the requirements for the degree of Master of Arts.

Wel Downey. Chairman

E. T. Bell

Richard E. Scammon

May 9th, 1918

THE UNIVERSITY OF MINNESOTA

GRADUATE SCHOOL

Report

of

Committee on Examination

This is to certify that we the undersigned, as a committee of the Graduate School, have given Emily Helen Payne final oral examination for the degree of Master of Arts. We recommend that the degree of Master of Arts be conferred upon the candidate.

Minneapolis, Minnesota

May 31, 1918

Hal Downey, Chairman

Richard E. Scammon

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The Omentum Of the Rabbit With Special Reference To the Origin and Structure of Plasma Cells.

A Thesis

Presented to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the Degree of Master of Arts.

by

Emily Helen Payne

June 1918.

Foreword

The following investigation was carried on under the direction of Professor Hal Downey, to whom I wish to express my sincere thanks for his helpful suggestions thruout the work.

Altho an enormous amount of work has been done on plasma cells, a survey of the literature shows that they have been studied almost exclusively either in pathologic human material or in animals under experimental conditions. Comparatively few studies have been made of plasma cells in normal animals. However, Maximow states that plasma cells are found in all normal warm blooded animals, and that they are especially abundant in certain definite regions. Also Downey ('09) described and figured them and their development from lymphocytes in the lympho-renal tissue of Polyodon, and again in 1911, ( ) gave a detailed account of their origin and structure in various other cold blooded vertebrates. Other workers have mentioned the presence of plasma cells in the omentum, bone marrow, spleen, lymph nodes, and submaxillary gland, as well as in the digestive tract of normal animals. But most of these investigators have only incidentally touched on plasma cells. The majority of the detailed accounts of these cells have been taken from pathologic and experimental material.

The omentum has long been considered an organ of great potential and protective powers. Ranvier and Weidenreich have described it as a greatly flattened lymph gland. Other authors have noted the development of blood cells in the omentum of the foetus and newborn animals, (Marchand, Schwartz, Pardi), and Schott, Downey, Weidenreich, Maximow, and Cornil have proved it to be a source of the free cells of the body cavity. But that the omentum of the rabbit is an easily obtained and most satisfactory source for the study of all types of lymphoid cells, particularly of plasma cells, has not been sufficiently appreciated, although Schwarz, Jolly, Dominici, and others have shown that the omentum of the rabbit contained numerous plasma cells. Also the rabbit was known to be a very lymphoid animal, and the omentum was known to contain not only all forms of lymphocytes but also various types of connective tissue cells.

Because these were the cells from which various authors had derived plasma cells, and because numerous plasma cells were said to be present even in normal animals, I chose the omentum of the rabbit for study. I found on investigation that plasma cells were even more numerous than I had anticipated. They were found lying along the large vessels, in the midst of capillary networks, in the center and at the periphery of tâches laiteuses, and scattered individually or in small groups, thruout the rest of the omentum. They were most numerous in the neighborhood of the vessels, but were occasionally found in the pale nonvascular connective tissue portions of the omentum. The larger nonvascular tâches laiteuses contained great numbers of them.

Just what constitutes a plasma cell continues to be a matter of debate. There are two main theories concerning the structure of a plasma cell. One group of workers headed by Unna and his followers holds the presence of strongly basophilic, amorphous granoplasm to be the chief characteristic of a plasma cell and include as such, round, irregular, or even spindle-shaped cells with a pale oval nucleus somewhat resembling that of a fibroblast, providing those cells have the characteristic basophilic granoplasm.

Others hold that the Marschalko type of cell is the only true plasma cell. It has a round and eccentric nucleus with its chromatin massed in several blocks which are chiefly in contact with the nuclear membrane, forming the so-called 'radkern'. At one side of the nucleus, towards the center of the cell, is a light space. The cell body is usually round or oval and must contain the densely basophilic granoplasm described by Unna.

That the Marschalko type represents the typical fully developed plasma cell is the view most prevalent today. However, Downey, Schwarz, Weidenreich, Maximow, and others have shown that there are other cells present in normal animals which, altho they differ from both of the above types, must be included with the plasma cells. Their cell bodies may be round, oval, or irregular in outline, sometimes bearing many pseudopodia. Their nuclei may resemble those of any of the lymphoid or connective tissue cells, but they are usually eccentrically placed and there is a clear 'Hof' or space at one side of the nucleus. The cytoplasm stains densely with basic aniline dyes.

The main theories concerning the morphology of plasma cells coincide with the chief views regarding their origin. Those who hold Unna's view as to the structure of these cells stand for a direct development from connective tissue cells (fibroblastic-perithelial cells), while those who consider the Marschalko type of cell the true plasma cell derive them from lymphocytes.

Those who uphold the lymphocytic origin of plasma cells are also divided in their views. Some hold that histogenous lymphocytes are the chief source of plasma cells, while others derive them from haematogenous lymphocytes. Still others hold that plasma cells can arise from many sources: from connective tissue cells (fibroblasts-perithelial cells, clasmatocytes) and from lymphocytes (small and large lymphocytes and large mononuclears). The nuclei in these cells necessarily differ a good deal, but their cytoplasm may be identical with that of the Marschalko type of cell.

The majority of plasma cells in the omentum of the rabbit contain a nucleus similar to that found in a small lymphocyte, and their cell outlines are very varied in shape.

Even a brief study of the omentum of the rabbit showed that the Marschalko type of plasma cell only rarely occurs. But to work out in detail the structure and origin of the plasma cells necessitated a rather extensive study of the omentum in general, and of the lymphoid areas (perivascular infiltrations and tâches laiteuses of Ranvier) in particular.

For this purpose I secured the omentum from animals of the following ages: 1 day, 3 day, 5 days, 10 days, 5 weeks, 8 weeks, 10 weeks, half grown, and adult. It proved to be not only a satisfactory place for the study of plasma cells but also showed the complete development of tâches laiteuses. For this reason I shall divide my paper into two parts. The first will consist of a general description of the omentum of the rabbit at different ages and under different experimental conditions, with special reference to the development and composition of the tâches laiteuses. The second part will deal primarily with the origin, structure, and distribution of plasma cells.

Methods and Materials.

In this investigation both whole preparations and sections of the omentum were studied. Instead of stretching the omentum over test tube tops in the usual way (Maximow), I found the following method much more satisfactory: rings of any desired size, usually the size of the cover slip to be used in mounting, were cut out of filter paper. These were slipped under the omentum and the tissue quickly cut out, care being taken to have the whole edge of the filter paper ring in contact with the omentum before cutting. The quickness with which this operation could be completed minimized the risk of drying and ensured good fixation. The omentum was cut from the filter paper while in xylol just previous to mounting.

Because the omentum of the young animal was too small and thin to be conveniently handled in the above way or by Maximow's method, small pieces were cut out and spread flat on cover glasses. Forty-five minutes in Helly's solution was sufficient fixation for these pieces.

The omentum from the older animals was fixed one hour in Helly's fluid (Zenker with 10% commercial formalin in place of glacial acetic acid) or two hours in absolute alcohol. Since the best results were obtained with Helly's mixture it was used almost exclusively. When foreign bodies had been introduced, they and the adhering omentum were fixed in cold Helly's fluid for five hours.

In staining the preparations, Pappenheim's methyl green pyronin, Ziehl's carbol fuchsin, May-Giemsa, Benda's iron haematoxylin, Dominici, and a combination of Ehrlich's triacid and toludin blue were used. Unna's methyl green pyronin following zinc chloride fixation was tried, but no satisfactory results were obtained. Pappenheim's methyl green pyronin gave the best and most useful results for my study as it brought out plasma cells and lymphocytes very clearly and left the 'mesothelium' and underlying tissue quite transparent. After one half hour in the stain, preparations were washed in distilled water, differentiated in 95% alcohol, and dehydrated in absolute alcohol. This was found more dependable than differentiation and dehydration in acetone.

Methyl green pyronin was not so satisfactory a stain for the omenta of the youngest animals because of the small numbers of lymphoid cells present.

When May-Giemsa was used, the preparations were placed in acetic acid (3 drops to 25 cc. of distilled water) for 10 minutes, stained 1 1/2 minutes in May Grünwald (1cc. of dye to 1cc. of distilled water) and 1 hour in Giemsa (1 drop of stain to 1 each cc. of distilled water). It was then differentiated in dilute acetic, and dehydrated in acetone.

The omenta of various animals have been studied by Klein, Ranvier, Renaut, Marchand, Goldman, and others, and the omentum of the rabbit has been investigated by Klein, Schwarz, Jolly, and Dominici.

Klein considered the omentum of the rabbit the most instructive and simple object for the investigation of the cellular elements, because it is flat, and for the most part, very slightly fenestrated compared with that of the guinea pig, dog, cat, and monkey. He finds that in the omenta of full grown animals, there occur richly distributed opaque tracts of lymphoid cells, forming a network. Besides these there also exist smaller patches situated laterally to these tracts, as well as more isolated ones. In the young animal the network of opaque tracts is less developed than the isolated patches. The isolated small patches are more numerous in the younger animals. They are larger in the older ones, and the tracts more confluent. Klein concludes from this that in the omentum there is a continuous growth of opaque patches which, by growing in length and coalescing in the direction of their long axis, form tracts. He also states that from their topographical arrangement the lymph nodules and tracts are the anlagen of the fat tissue of the omentum.

Dominici describes the omentum as composed largely of two plasmodia. One forms the surface covering and the other is in the deeper portions of the membrane, and is found especially in the neighborhood of the tâches laiteuses. Besides these plasmodia, the omentum contains fibers, endothelial cells of the capillaries, perivascular cells, vasoformative cells, and rounded free "primitive" cells. The small round cells predominate in the tâches laiteuses. Dominici is unable to find any great differences between them and plasma cells.

Schwarz, studying fresh preparations of the omentum, finds in the neighborhood of the vessels, clearly distinguished white flecks which are usually oval and macroscopic in size. They are scattered very irregularly over the omentum, and range from only a few cells up to patches 2-3 mm. in length. In the newborn rabbit he finds large vessels surrounded by thick adventitial sheaths. Running parallel with these are spindle-shaped connective tissue cells with numerous wandering cells among them.

Observations.

