THE INDUCED DEVELOPMENT AND HISTOGENESIS OF PLASMA CELLS

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PLATES 30 AND 31

It is known that plasma cells occur normally in the connective tissues of warm blooded animals and that they are increased in numbers around various pathological lesions. In a study of the cellular reactions to the different chemical fractions of the tubercle bacillus, Sabin, Doan, and Forkner (1) reported the presence of these cells in rather large numbers in the omenta of rabbits after intraperitoneal injections of tuberculo-protein.

The present work was undertaken to determine the effectiveness of the tuberculo-protein as a stimulant for plasma cells; and to use the resulting proliferations of plasma cells for a study of their histogenesis.

If the plasma cell is accepted as a definite cellular entity, it must have a maturation cycle, as have the myeloid elements and the lymphocyte (2). The cellular reaction following intraperitoneal injections of tuberculo-protein has made it possible to follow the evolution of plasma cells from primitive undifferentiated mesenchymal cells, through maturity, into Russell body cells and other degenerative forms.

The name plasma cell was introduced by Waldeyer (3) in 1875. From his work it is not clear that he described a specific type of cell. A definite cell strain was first recognized by Cajal (1890 (4)) in the condylomata of syphilis. He named them *cells cyanophils*. Unna (1891 (5)) found cells in the lesions of dermal tuberculosis which he called plasma cells. He described them as having a basophilic, spongy, or granular cytoplasm, the granuloplasm. Their nuclei were either centrally or eccentrically placed, and the chromatin content and arrangement were variable. His only constant specializing criterion was basophilic granuloplasm, and as a result of this he included under the category of plasma cells many cells with basophilic cytoplasm, which were probably derivatives of other strains.

Marshalkó (1895 (6)) selected certain morphological characteristics as the essential criteria of the typical plasma cell. By his definition such a cell must have basophilic cytoplasm, showing a clear area in the center, be round or oval, have a round, eccentrically placed nucleus with the chromatin condensed near the nuclear membrane and arranged radially in blocks. Cells that have these criteria are known today as typical plasma cells. It was Marshalkó's belief that they originated from hematogenous lymphocytes.

Downey's (7) discussion of the controversy over the origin of plasma cells shows that many believe them to be derived from lymphocytes, either hematogenous or histogenous, while others think they take origin from primitive mesenchymal cells. He gives evidence to support the view that they are derived from both types of lymphocytes, but in greater numbers from the hematogenous variety. In describing plasma cells in the mesentery of the frog, he shows that the Russell body cells are the end stage of their development and are present normally. The Russell body cells are plasma cells which have fulfilled a cellular secretory function, having built up some material in their cytoplasm, which first appears as granuloplasm, and later, becoming hyalinized, is present as the Russell bodies. An excellent review of the literature has been given recently by Michels (8).

Although plasma cells are found in normal connective tissues, they are present in the greatest number in organs which act as bacterial filters or which presumably have a detoxifying function, notably the lymph nodes and omentum. This, together with their presence in certain pathological lesions, suggests that they act to detoxify bacterial and other toxins.

Methods

Three tuberculo-proteins were used to stimulate the production of plasma cells, as follows: (a) one isolated by Johnson and Coghill (9), designated water-soluble 304; (b) an alkali-soluble fraction, also isolated by Coghill (10); and (c) a water-soluble material similar to that of Johnson but prepared by the Mulford Company (MA-100). The first two, because they were slightly acid, were suspended in distilled water or salt solution and caused to dissolve by the addition of enough 1 per cent NaOH to give a neutral reaction to litmus. The Mulford protein, MA-100, was received in salt solution and injected in this form.

Eighteen animals were employed in the experiments. To stimulate the cells in the omentum, seventeen of them were given intraperitoneal injections of one of the proteins. Two of the seventeen animals were also given intravenous injections, and three were injected subcutaneously. The remaining animal was given intravenous injections only.

Table I indicates the number of injections, the type and amount of protein each animal received, and the interval between the last injection and autopsy.

After its course of injections, each animal was killed by intravenous injection

of air and an autopsy was performed. The omentum was spread over a slide prepared with neutral red and Janus green for study by the supravital method. Lymph nodes were scraped and prepared for supravital study. Parts of the various