Apart from the thickenings due to the accumulations of fat and the presence of large blood vessels, the surface of the omentum of the normal adult rabbit is unusually flat and only slightly fenestrated. In the youngest animals, perforations are very small and infrequent. In animals 5-7 weeks old the perforations have increased in number and many of them have lost the even outline which they had in the younger animals. In some perforations we find one or more large partially attached cells extending into the opening, while in others the cell, or cells, which may be greatly elongated are attached at either side of the perforation, thus forming a bridge-like strand. These 'strands' may be narrow and smooth in outline, or they may show one or more partially attached cells clinging to their sides. These cells and sometimes the whole 'strand', seem to be separating from the surrounding tissue. If they should pull themselves free, it would leave the perforation larger than before, or one large opening would take the place of two smaller ones. Similar conditions are not infrequent in the omenta of full-grown rabbits, and they may indicate the way in which the omentum becomes fenestrated.

The separation of the cells, or strands of cells, from the surrounding syncytium may be due to the activity of the cells themselves, or it may be merely a wearing off process, resulting from the friction produced by the rubbing of the omentum over the internal organs.

Few or no perforations are present in the omentum of a newborn rabbit, but their number and size increase with the age of the animal.

From the observations described above, I conclude that the perforations have been formed by the separation of individual cells or groups of cells from the surrounding syncytium, and that their increase in size is due to the subsequent stretching and widening of the openings resulting from the growth of the omentum. The continued liberation of cells from the margins of the openings is another factor determining the increase in size of the perforations, particularly of the smaller ones.

Altho the perforations in the omentum of the adult are larger and more numerous than those of the young animals, they are still comparatively small and inconspicuous. Large openings are found occasionally in the nonvascular fibrous parts of the omentum.

but, even here, the tissue seldom forms a true network as it does in the case of the cat, dog, gopher, monkey, and man. Klein noted the true fenestrated appearance of the omentum of the cat, dog, and monkey, and it is well known that the human omentum is an open net. In order that I might understand the omentum of the rabbit more clearly, a study was made of the omenta of various animals. They consisted of a true net in the case of the cat, dog, and gopher.

The omentum of the adult rabbit is also characterized by elongated outgrowths, 1-3 cells wide (fig. 5) which arch over the surface in the form of a bridge. Usually both ends of the 'bridge' are attached to the omentum, but sometimes one end may lie free in the body cavity. Occasionally these bridges assume enormous dimensions and fantastic shapes (fig. 2a).They are composed of masses of basophilic fibroblasts, some of which seem to have pulled themselves free from the surrounding tissue. They may or may not contain blood vessels. Other growths are seen which appear to be great thickenings or ridges projecting from the surface of the omentum. They are composed of basophilic fibroblasts surrounding free basophilic lymphoid cells. Many of the cells contain two nuclei, and transitions are seen from the fixed surface cells to the smaller inner free cells.

The blood vessels ramifying thru the omentum break up into loose networks (fig. 1a) or branching capillary tufts (fig. 1b). Sometimes practically every arteriole in the preparation will end in a spreading tuft or ball of capillaries. These capillaries converge to form a venule which leaves the field along with the corresponding artery. There are sometimes as many as 20-30 capillary tufts in a preparation an inch square.

Both surfaces of the omentum are composed of large, flat, protoplasmic cells having large, pale, oval nuclei. According to the usual conception these cells are combined to form a simple pavement epithelium (mesothelium of Minot) which covers the underlying tissue composed largely of fibers and fibroblasts. This 'mesothelium' is particularly evident in the familiar silver nitrate preparations, but when other methods are used it is difficult to demonstrate anything like a continuous epithelium on the surface of the organ. Weidenreich, Schott, Cornil,etc.have concluded that the surface of the organ is made up of cells which are identical, excepting for size, with those of the underlying connective tissue. The latter is composed of fibroblasts, the slender processes of which anastomose with one another forming a veritable network. Some of the fibroblasts are long and slender; others are broad and flat, closely resembling the covering cells. Scattered among them are numerous free cells of all types (clasmatocytes, lymphocytes, plasma cells, eosinophils, and, occasionally, a special cell). The free cells are not evenly distributed but are found concentrated along the blood vessels and in the tâches laiteuses. Large areas of the omentum may be composed almost wholly of connective tissue cells and fibers.

The larger blood vessels of the omentum are usually surrounded by fat, or a dense sheath of fibroblasts, but the smaller ones are accompanied by a body guard of perithelial cells (Marchand Herzog-). Surrounding the perithelial cells and sometimes completely obscuring them are numerous lymphoid cells. Altho all types of lymphocytes are usually found, these aggregations may be composed almost exclusively of small lymphocytes or plasma cells. The cells of such an aggregation may proliferate to form a definite nodule or tâches laiteuses.

In the adult rabbit the milky flecks, or tâches laiteuses of Ranvier, may be divided into three types:

1) definite patches in close association with the vessels. They are composed almost wholly of lymphoid cells.

2) less distinct patches composed of lymphocytes and fibroblasts. These are usually found in nonvascular areas but may be associated with capillaries.

3) tâches laiteuses ranging from the smallest to the largest forms, composed of 'mesothelial' covering cells, both fixed and free, and all types of lymphoid cells. Spindle-shaped fibroblasts and clasmatocytes may also be present. In the first type, the patches may be in the form of definite nodules, or they may be more diffuse and elongated, resembling the lymphoid sheaths.

These nodules are sometimes very thick and they may project as great masses from the ends or sides of the vessels. They may be found anywhere along a vessel or surrounding it. Usually they occur where a vessel branches (fig.1,c) or they are imbedded in a tuft of capillaries (fig.1,d).

The small vascular tâches laiteuses are composed chiefly of small lymphocytes. The larger ones consist of a core of small lymphocytes, surrounded by larger lymphocytes, large mononuclears, and plasma cells, with a few small lymphocytes and large mononuclears intermingled.

Type two consists of less distinct patches, which may be in the vicinity of the capillaries but are more often found in the nonvascular parts (fig.1). They are composed of lymphocytes and fibroblasts and all intermediate forms are found between the fixed and the free cells. The surrounding connective tissue is slightly basophilic. The fibroblasts appear very active. Some of them are attached by only one slender process, while others are entirely free.

In slightly larger patches, larger, more basophilic lymphocytes and plasma cells are found. These may be scattered indiscriminately among the smaller lymphocytes, or they may form a wide border about the smaller cells, almost obscuring the active fibroblasts. If vessels are present, the larger tâches laiteuses may resemble those just described under type one.

The majority of tâches laiteuses are of the third type. They vary greatly in size, form, and contents; but slightly basophilic 'mesothelial' cells, both fixed and free, are always present. In some cases these make up the entire milky fleck. The latter may consist of only a few cells (4-10), or they may cover the entire field as seen with low power. In other cases, particularly the larger tâches laiteuses, the 'mesothelial' covering cells merely surround a basophilic patch of small lymphoid cells. These covering cells hang from the lymphoid patches like bunches of grapes and give a characteristic scalloped appearance to the tâches laiteuses.

Summary

1) The omentum of the adult rabbit is characterized by small infrequent perforations, elongated outgrowths (fig.2,3) and great thickenings or ridges containing many free lymphoid cells which stain densely with basic anilin dyes (fig.2,b).

2) The blood vessels of the omentum terminate in loose network (fig.1,a) or branching capillary tufts (fig.1,b).

3) Both surfaces of the omentum are composed of large, flat, protoplasmic cells having large, pale, oval nuclei. These cells are identical, excepting for size, with those of the underlying tissue

(Weidenreich, Schott, Cornil, etc.).

4) Besides the surface and underlying fibroblasts, the omentum also contains clasmatocytes, lymphocytes, plasma cells, eosinophils, and occasionally a special cell. Plasma cells and the other lymphoid cells are extremely abundant.

5) The lymphoid cells are not evenly distributed thruout the omentum but are concentrated along the blood vessels and in the tâches laiteuses.

The Omenta of Newborn and Young Rabbits.

Unlike the omentum of the adult rabbit, the omentum of the newborn animal can hardly be called a lymphoid organ. It is small and thin, and is composed almost entirely of connective tissue cells. It proved to be beautiful material for the observance of developing capillaries, but was of little use in the study of plasma cells or tâches laiteuses.

The omenta of five newborn rabbits from different litters were examined. They contained a few large and small lymphocytes but no plasma cells, and no tâches laiteuses were present. Many mitotic figures were seen in both the small and the large lymphocytes, but there was no clue as to the source of these cells. Over small areas the surface cells were slightly basophilic and the cells appeared to be separating from the surrounding tissue. The rest of the preparation consisted almost wholly of pale, flat connective tissue cells. One small patch was present which appeared to be a developing tâches laiteuses. On close observation, however, this proved to be only a dense network of capillaries. The endothelial cells of the vessels were very basophilic, and as the capillary network was very closely woven, the area resembled a tâches laiteuses. However no free cells were present, and the connective tissue between the capillaries showed no special activity.

The omentum from an animal 5 weeks old was literally covered with small lymphoid patches. They ranged from those consisting of only a few pale cells (2-6) up to fairly well developed tâches laiteuses. The smaller patches consisted only of partially free surface cells. Slightly larger patches were composed of a few large lymphocytes and larger lymphoid cells in the central portion, and partially free surface cells at the periphery (fig. 17). The largest tâches laiteuses contained many free lymphocytes of all sizes in the center, larger paler lymphoid cells farther out, and at the periphery the same partially free and attached surface cells. All of these patches contained many mitotic figures. The tâches laiteuses were very irregular in shape and seemed to have sprung up anywhere from the pale surface of the omentum.

A few of the larger patches contained capillaries but the majority of them occurred in the non-vascular parts. Only a small number of plasma cells were seen and very few lymphoid cells were present outside of the tâches laiteuses. The endothelial cells of the capillaries were extremely basophilic and active.

Preparations from a 7 week rabbit showed an enormous number of small blood vessels terminating in a particularly dense capillary network. The endothelial cells were extremely large and basophilic, and numerous mitotic figures were seen in them. Many blind endothelial sprouts were present, showing that vascularization of the omentum was still going on.

In this animal the tâches laiteuses ,which in the 5 week omentum were isolated, had grown in length and fused with one another to form a network composed of strands of lymphoid cells.

Most of the cells of these strands were of the type of large, pale mononuclear macrophags, but some small and large lymphocytes were also present. On the surface of these patches the 'mesothelial'cells were rounding off and pulling themselves free.

Evidently the tâches laiteuses were being formed in the same manner as those of the 5 week rabbit, only here the activity on the part of the surface cells was more widespread, and differentiation was less rapid. The patches, altho larger and more confluent than those of the 5 week rabbit, were younger and less mature, and none of them showed the central core of lymphocytes so characteristic of the older tâches laiteuses. However, nearly all of the patches and lymphoid strands contained a few blood vessels. In some the capillary network was extremely dense. As many of the capillaries ended blindly, they had probably but recently grown in, and their development was not yet complete.

Only four plasma cells were found in the preparation of the 7 week old rabbit, but lymphocytes were numerous both within and between the vessels. Free and partially free surface cells were very common, the cutting-off process being particularly active over the lymphoid strands. The preparations of omentum from a 10 week old rabbit contained relatively fewer vessels. One contained two or three large strands of lymphoid cells. Many of the cells of these lymphoid masses were related to typical fibroblasts rather than to the large, flat surface cells. The overlying surface lacked the characteristic knobular appearance due to the usual freeing of these large surface cells. The larger tracts contained a very dense capillary network, but the smaller patches contained few or no blood vessels. A few typical plasma cells were present in the tâches laiteuses.

Another preparation showed the typical formation of small lymphoid patches or nodules from the surface cells, but no large patches or tracts were present.

It is interesting to note that here the majority of the tâches laiteuses contained a loose capillary network, but they were in all cases the larger patches. One rather small patch was seen with but one vessel entering it. Within the patch the vessel broke up into a loose network of capillaries which ended blindly. There was no efferent vessel present. Other small patches were present which contained no blood vessels. In one case an endothelial sprout was seen reaching almost to a tâches laiteuse. Evidently the capillary was either just growing in, or its former connection with the patch had been severed owing to retrogressive changes. However, there was no evidence of the latter, for neither the endothelial cells of the capillaries, nor the contained blood cells showed any signs of degeneration, and the cells of the surrounding tissue contained no phagocytosed products which might have been the remains of dead cells.

No tâches laiteuses were found in the newborn. The majority of those present in young animals were without vessels, and they were being built up from the connective tissue in the nonvascular portions of the omentum. The older the animal the greater were the number of tâches laiteuses which contained blood vessels.

In the full grown animal the large lymphoid patches and strands (fig. 1 and a) almost invariably contained blood vessels. But the smaller immature patches were often totally free from them. One frequently finds large numbers of such patches in various stages of development, out in the nonvascular parts of the adult omentum. Therefore, it seems most reasonable to believe that as a rule, the lymphoid patches or tâches laiteuses, develop first (Klein) and that the vessels grow in afterwards. However, this may not always be the case, for it is difficult to see why the presence of vessels should prevent the formation of tâches laiteuses from the neighboring surface cells. However, there is no doubt that this is the exception and not the rule in both young and old animals. The majority of the tâches laiteuses were formed from the connective tissue in the nonvascular parts and had, therefore, no special relation to the blood vessels. When capillaries are present, they have usually grown in after the development of the tâches laiteuses has begun. Perhaps the activity on the part of the connective tissue cells was the immediate cause of their growth.

Goldmann finds that nonvascular tâches laiteuses are quite common in young animals, but he thinks that they were all supplied with blood vessels at one time. He explains this by saying that in the newly born animal the omentum is supplied with an uncommonly dense capillary plexus, which retrogresses with further development. From this primitive transitory plexus a secondary definite one arises. In the newly born all the tâches laiteuses are attached to blood vessels, but in the young some of them remain behind after retrogression of the capillaries. Goldmann worked on the mouse and the rat.

In the rabbit I find no tâches laiteuses in the omentum of the new born. One occasionally sees a small patch which looks like a tâches laiteuses, but it proves on closer observation to be nothing but a group of capillaries buried by basophilic endothelial cells. Free lymphoid cells are seldom seen in these areas, and they cannot be considered true tâches laiteuses of Ranvier. They are not accumulations of free lymphoid cells, and they do not appear white and opaque in the fresh omentum as the true milky patches do.

Summary

1) The omentum of the 1-5 day old rabbit is much thinner, and less fenestrated, than that of the adult animal. It contains a few lymphocytes, but no plasma cells, and no tâches laiteuses were present.

2) Plasma cells were first seen in the omentum of the 10 days old rabbit. Lymphocytes were numerous thruout a small area, and the preparation contained what might be called a small tâche~~s~~ laiteuse~~s~~.

3) The omentum of the 5 week old rabbit contained an enormous number of small developing tâches laiteuses. The smaller patches were found almost exclusively in the nonvascular portions of the omentum but a few of the larger ones contained blood vessels. Only a small number of plasma cells were seen and very few lymphocytes occurred outside of the tâches laiteuses.

4) The preparation from a 7 week old animal showed an enormous number of developing blood vessels. The tâches laiteuses which in the omentum of a 5 week old rabbit, were isolated, had grown in length and fused to form a network of lymphoid strands. Four plasma cells occurred, and numerous lymphocytes were present in the strands, as well as in the included blood vessels.

The omenta from the 10 week rabbits contained relatively fewer blood vessels than that of the 7 week old rabbit. Those present terminated in an extremely dense network of capillaries, surrounded by numerous free lymphocytes and some plasma cells.

Small developing tâches laiteuses were most numerous in the omentum of animals 5-7 weeks old. A study of the omenta from those animals, showed clearly that the majority of the tâches laiteuses are formed from the connective tissue in the nonvascular parts, and have, therefore, no special relation to the blood vessels. Where capillaries are present, they have usually grown in after the development of the tâches laiteuses has begun.

The Omentum of the Rabbit under Experimental Conditions.

The effects of the irritation caused by bringing the omentum in contact with a foreign body were next studied. For this purpose two small pieces of sponge were placed in the body cavity in contact with the omentum five days previous to the removal of the organ. Sections of the foreign body and adhering omentum were studied and also whole preparations of the omentum.

The tissue immediately surrounding the foreign bodies was very dense, thick, and vascular. The surface cells were rounding off and pulling themselves free. Everywhere surrounding the vessels were great hordes of plasma cells and other lymphoid cells.

That part of the omentum located some distance from the foreign bodies showed no great numbers of plasma cells. The latter were either free in the tissues or contained in definite tâches laiteuses. Out in the nonvascular, open part of the omentum, the connective tissue was thick and fibrous. Scattered thru the pale areas were many accumulations of basophilic fibroblasts and smaller lymphocytes. In the larger patches large lymphocytes and plasma cells were also seen. Many of the fibroblasts were pulling themselves free, and all transition forms were seen from the fibroblast to the smaller lymphoid cells. Here as in the 10 week old rabbit, it was the spindle-shaped fibroblasts and not the large pale surface cells which were forming the tâches laiteuses. A study of the omentum in such places will explain the reason for this.

The omentum of the experimental animal was very tough and fibrous, and it also contained many large perforations. Over large areas the 'mesothelial' cells appeared stretched out lengthwise until they were very narrow and crowded. Their flat branches appeared pulled out in one thickened process. In other places the omentum was made up entirely of typical fibroblasts. No large flat 'mesothelial' cells were seen with the most careful focusing. In these areas the surface of the organ was, therefore, composed of typical fibroblasts in place of the usual large, flat, 'mesothelial' cells.

Weidenreich, Schott, and Cornil have shown that there is no essential difference between the underlying fibroblasts and the large flat surface cells. When worn off or detached to form the cells of the serous cavity, these may be readily replaced by the underlying fibroblasts. These fibroblasts may change their characters to such an extent that they become 'mesothelial' cells, or they may keep their fibroblastic structure.

Summary

1) The tissue of the omentum immediately surrounding the foreign bodies was very thick, and vascular, and dense, and contained great numbers of plasma cells and other lymphoid cells. The surface cells were rounding off and separating from the underlying tissue.

2) The omentum located some distance from the foreign bodies was more perforated and less vascular than that of the normal animal. The tissue was very fibrous and contained no great numbers of plasma cells. Numerous small tâches laiteuses were developing from underlying fibroblasts.

to be considered chiefly as lymphatic elements.

Renaut divides the tâches laiteuses into two kinds: 1) primary, which are associated with blood vessels, and, 2) secondary, which occur in the nonvascular parts of the omentum. The latter type ultimately develop into islands of fat cells. Both the vascular and nonvascular tâches laiteuses are composed for the most part of "rhagiocrine cells" and their derivatives. He derives the rhagiocrine cells from lymphocytes which have left their respective lymph and blood vessels, and entered the serous membrane, where they accumulate in large numbers as tâches laiteuses. These cells have a glandular function. Later they may form the fixed connective tissue cells of the omentum, and loose their glandular function. In short, the rhagiocrine cells of the tâches laiteuses furnish the bulk of the free and fixed connective tissue cells of the omentum, and also a large portion of the free cells of the body cavity.

Jolly describes the tâches laiteuses as miniature lymph glands, built up thru a setting together of lymph cells, which probably originate in loco. Mitotic figures are frequent in the lymph cells. Typical plasma cells also occur which originate thru protoplasmic differentiation of the lymphocytes.

According to Marchand, the tâches laiteuses are composed of large round or polygonal cells which resemble large mononuclear leucocytes. He finds all transitions from these cells to the long stretched-out forms. (Marchand's adventitial cells or clasmatocytes) The tâches laiteuses originate from layers of elongated clasmatocytes.

This is contrary to Schwarz, who can nowhere find tâches laiteuses developing from clasmatocytes. He derives them from leucocytoid mononuclear wandering cells, which continue to furnish

The Tâches Laiteuses of Ranvier.

In the vascular and nonvascular parts of the fresh omentum one sees macroscopic white flecks scattered irregularly over the surface. They may consist of only a few cells or they may be 2-3 mm. in size (Schwarz).

These flecks were first mentioned by Recklinghausen. He describes them in the omentum of the rabbit as "weissliche Flecken, die eine sehr dichte Anhäufung von Bindegewebskörpern in den verschiedensten Formen zeigen. Einzelne sind sehr gross, matt, spindelförmig oder etwas ramifiziert, andere rundlich, aber ebenfalls gross, andere klein, glänzend und den Lymphkörperchen ähnlich."

The flecks were next described by Ranvier, who named them "tâches laiteuses". According to him they make their appearance in animals 4-5 days old. They are composed of vasoformative cells, closely surrounded by numerous lymphocytes, and strongly branched connective tissue cells similar to those found in the remaining portions of the omentum.

Contrary to Ranvier, Francois holds that the tâches laiteuses are present in the newborn. They originate thru the close approximation of ramified connective tissue cells, which later assume a polygonal shape. The protoplasm of these cells becomes roughly granulated and vacuolated, and it may contain foreign material. The nuclei can round themselves off and binucleated cells may appear. Francois thinks the milchflecken are concerned with the vessel building and probably also with fat formation.

According to Spuler the tâches laiteuses build themselves up from young mesenchyme cells, which develop partly into connective tissue cells and partly into vessel cells. However, the latter are leucocytoid mononuclear cells. Schwarz notes that the tâches laiteuses of the adult differ from those of the young animal in the absence of sharply marked out boundaries. The older ones blend off gradually into the surrounding tissue.

Schott finds lymphocytes more or less abundant in every tâche laiteuse. These elements, for the most part, differentiate into large mononuclear macrophags, but may also furnish small lymphocytes. The macrophags may also develop from the fixed connective tissue cells. He sees no essential difference between the free elements of the tâches laiteuses and the surrounding fixed connective tissue cells. They are all genetically connected and belong to the same cell species.

Goldman accepts Renaut's classification of the tâches laiteuses. He finds in the nonvascular portions of the omentum small cell masses which act as tho they were gradually detaching themselves. These secondary tâches laiteuses take no active part in the function of the omentum in the adult animal, whereas the 'primary' ones do. Nothing could be more variable than the structure of these tâches laiteuses under manifold normal and pathologic conditions. At times they resemble perfect small "secondary nodules" with well defined inner and outer zones. Unlike the germinal centers and follicles of a lymph nodule, the small cells are central and large ones peripheral.

Only the outer zone takes the vital stain. Besides the various types of large and small lymphocytes, Goldman finds the tâches laiteuses composed of a framework of branched connective tissue cells. However, contrary to Schott, Maximow, Weidenreich, and Cornil, he declares that there is an essential difference between the lymphocytes and the neighboring connective tissue cells. They do not belong to the same cell species.

Observations

It is important to note that in the omentum, as well as in the other lymphoid organs, the development of the lymphoid patches or nodules is closely associated with changes in the connective tissue. Downey and Weidenreich have shown that the cells of the reticular tissue of the lymph nodes and spleen round off and pull in their processes, to form free lymphoid cells. This process is most prevalent in certain definite areas. These areas may be located in the center of the follicles (germ centers), or at the periphery of the follicles, as in the lymph nodes of the mole and bat (Downey and Weidenreich). The cells thus formed may divide and redivide by mitosis to form the free cells of the lymph nodules and interfollicular tissue. Therefore, the free cells of the follicles and interfollicular tissue of the lymph nodes and spleen have originated from either the fixed connective tissue cells (reticular cells) or from their derivitives. The same thing was found to be true for the free cells of the tâches laiteuses or lymphoid nodules of the omentum.

The Development of the Milky Flecks or Tâches Laiteuses.

The tâches laiteuses of the omentum of the rabbit may develop in two different ways, i.e., by a freeing and subsequent proliferation of (a) the 'mesothelial' covering cells of the omentum and (b) the spindle-shaped fibroblasts, or by a combination of both. Their formation from the large pale 'mesothelial' cells occurs in both young and old animals, and it is extremely common in rabbits 5-7 weeks old.

The so-called 'mesothelial' cells are large, flat, branched protoplasmic cells covering both surfaces of the omentum. Their nuclei are large, pale, and oval, with the chromatin in evenly distributed granular masses. The nuclear membrane is thin and indistinct.

The tâches laiteuses originate as small masses of these surface cells which have taken on a slight basophilic tone. These sometimes appeared fully attached, but on close observation a slight separation of these cells from the surrounding tissue was usually noticeable. The nuclei were still identical with those found in the pale inactive surface cells. Other, perhaps larger masses, were seen, composed of more rounded cells which, on account of their spherical form, projected above the general surface of the organ. Some of these cells were nearly free, but were still attached to their neighbors by delicate cytoplasmic threads. (fig.) The rounded bodies of the other cells were attached by only one stalk-like process. Their cytoplasm was decidedly basophilic and, as compared with the surrounding fully attached cells, their nuclei were slightly smaller and denser, and the nuclear membrane was more distinct. The chromatin masses, which were still evenly distributed thruout the nucleus, were fewer and larger.

More distinct patches occurred which consisted of a few large, comparatively pale, free cells in the center, surrounded by partially attached cells resembling those just described (fig. 17). Excepting for their rounded contour, some of the free cells were identical in structure with the surrounding attached cells. But the cytoplasm of many of them was darker, and their nuclei were frequently smaller, denser, and more rounded than those of the attached cells; while the nuclei of others were pale and indented. Next, larger patches containing a central core of typical large and small lymphocytes were seen. These cells have originated from surface cells either directly or via the large mononuclear cells, thru division and differentiation. All intermediate stages were seen between these patches and the large definite ones illustrated in figs.(2 and 3) There were no definite boundaries to these patches. Their peripheral portion blended with the surrounding tissue. There we find the same large, pale, fixed, surface cells that are present everywhere in the omentum. At the edge of the patch these same cells were seen to be separating from their neighbors and rounding off. Many of them were attached by only one stalk-like process. These cells correspond to those described for the youngest tâches laiteuses, where all the cells were of this type (fig. 4). Further in, the patch was composed chiefly of many layers of large pale cells. They were slightly basophilic and were either fixed or partially free, but, in other respects, they were similar to the surface cells of the omentum. These were sometimes heaped up over large areas forming low mounds on the omentum.

Toward the center of the tâches laiteuses there were many free cells, including large and small lymphocytes, clasmatocytes, and plasma cells (fig. 7-16). These were either rather evenly distributed among the surface cells or heaped together as a dense core or nodule. This latter type of tâches laiteuses, which undoubtedly represents an older form, was most frequently seen in full grown animals.

Tâches laiteuses in all the earlier stages of development could also be found in normal adult omentum. However, they were so infrequent, and the stages so scattered, that one would not correctly interpret them as developing tâches laiteuses unless he had first studied their development in the younger animals, where they were very numerous and where all intermediate stages could be found in one preparation.

The omentum from a 5 weeks old rabbit gave the most beautiful examples of their development. In this case, the entire omentum had been removed, stretched flat on a large cover glass, and fixed. The whole omentum was covered with small white flecks which stained red with methyl green pyronin. These proved, on microscopic examination, to be developing tâches laiteuses, from the smallest (2-6 cells) to those of medium size. Mitotic figures were numerous in the regions of the patches, and there can be no doubt that the masses of free cells originating from the large flat 'mesothelial' cells, represent the anlagen of the tâches laiteuses. In the younger animals many of these mitotic figures were undoubtedly associated with the growth of the organ, but others, in both young and ~~adult~~ adult animals, were associated with the budding-off of free cells into the body cavity. Evidence for this was obtained from several late stages of mitosis in which one of the daughter cells still formed a part of the surface layer, while the other one projected above the surface, and was free from the surrounding tissue, excepting for the narrow connection with the fixed daughter cell. In such a case, completion of the division would undoubtedly liberate one of the daughter cells, while the other one would remain as a part of the general surface of the organ.

While many cells are liberated during division, many more are cut off directly from the fixed tissue during the resting stage. Usually this process is confined to a distinct localized area involving several cells, although individual cells may become isolated from almost any portion of the surface of the organ. Where the process becomes most active, one usually sees several more-basophilic and more-rounded cells which have separated slightly from their neighbors. Study of many such areas and of many individual cells shows clearly that the cells become more rounded, pull in their processes, and finally separate completely from their neighbors and from the surrounding fixed cells which may show no indication of this activity. Frequent mitotic figures in the immediate neighborhood of such areas probably represent an effort on the part of the fixed cells to replace those which have separated from the general syncytium. The tâches laiteuses were also formed from typical fibroblasts. The fibroblasts differ from the 'mesothelial' cells in being smaller, more elongated or spindle-shaped, and containing a smaller, more oval nucleus. They resemble the mesothelial cells in being only very slightly basophilic, and in having processes which anastomose with those of the surrounding tissue. All transition forms are seen from the one to the other, and, as will be explained farther on, the 'mesothelial' cells in the more fibrous areas may so change their shape as to resemble the underlying fibroblasts. In other portions of the omentum, the fibroblasts may enlarge and replace the overlying 'mesothelial' cells which are being constantly worn off. However, in describing the development of the tâches laiteuses, I have been careful to select those places in which there could be no question that the parent cells represent, on the one hand, the so-called 'mesothelial' cells, and, on the other, typical fibroblasts. Scattered thru the omentum of an adult rabbit were small groups typical of basophilic fibroblasts. The processes of most of these cells were bound to the surrounding tissue. Other fibroblasts, however, were attached at only one end, while the other end was rounded or slightly elongated and contained the nucleus. Here and there among these groups of active fibroblasts were other patches composed of the same active fibroblasts plus numerous free cells. Most of the free cells were typical small lymphocytes. Others had the small lymphocyte form, but a nucleus more like that of the fibroblasts. Stil other cells had a nucleus identical with those found in the surrounding fibroblasts, but the cell body was rounded at one end and slightly elongated or sharply pointed at the other. A few cells occurred which appeared to be separating from the surrounding tissue. Plenty of mitotic figures were also present, and there was no doubt that the lymphocytes present had come from the surrounding fibroblasts, either by division or by the pulling in and rounding off of their processes. Mitoses were even more numerous in the free cells. Therefore, the tâches laiteuses which had arisen thru the activity of the fibroblasts must have been further built up and enlarged by the repeated division and growth of the small lymphocytes.

This proved to be the case, for larger patches, which represented well defined tâches laiteuses, contained, besides all of the cells just described, numerous medium sized and large lymphocytes. A few of them also contained plasma cells. In these larger tâches laiteuses, mitotic figures were frequent in both the large and small lymphocytes.

It is impossible to here regard the small lymphocyte as the older fully differentiated lymphocyte, incapable of further growth and differentiation (Ehrlich, Pappenheim); for plenty of mitotic figures were present in the smallest lymphocytes, and there were all intermediate stages between small lymphocytes and large lymphocytes, showing that the latter were formed by the enlargement and differentiation of the smaller cells. The larger lymphocytes in turn either divided to form small lymphocytes or further differentiated to form plasma cells and large mononuclears.

While most of these tâches laiteuses were developed in non-vascular areas, a few of them were found in the neighborhood of capillaries. Also over the overlying surface of some of these tâches laiteuses, the large pale 'mesothelial' cells were pulling free and rounding off, so that it was sometimes impossible to tell whether the large lymphocytes present had come from the fibroblasts by way of the small lymphocyte, or whether they had originated from the large pale 'mesothelial' or surface cells thru division of the large free lymphoid cells. Evidently the two parent forms, fibroblasts and surface cells, are not only endowed with the same potentialities, but the free cells which they form may so resemble each other that one cannot see any difference between them. Thus tâches laiteuses which originate thru the activity of fibroblasts and the subsequent lymphocytes may be further enlarged thru the rounding off and pulling free of the overlying surface cells. Also the reverse of this may be the case, and it is quite probable that the majority of the tâches laiteuses present in the omentum have been built up in more than one way.

But, however they have been built up, they show the same close association with the connective tissue. That is exactly what we find in the other lymphoid organs. Only there the lymph nodules usually contain what is known as the germ center. Germ centers, according to most investigators, are found in the center of the nodule, and the lymphocytes out at the periphery. Therefore, the younger, less differentiated cells are found in the center of the lymph nodules, and the more mature forms occur toward the outside. But Downey and Weidenreich have shown that the follicles of the lymph nodes and spleen in the mole and bat contain no germ centers, but that the germ center tissue is located at the periphery of the follicle. The reticular cells of the germ-center tissue divide by amitosis, giving rise to the free lymphoid cells of the lymph nodules. The lymphocytes thus formed may divide, and enlarge, and redivide to form other free cells. However, whether the site of proliferation is in the center or at the periphery of the nodule, the lymphocytes which originate there continually migrate out into the surrounding tissue.

In the omentum it is the cells at the periphery of the nodule which, proliferating, and separating from the surrounding syncytium, ~~that~~ represent the younger and more immature forms. In the center of the nodule are usually found small lymphocytes, or small and large lymphocytes, and plasma cells. They have developed from the large lymphoid cells found at the periphery and but recently cut off from the connective tissue. They have originated from them by division and differentiation, and, therefore, represent older, more specialized forms.

Therefore, if the lymph nodules or tâches laiteuses of the omentum have 'germ centers', they must be located at the periphery of the tâches laiteuses, as they are in the lymph nodules of the mole and bat. The essential difference between the nodules in the omentum and those in the lymph nodes is that in the omentum the majority of the cells do not migrate out into the surrounding tissue, but remain in place and collect to form larger and larger nodules or tâches laiteuses. Here they may divide or differentiate to form small and large lymphocytes and plasma cells. Thus the development of the tâches laiteuses becomes essentially a 'piling up' process, new cells being formed at the periphery and older cells piling up in the center to form the dense core charecteristically found in many of the tâches laiteuses.

According to Kiyono the tâches laiteuses are composed of two totally different kinds of cells. The small cells occupying the center of the nodule fail to stain vitally with lithium carmine and are lymphocytes, while the larger cells at the periphery take up the dye and are therefore 'Histocytes'. The latter can never form lymphocytes.

If it is the large cells at the periphery of the tâches laiteuses which always take up the dye, then this, too, corresponds to what we find in the lymph nodes. Here it is either the fixed reticular cells or those which have but recently separated from the connective tissue, which take up the dye. That is, in the case of both the lymph nodules of lymph nodes and the tâches laiteuses of the omentum, it is the younger less differentiated cells still connected with or most recently separated from the connective tissue which take up the dye. In their failure to take up the dye, the small and large lymphocytes and plasma cells in the center of the tâches laiteuses, behave like the corresponding cells of the spleen and lymph nodes. There is no evidence from the vitally stained omentum that the failure on the part of certain lymphocytes to take up the dye is due to their belonging to a different cell species from those which do take up the dye. The failure to take up the dye seems rather to be due to a difference in conditions, either in the cell itself (stage of differentiation) or in its location (environment). Downey has shown that the reaction of the tissues toward vital dyes is by no means specific; and after a study of the tâches laiteuses, there can be no doubt that large lymphoid cells at the periphery of the tâches laiteuses (Kiyono's Histocytes) can and do constantly proliferate to form the inner lymphocytes. Also, some of the cells in the center of the nodule (lymphocytes) normally enlarge and wander out into the periphery, where they can not be distinguished from those which have more recently been cut off from the connective tissue. All transition forms are found between the small and large lymphocytes and plasma cells, and the large lymphoid cells which have but recently separated from the connective tissue and the surface cells themselves.

To sumarize the foregoing discussion, it has been shown: that the origin of the tâches laiteuses or lymphoid nodules of the omentum, like those of other lymphoid organs is closely associated with important changes in the connective tissue. In the omentum of the rabbit the tâches laiteuses arise from either (a) the large, pale, flat mesothelial covering cells, or from (b) typical spindle-shaped fibroblasts, thru the separation of individual or small groups of cells from the surrounding syncytium. As these cells divide, grow, and redivide to form distinct patches, the cytoplasm of the cells becomes more basophilic, the nuclei change their character, and the cells become typical small and large lymphocytes. All intermediate stages are seen between these small patches and the larger, more definite ones containing the characteristic core of small lymphocytes. The largest tâches laiteuses are composed of from one to many layers of partially attached cells, surrounding a dense mass of lymphocytes, plasma cells and fibroblasts. The latter type of tâches laiteuses probably represents an older form, and is most frequently met with in the adult animal.

Plasma Cells

I shall now pass on to the second part of my paper:i.e.the origin, structure, and distribution of plasma cells in the omentum of the rabbit. In the foregoing discussion, I have frequently noted the abundance of plasma cells in the omentum of the adult animal. As their exact morphology is still a matter of considerable debate, I shall take up their structure first.

The theories concerning the structure of plasma cells, like those of their origin, may be divided into two groups,i.e., 1)those which are embodied in Unna's views concerning the morphology of a plasma cell, and 2) those which set forth the Marschalko type of cell as the only true plasma cell. However, both Pappenheim and Downey have pointed out that the modern conception of a plasma cell is very much broader than it was in either Unna's or Marschalko's time. Plasma cells not only originate from several different sources, but they may differ also in size, structure, and staining reaction according to the cells from which they have been derived(Downey, Schwarz, Schlesinger, Weidenreich, and others).

According to Unna, the presence of basophilic, amorphous granoplasm is the chief characteristic of a plasma cell and he regards as such all cells of the granulation tissue which show this reaction. He derives the plasma cells exclusively from connective tissue cells (fibroblasts and perithelial cells), and includes round, irregular, or even spindle-shaped cells, with a clear, oval nucleus somewhat resembling that of a fibroblast.

Leo Ehrlich, investigating pathologic human material, likewise regards them as hypertrophied connective tissue cells in which the granular condition of the protoplasm has been greatly increased.

Both he and Unna describe and figure plasma cells actually budding off from fibroblasts, but they say nothing about what happens to the nucleus of the fibroblast during this budding or fragmentation process.

Schlesinger also finds plasma cells corresponding in all particulars to Unna's forms, but thinks that they represent only one type of plasma cell. He finds all intermediate stages between them and those of the typical Marschalko type, and regards them all as different forms of plasma cells.

The Marschalko type of plasma cell (fig. -) is either round or oval in shape, and contains a small, round, eccentrically-placed nucleus, with its chromatin massed in several blocks against the nuclear membrane, forming the so-called 'Radkern'. On one side of the nucleus and towards the center of the cell is a light space or 'Hof'. According to Marschalko the above morphological characteristics must be accompanied by Unna's tinctorial properties. He derives his plasma cells exclusively from haematogenous lymphocytes which have emigrated from the vessels, but admits the possibility of their development into connective tissue cells. Otherworkers who describe the development of connective tissue cells from plasma cells are Schottländer, Krompecker, and Weishaupt.

Unna, Schlesinger, Leo Ehrlich, and Herbert hold the reverse to be the case, i.e., that plasma cells develop from connective tissue cells; and Pappenheim ('02) is inclined to derive them chiefly from perithelial cells. Later, in 1906, he states that true plasma cells have no relation to connective tissue cells; they originate from lymphocytes only. Pappenheim has many articles on the plasma cell question, and he also has as many different ideas as to their definition and origin. For a complete discussion of his views concerning plasma cells, the reader is referred to the paper on plasma cells by Downey('11).

As mentioned at the beginning of this paper, those who uphold the lymphocytic origin of plasma cells are divided in their views. Some workers derive these cells from histogenous lymphocytes, while others maintain that they develop from haematogenous lymphocytes only. The majority of workers hold the latter view, basing their conclusion largely on the results of investigations of pathologic or experimental material.

The most important workers upholding the haematogenous origin of plasma cells are Marschalko, Baumgarten, Nissl, Schottländer, Krompecker, and Maximow. Schottländer and Krompecker regard them as intermediate stages between haematogenous lymphocytes and fixed connective tissue cells.

Ribbert and his followers believed that there existed everywhere in the connective tissue of the normal animal, small accumulations of lymphoid cells (perivascular lymphomata). He, as well as Joannovics, Schaffer, and Veratti, derive plasma cells from histogenous lymphocytes. Others, including Downey, Weidenreich, Schwarz and Porcile, find plasma cells developing from both sources, but believe that histogenous lymphocytes are of chief importance. The last named authors have made the most detailed and recent studies of plasma cells. According to Weidenreich, and Downey, plasma cells may also be developed from connective tissue cells. These workers who find plasma cells developing from many types of cells also see a great variance in the size, shape, and structure of these cells.

From the brief account above, it has been shown that the most recent workers on plasma cells include cells other than those of the Marschalko type. However, most of them are inclined to regard the Marschalko type as the fully differentiated form of plasma cell. It is also important that the most modern workers, while admitting that plasma cells may originate from a haematogenous source, believe that the lymphocytes of the tissues furnish the bulk of the plasma cells. Altho fibroblasts and perithelial cells may also form plasma cells, the number formed in this way is of little significance.

I shall now proceed to describe plasma cells as I find them in the omentum of the rabbit. They vary considerably in size, varying between 4 and 13 in diameter. The majority of them contain a nucleus similar in structure to those of the smaller lymphocytes (figs. [illegible]). It is usually eccentrically placed and surrounded by a more or less round or oval cell body, often irregular in shape, or prolonged in knoblike or finger-like pseudopodia. The cytoplasm of the cell contains a fine dust-like granoplasm, which stains densely with all basic anilin dyes. This granoplasm is not always so evident as Unna maintained; it is brought out most distinctly with the alcohol or zinc chloride fixation which Unna used, but it is sometimes barely visible when the material has been fixed in Helly's fluid. Altho always present in the plasma cells of the omentum of the rabbit, it is by no means as characteristic of them as Unna, Nissl, Scwarz, and others have supposed. It is common in large lymphocytes and may also be found in other types of lymphoid cells, in endothelial cells, and perithelial cells, and even in fibroblasts under experimental conditions. (Maximow, Weidenreich, Pappenheim, and Downey)

Besides several small, round or irregular vacuoles, there is usually a large clear area near the central portion of the cell at one side of the nucleus (fig.22,23). This is the 'Zellhof' described by many authors which, according to Pappenheim, Maximow, Weidenreich and Wallgren, contains the centrosome apparatus. It is quite variable in shape and size figs.(23,14,27). It may be absent from some cells which in other respects are typical plasma cells, or it may be replaced by a group of several smaller vacuoles (fig. 24). This corresponds to what Downey finds for plasma cells in cold blooded vertebrates. There, the large space may be at one side of the nucleus and nearly in the center of the cell, or it may be out at one end of the cell.

Both the 'Hof' and the vacuoles contain a homogeneous acidophilic substance (fig.) which may increase in amount and density until it assumes the form of Russel's 'fuchsin bodies' (fig.) It develops at the expense of the granoplasm and finally appears as a homogeneous, semifluid, colloid-like substance which has a strong affinity for acid dyes. This substance finally forms the round or oval bodies known as Russel's 'fuchsin bodies' (Downey). These bodies were found in small numbers in the plasma cells of the normal omentum and in greater numbers in the abnormal and experimental material.

Besides the plasma cells just described, there are others which have a nucleus resembling that of a large lymphocyte. It is larger and more vesicular, and the chromatin, instead of being massed in large, triangular blocks against the nuclear membrane, is found in smaller masses partially distributed thruout the nucleus. The outline of the cell may be similar to that of the cell first described, or it may be larger and more irregular; and the basophilic granoplasm is usually more distinct than it is in tha cells having a small lymphocyte type of nucleus. One or more nucleoli are occasionally present. Preparations of omentum in which small pieces of sumac pith had been preveiously embedded , and also a preparation from the omentum of a normal rabbit show numerous lymphoid cells with lobulated nuclei. There are all transitions from those with a slightly indented, kidney-shaped nucleus (fig. 29) to those which posess 4-6 lobes (fig. 30). In some of these nuclei the chromatin is massed against the nuclear membrane, so that the whole nucleus resembles several small lymphocytes nuclei which have become confluent. In other cells the lobes of the nuclei are larger, and the chromatin is evenly distributed. Some of these are plainly only medium-sized or large lymphocytes, but others posess all of the cytoplasmic characteristics of a plasma cell. These have been described by Maximow ('05) and Weidenreich ('09). Maximow figures them in the capsule of a celloidin chamber and states that they are degenerating plasma cells. Weidenreich also regards them as plasma cells, but thinks that the lobulation of the nucleus is either the result of amoeboid activity, or that it represents a retardation in the nuclear differentiation of a plasma cell which has developed from a lymphocyte having a lobulated nucleus. Many of the cells which contain a lobulated nucleus in my preparation, are undoubtedly plasma cells. As they show no signs of degeneration and as all transitions are seen between the cells with one lobulated nucleus (fig. 30) and those with two and three separate nuclei, (fig. 31), it is more likely that they are young and especially active plasma cells in which the nuclei are dividing and differentiating faster than the cell body can divide. This necessitates the acceptance of the view that plasma cells may divide by amitosis, and while I hold that both mitotic and amitotic division rarely occurs in these cells, I believe that amitosis may take place in areas where there is rapid proliferation of lymphoid cells. Leo Ehrlich had somewhat the same view for the binucleated plasma cells when he said,"Die Zellen haben zwei und mehr

Kerne an den Orten der Präparate, wo die Proliferation dieser Zellen besonders stark ist." Maximow, Weidenreich, and Schwarz also describe and figure bi-nucleated plasma cells. I do not regard them as having any special significance for there is no reason why two or three nuclei should not occur in plasma cells as well as in other lymphoid cells and fibroblasts. Many investigators (Unna, Ehrlich, Schottländer, Krompecker, and Schlesinger) studying plasma cells in foreign body or experimental material figured and described the presence of densely basophilic cells which they called plasma cells. These cells contained a large, clear vesicular nucleus with small masses of chromatin mostly in contact with the nuclear membrane. Unna and Ehrlich derived these directly from connective tissue cells by the process of bridging or fragmentation. As I could find no signs of such cells in the omentum of normal rabbits, and as I could find no evidence for the direct development of plasma cells from fibroblasts, I resorted to the "Kieselgur" experiments. After removing a small piece of omentum to use as a check on the normality of the tissue, I rubbed infusorial earth over the surface of the omentum, and allowed the animal to live. Small portions of the omentum were removed from the rabbit 2 days and 5 days later. The latter preparation showed a small number of very basophilic cells with round or slightly oval, eccentrically placed nuclei. These nuclei were large and clear, and contained only a sparse amount of chromatin, lying against the nuclear membrane. The center of the nucleus contained one or more prominent nucleoli. In fact, they were identical with the plasma cells described above except for their rounded outline, the eccentric position of the nucleus, and the presence of a clear 'Hof', these cells were identical in structure and staining reaction with the fixed or partially attached connective tissue cells, from which they were plainly being derived. However, the eccentric position of the nuclei together with the distinct 'Hof' was so marked as to necessitate that the cell be classified as a plasma cell.

Altho the plasma cells hve been described in the omentum of the normal rabbit by Schwarz, Jolly, Weidenreich, Marchand, and Maximow, I found them to be even more numerous than I had expected from the descriptions of these men. Some of them are found in the center and at the periphery of the taches laiteuses (Schwarz and Dominici). Others are characteristically embedded in the midst of capillary network, or scattered, individually or in small groups, thruout the less vascular portions of the omentum. But the majority of the plasma cells are found lying along the smaller vessels (Weidenreich) and also surrounding the larger ones. Sometimes they are arranged in a single row on either side of a vessel, and again they accumulate in dense masses or nodules about the walls of the larger ones. The largest accumulations usually occur where a vessel branches. In this particular, they resemble the lymph follicles of the lymph nodes and spleen. From my study of the omentum in general, and of the taches laiteuses in particular, I find that plasma cells can develop from the following sources: from small, medium-sized, and large lymphocytes directly, and from fibroblasts and 'mesothelial' covering cells indirectly via various lymphoid cells. Those in the thin connective tissue areas originate chiefly in the nonvascular taches laiteuses, while those in the regions of the vessels have probably either originated in loco from the lymphoid sheaths or vascular taches laiteuses, or they have wandered into the vascular areas from the nonvascular parts. Altho it has been shown by Mallory, Schwarz, and others, that plasma cells may migrate thru the walls of a vessel, it is unlikely that many of those in the omentum have originated directly from the blood stream. Maximow derives plasma cells chiefly from emigrated haematogenous lymphocytes, but also from lymphocytes which have been in the connective tissue for a long period of time, He makes no distinction between the histogenous,and haematogenous forms. Other workers hold that plasma cells originate from haematogenous lymphocytes and large mononuclears only. (Baumgarten, Schottländer, Krompecker, Enderlin, Justi and Schwarz) However, all of their work has been done on abnormal and experimental material.

The origin of plasma cells, as well as their structure, ought not to be decided wholly from a study of pathologic tissues. It is common knowledge that many cells occur in areas of chronic and acute inflamations which are not present in these areas under normal conditions, and it does not seem reascnable to regard these foreign cells as the parent forms of those found normally in the tissues of healthy animals. For this reason I restricted my investigations almost wholly to the omentum of normal animals.

There I find that plasma cells arise chiefly from small and medium-sized lymphocytes. Altho the nuclear structure of the plasma cells would indicate that they have usually come from lymphocytes, one cannot be sure of this until he has found all intermediate stages between these cells and plasma cells. This was not at all difficult and I was even fortunate enough to discover a single field which showed all intermediate stages between both the small and the large lymphocytes and plasma cells. This field, drawn from the omentum of a normal rabbit (adult) is pictured in figure 6. The preparation was stained in methyl green pyronin, and every cell in the field was drawn. It shows all transition forms between small lymphocytes and true plasma cells.

A typical small lymphocyte having only the barest rim of faintly stained cytoplasm is pictured at 'a'. It possesses a small nucleus with the chromatin arranged in triangular blocks against the wide nuclear membrane, plus a large chromatin mass in the center of the nucleus. 'b' has a slightly larger, more irregular nucleus and a more noticeable cytoplasmic border, but it is still clearly a small lymphocyte. 'c' is a typical medium-sized lymphocyte; its nucleus is larger and paler, and the chromatin is more evenly distributed thruout the nucleus. The cell has a distinct rim of cytoplasm which has taken on a distinct pinkish color. A few small vacuoles are present. d and d')are cells with similar nuclei but a slightly larger amount of cytoplasm which stains distinctly red with the pyronin of the staining mixture. The cytoplasm contains the amorphous granoplasm supposed by Unna, Nissl, and Schwarz to be characteristic of the plasma cell. Yet this cell is plainly only a rather small large lymphocyte. Small vacuoles are evident but the nuclei are still centrally placed and no clear 'Hof' is seen. e and e') are ordinary large lymphocytes. A large cell, in which a nucleus similar to that of a medium-sized lymphocyte is eccentrically placed, and the vacuoles in the cytoplasm are becoming confluent, is shown at f). The granoplasm is strongly basophilic. f') represents a cell with a large lymphocyte type of nucleus in which the same 'running together' of vacuoles to form one larger vacuole is seen. g and g') are cells in which this process has progressed still further, the vacuole appearing as a small indistinct 'Hof'. At h and h') are typical plasma cells. The one at h) contains a nucleus resembling that of a small lymphocyte, while the one labeled h') shows a nucleus similar to those pictured in the large lymphocytes e and e'). They have origiinated from small and large lymphocytes respectively, by a process of enlargement and differentiation. Both of these plasma cells, as well as the others in the field, show the basophilic amorphous granoplasm, the eccentrically placed nucleus, and the clear 'Hof' usually assigned to a plasma cell.

Another way in which plasma cells may originate is by differentiation from the 'mesothelial' covering cells. They may arise from covering cells anywhere in the omentum, thru separation from the underlying tissue and subsequent differentiation. But their most frequent place of origin is in the taches laiteuses of Ranvier.

The process may be a long one, involving many intermediate forms between the large, fixed, so-called 'mesothelial' cells and the typical plasma cell, or differentiation may be more rapid, with possibly only one transition stage.

Fig. 19 is a low power drawing of a medium sized tache laiteuse located out in a nonvascular, plain connective tissue area. The thickening and slightly basophilic character of the connective tissue over the area of the taches laiteuses (b) is quite noticeable when compared with the rest of the omentum (a). c) represents the peripheral margin of the taches laiteuses, which is characterized by the presence of only partially attached, surface cells. The large, slightly darker cells at (d) are the large mononuclear cells which have but recently separated from the underlying syncytium. In the center of the tache laiteuse is a dense mass composed of all types of lymphoid cells, including plasma cells (e). A study of the cell forms found in the taches laiteuses shows that the plasma cells have been derived from the large pale 'mesothelial' cells. To show tha transition from the 'mesothelial' covering cells to plasma cells, I have figured the intermediate stages in figs.7-16.

The cells drawn are taken from the tache laiteuse just described. Fig.7 is a mesothelial covering cell. It is large, flat, and pale, and appears to be securely attached to the surrounding tissue by six rather broad processes. Its large oval nucleus is surrounded by a lightly stained nuclear membrane, and contains small, evenly distributed masses of chromatin. Fig.8 represents a slightly smaller cell with thinner, more pointed processes. The cytoplasm is darker on one side of the cell, and the nucleus contains several deeply staining masses of chromatin. There are two cells represented in fig.9. Here, the processes of both cells are extremely delicate, as if they were about to break away from the underlying tissue. In (a) the nucleus resembles that of fig.8, while in (b) the nucleus, like the cell, is decidedly smaller. (b) is a good example of the way in which large lymphocytes are formed directly from the attached surface cells. The cell, altho still attached, is small, and the cytoplasm as dense as that of many large, lymphocytes. Even the nucleus is further differentiated than that of the neighboring cell(a). Numerous mitotic figures are found in both the fixed and the free cells. Fig. 10 shows a large rounded cell in mitotic division. It is about to pull itself free. Both the cytoplasm and the nucleus of a free cell may stain as lightly as those of the fixed cells, but they are apt to be darker and more distinct, as in fig.11. The lymphoid cell shown in fig.12 has probably been derived from a smaller attached cell such as b),fig.9. The cytoplasm is moderately basophilic and contains a bare indication of granoplasm in the upper part of the cell. In fig.13 the granoplasm has increased in amount until it occurs thruout the periphery of the cell, leaving a pale, homogeneous area immediately surrounding the nucleus. But as there is no real 'Hof' present, and as the nucleus is still pale, I would not consider it a plasma cell. The next cell, however, (fig.14) shows true plasma cell characteristics. The nucleus is eccentrically placed, and its distinct chromatin masses are lying against the nuclear membrane. The increase in the amount of basophilic granoplasm brings out the clear space at the side of the nucleus more distinctly, and it can now be considered a true 'Hof'. However, there are workers who would not admit that this cell is a plasma cell. For this reason, I have pictured two further stages in differentiation (figs.15 and 16). In both of these cells the nucleus is eccentrically placed, the cytoplasm contains extremely basophilic granoplasm, there is a distinct 'Hof' at the side of the nucleus, and the latter,altho not of the Marschalko type, is identical in structure with many of the plasma cells found elsewhere in the omentum of the rabbit. In fact, there can be no doubt that they are true plasma cells, and that they have differentiated from pale fixed,'mesothelial' cells which have pulled themselves free from the underlying syncytium.

In the section concerning the development of the taches laiteuses, I figured and described the formation of small, medium-sized, and large lymphocytes from typical spindle-shaped fibroblasts. In a few of the larger taches laiteuses, there was a fair number of large basophilic lymphocytes, the nuclei of which were very similar to those of fibroblasts. Occasionally, there were one or two plasma cells also present. Thes appeared clearly to have been derived from the fixed fibroblasts via the small, and large basophilic lymphocytes.

But, this was an indirect transformation of fibroblasts into plasma cells; it was not according to the process of fragmentation or "Abbau" described by Unna and Ehrlich. Altho neither Unna's nor 3hrlich's figures and descriptions were convincing, I decided to try experimental methods, to see if I could get the type of plasma cells described by them.

In the omentum of the animal in which infusorial earth has been placed, as described on page 40, the whole tissue appeared to be composed of fixed, extremely basophilic fibroblasts, partially free cells, and free mononuclear cells. The latter possessed a nucleus similar to the nucleus in the fixed and partially free cells, and identical with those described and figured by Unna and Ehrlich, except for the fact that it was eccentrically placed, and that a distinct 'Hof' was present. I must conclude with Unna and Ehrlich that the clear nucleated cells described by them are plasma cells, and that they have been derived from fibroblasts. However, the corresponding cells in my material did not originate directly from fibroblasts by the process of fragmentation, and they are not found in the normal rabbit omentum.

To summarize the foregoing discussion, it has been shown that plasma cells in the omentum of the rabbit can be derived from small and medium-sized lymphocytes, and large lymphocytes directly, and that they may arise indirectly from 'mesothelial' covering cells, and fibroblasts via various types of lymphoid cells.

Until recently this would not have seemed possible. Older investigators held the above forms to be widely separated and distinct species of cell forms; but the late investigations of Ranvier, Dominici, Downey, Weidenreich, and Schott have shown that fibroblasts, 'mesothelial' covering cells of the omentum and mesentery, macrophages, lymphocytes, and wandering cells all belong to the same family, and that their different morphological appearance is an expression of their immediate functional activity. Therefore, it is not strange thatplasma cells should be derived from all of them, and that they should represent a special state of activity in various cells which are genetically and functionally the same. (Pappenheim and Downey)

The majority of works on plasma cells have been concerned with their structure and origin, rather than with their function. Plasma cells are most characteristic of chronic processes where they constitute an important part of the round cell infiltrations, and they are abundant about tumors, cancers, infectious granulomata,etc. A small number of them are also found in the tissues of normal animals,-i.e., in lymph nodes, spleen, bone marrow, omentum, submaxillary gland, and digestive tract. They are seldom or never present in acute inflammatory conditions and especially in acute suppuration. (Joanovics) It is almost iniversally believed that plasma cells are not phagocytic, and Councilman states that they are found, not in lesions produced by bacteria, but in the periphery of the purulent foci. However, Beattie, studying the effects of tubercle bacilli and B.Coli on the peritoneal exudate and internal organs of guinea pigs, declares that plasma cells are phagocytic to bacteria and to other cells. As he gives no figures, and as he maintains that plasma cells are identical with the phagocytes derived from large mononuclear leucocytes, it is quite probable that Beattie included as plasma cells many forms which were not true plasma cells. My study of the omentum of the rabbit gave no evidence of plasma cells, with phagocytosed inclusions in either my foreign body or vitally stained material, and they were not called forth by the injection of foreign matter.

Regarding the role which plasma cells play in both normal and abnormal material: Marschalko regards his cell as a young and particularly active cell, while Unna states that the Marschalko plasma cell represents an atrophic degenerating cell. This is directly opposed to Krompecker who holds that Unna's plasma cell is degenerative. Councilman examined diseased kidney tissue for fatty degeneration and found no fat in the plasma cells. He states that eviidence of cell necrosis, as shown by nuclear detritus, is not found. The only evidence of degeneration is the occurence of vacuoles or hyaline droplets which stain homogeneously with methylen blue. I find that plasma cells are not only present in the normal omentum but that there is no evidence for the presence of degenerating elements among them. One may look thru many slides before he finds a plasma cell with a degenerating nucleus. Even tho I do not find Unna's type of plasma cell in the normal omentum, I do not regard it as a degenerating type. It should be looked upon rather as indicative of a new source from which plasma cells may be derived under abnormal conditions.

Russel's fuchsin bodies are regarded by some as a product of degeneration, and by others as, "a special kind of secretion, or the accumulation and thickening of the normal secretion", (Downey). I have made no special study of these structures, but I do not think that they are degenerating bodies, for, altho my material shows comparatively few plasma cells containing Russel's fuchsin bodies, not a single nucleus in any of the cells seen was degenerating. Also, as these bodies are built up from the homogeneous substance in the small vacuoles and 'Hof', and as they are occasionally found free in the tissue, it is more lokely that they represent a kind of secretion.

There is another type of secretion, however, which is more common for the plasma cells of the omentum than the one just described. This is formed by the process of 'fragmentation'. It is not characteristic of plasma cells alone, but is found in other lymphoid cells (Downey, Weidenreich,Maximow). The cells may send out portions of their protoplasm which become pinched off from the cell body. Such detatched fragments are frequently met with in the omentum of normal animals, and are even more numerous under experimental conditions. The small drop-like masses of protoplasm which are being given off are usually more basophilic than the cytoplasm of the rest of the cell, and the granoplasm is extremely distinct. The proto plasmic attachment to the cell body is pale and homogeneous(fig. 27) showing that the unusually dense granoplasm of the knobules has been increased at the expense of that in the area of attachment.

I believe that the granoplasm is a form of secretion,which is liberated by the fragmenting or 'pinching off' of portions of the cell body. This is in accordance with Weidenreich's view that both lymphocytes and plasma cells may give off portions of their cytoplasm, which represent a kind of secretion. Some of the loose fragments may be pale in color while others have a clear homogeneous appearance. I conclude from this that the granoplasm dissolves or is used up in some way after the small drop-like masses have become detatched.

Plasma cells which are about to give off pieces of their protoplasm must not be confused with those in the act of amoeboid motion, which they may resemble. Various workers have denied that plasma cells are amoeboid. However, altho I have not studied plasma cells in the living material, there is considerable evidence from my fixed preparations that plasma cells are able to migrate freely thru the tissues. Fig.6,1 and 23 show the difference between migrating plasma cells and those undergoing the process of fragmentation (fig. 27)

What happens to the vast number of plasma cells normally present in the omentum of the adult rabbit? Schottländer, Krompecker, and Weishaupt all believed that plasma cells were merely intermediate stages between haematogenous lymphoid wandering cells and connective tissue cells. According to these men plasma cells constantly develop into fibroblasts and may even form fibers.

Several other investigators have shown that plasma cells may further differentiate into other cells, particularly into granular leucocytes. The frequent development of mast cell granules in their cytoplasm, thus forming the so-called 'plasma mast cells', has been described by Schridde, Downey, and Greggio. Shridde also favors the development of special cells and eosinophils from plasma cells. This is opposed to Weidenreich who believes that plasma cells are merely the temporary structural expression of a special functional condition of various types of lymphocytes. They can lose their granoplasm and again become lymphocytes.

My material gives no evidence for any of these views. The only examples of the local development of granular cells were in cases of myloid metaplasia, and plasma cells were in no way connected with their formation. Also, I saw no instances where plasma cells were losing their granplasm and again becoming lymphocytes, and it seems more likely that they are a highly specialized cell with a secretory function. (Downey)

Evidence of degeneration in cells with a small amount of cytoplasm, exists in perfectly normal conditions, and while these cells are commonly regarded as small lymphoid cells, they can not be distinguished from plasma cells which have lost their granoplasmic cytoplasm. The nuclei of the plasma cells may degenerate after the almost total fragmentation of their protoplasm, and many of the cells are probably disposed of in this manner. It is possible that others are destroyed upon the formation of Russel's fuchsin bodies.

There are two other facts gained from my study of the omentum which may be of general interest. One of them is the finding of abundant mitotic figures in lymphocytes within the blood stream, and the other is the not infrequent occurence of myeloid metaplasia.

It is the generally accepted view that mitotic figures do not occur in the circulating blood of normal animals,(Maximow, Pappenheim). This is not true of the rabbit. While only a few mitotic figures (3) were found in blood vessels of the omentum of normal adult rabbits, they were more numerous in the newborn, and quite frequent in the lymphocytes of the omentum of 5 week and 7 week rabbits.

As many as twenty-one different examples have been seen during a half hours study of the omentum of a 5 week rabbit which were distinctly in the vessel. They were found both in the capillaries and in the large vessels, chiefly in the veins. In only one instance was a mitotic figure (telophase) found in an artery. In the surrounding tissue, all phases of mitosis were numerous, but the metaphase or telophase, with the cells frequently divided, were the only stages seen among the dividing cells within the vessels. This, and the fact that mitotic figures have rarely been reported in the general circulation, indicates that the mitotic division begun in the tissues is completed after the cells have migrated into the vessels.

While the capillaries and veins of both the 5 week and 7 week omentum contained great numbers of lymphoid cells, often literally gorged with lymphocytes, it is important that the corresponding arteries in every case but one contained only the normal number of lymphoid cells.

An unusual number of lymphocytes in the capillaries might point to emigration as well as to immigration, or it might mean that lymphocytes had merely accumulated in the cappillaries where the blood current was slow. And if both arteries and veins had great numbers, it might mean simply that animals of this age had more lymphocytes in the blood than older animals (as in man). However, in a systematic study of the lymphoid contents of veins and their corresponding arteries, I found only one instance where the artery contained more than the usual number of lymphocytes- and this seemed to be merely a local condition extending for a short distance only. The majority of veins and capillaries ~~in the veins and capillaries~~ in the omentum of the 5-7 week rabbits contained large numbers of lymphocytes.

This and the presence of mitotic figures in the capillaries and veins would point to immigration of lymphocytes into the circulation, rather than an emmigration out. The lymphocytes of the vessels are morphologically identical with those of the tâches laiteuses and perivascular sheaths, and if we consider the large number of lymphoid cells which are produced in the omentum, and look upon it as a lymphoid organ (Schott, Weidenreich), or as containing "extravascular lymphomata" (Ribbert), it is only natural to suppose that at least some of the lymphocytes produced get into the circulation here as in the lymph glands (Schwarz).

Regarding the myeloid metaplasia, one case was found in the omentum of an apparently healthy 5 day rabbit. There, special granulocytes were developing from large mononuclear cells, identical in structure with those which were separating from the surface of the organ. It appeared to be an example of the development of granuloocytes from 'mesothelial' covering cells.

Another case was found in the otherwise normal omentum of an adult rabbit. Here, the developing myelocytes were eosinophils. The preparation was stained in a combination of Ehrlich's triacid and Toluidin blue, and showed the earliest development of basophil granules in large, round nucleated lymphoid cells. In the smaller cells, containing indented or saddle back nuclei, the granules were either part blue and part red, or they were all eosinophilic. Several other examples of what was undoubtedly the local development of granulocytes were noted, but as they were not stained in a way which would bring out the granules, nothing definite could be determined.

Marchand states that the omentum of young animals and human foetuses is very similar in character to mesenchyme tissue. The universal formation of all types of lymphocytes and plasma cells from the fixed cells of the omentum, and the occasional local development of granulocytes from the various lymphoid cells of the otherwise normal omentum is in favor of the above view. It must be that the elements of the omentum are less specialized than those of other organs, and that even in the adult animal they still retain the potentialities of their younger, less mature mesenchymatous forms.

Summary

The omentum of newborn and young animals is thinner and less fenestrated, and contains fewer free cells, than that of the adult rabbit. Both surfaces of the omentum are composed of large, flat protoplasmic cells having large, pale oval nuclei. These cells are identical with those of the underlying tissue (Weidenreich, Schott, Cornil, etc.).

Besides the surface cells and underlying fibroblasts and fibers, the omentum may contain clasmatocytes, lymphocytes, plasma

cells, eosinophils, and, occasionally, a special cell.

The lymphoid cells are not evenly distributed thruout the omentum but are concentrated along the blood vessels and in the tâches laiteuses.

The latter were not found in the omentum of the newborn, but were seen first in the 10 day rabbit. They originate from either (a) the large, pale, flat, 'mesothelial' covering cells, or from (b) typical spindle-shaped fibroblasts, thru the separation of individual or small groups of cells from the surrounding syncytium. As these cells increase in number, to form distinct patches, theychange their character and become typical small and large lymphocytes. These patches grow in size and may fuse to form a network of lymphoid strands In the larger patches, or tâches laiteuses, which are most frequent in the adult animal, the lymphocytes may further differentiate into plasma cells.

Altho the majority of the tâches laiteuses in the adult animal are connected with blood vessels, this connection is usually only secondary. In most cases the tâches laiteuses develop first and the vessels grow in later.

Plasma cells were first seen in the omentum of a 10 week old rabbit, but a sparce number of lymphocytes were present in the newborn animal. Both plasma cells and lymphocytes increase in number with the age of the animal, and they are extremely abundant in the omentum of the adult rabbit.

The placing of foreign bodies in contact with the omenta of rabbits resulted in a separation of both fibroblasts and 'mesothelial' covering cells from the underlying tissue, and in the proliferation of the free cells to form lymphocytes and plasma cells.

Plasma cells are found in all normal warm blooded animals

(Maximow), and in various normal cold blooded animals(Downey). The study of the rabbit's omentum shows that they are abundant in the adult animal in the regions of the tâches laiteuses and perivascular sheaths. They are less frequent in the pale nonvascular connective tissue areas.

The structure of a plasma cell varies according to the cell from which it has been derived. Typical Marschalko plasma cells seldom occur. The majority of the plasma cells have a nucleus similar to that found in small lymphocytes.

Plasma cells are derived from small and medium-sized lymphocytes and large lymphocytes directly, and,indirectly, from 'mesothelial' covering cells and fibroblasts via various types of lymphoid cells.

The present investigation shows that plasma cells are not phagocytic, and that they are not called forth in aseptic, inflammatory conditions produced by the introduction of sterile foreign matter.

They are secretory in function, and the granoplasm which is liberated by the fragmenting or 'pinching off' of portions of the cell body, represents a form of this secretion. (Weidenreich)

The omentum of the rabbit gives considerable evidence for the amoeboid motion of plasma cells. The presence of plasma cells in the vessels of the omentum, since they are not present in the general circulation, is further evidence of their migratory ability.

My material gives little evidence to show that plasma cells are degenerating elements. It is ~~more~~ probable that they represent a more highly specialized cell than the various cells from which they have been derived(Downey).

The presence of abundant mitotic figures in the blood vessels and the not frequent occurence of myeloid metaplasia are further interesting facts noted in connection with the study of the omentum.

Explanation of Plates.

Fig.1. Whole preparation of omentum from a normal, adult rabbit, showing the distribution of vessels and lymphoid tissue. a= loose capillary network; b=capillary tufts; c= tâches laiteuses characteristically located at the point in the forking of the vessel where the vessel branches; d= tâches laiteuses embedded in a capillary tuft; e=fat.

Fig.2. Large area of omentum from a normal adult rabbit. a=outgrowths or 'bridges' which have here assumed enormous dimensions.

Fig.3.Dense capillary network from the omentum of a 10 week old rabbit.

Fig.4. Developing tâches laiteuses composed of fine cells which are separating from the surrounding syncytium. They are shown attached only by very delicate processes. From the omentum of a 5 week old rabbit.

Fig.5. An elongated outgrowth from the omentum. (1-3 cells wide)

Fig.6. Development of plasma cells from small and large lymphocytes in the omentum of a normal adult rabbit.

Fig.7-15 and 16. Plasma cell development from 'mesothelial' covering cells via various types of lymphoid cells.

Fig.17. Developing tâches laiteuses composed of a few large, pale, free cells in the center, surrounded by partially attached surface cells. From omentum of a 5 week old rabbit.

Fig.18. Developing tâches laiteuses of medium size. Note all types of free lymphoid cells and fibroblasts surrounded by partially attached surface cells. From the same preparation as Figs.4 and 17.

Fig.19. Large nonvascular tâches laiteuses from the omentum of a normal adult rabbit.

Fig.21. Development of lymphocytes from spindle-shaped fibroblasts.

Fig.22. The Marschalko type of plasma cell from a normal adult omentum.

Fig.23. Plasma cell with a large amount of basophilic cytoplasm and a nucleus similar to that of a small lymphocyte. Same as above.

Fig.24. Plasma cell containing a large nucleus resembling that of a large lymphocyte. Same as above.

Fig.25. Small plasma cell from the omentum of a 10 day old rabbit.

Fig.26. Plasma cell which was derived from a fibroblast under

abnormal conditions. Infusorial experiment.

Fig.27 a and b. Two plasma cells from the normal omentum of different rabbits, showing the giving off of portions of their cytoplasm, probably a secretory process.

Fig.28. Plasma cell in amoeboid motion. Normal adult omentum.

Fig.29.Plasma cell with kidney-shaped nucleus. Same as above.

Fig.30.Plasma cell with a nucleus consisting of 5 lobes. Same as above.

Fig.31.Binucleated plasma cell. Same as above.

Fig.32. Plasma cell within a blood vessel. Cells resembling plasma cells, known as Türk's irritation forms, are sometimes found but they are of myelogenous origin. True plasma cells rarely occur in the general circulation. However, several have been seen in the blood vessels of the omentum. Whether thay are evidence for Weidenreich's view that plasma cells can again become lymphocytes and enter the circulation, or whether their presence is merely a chance occurence, must be decided by further investigation.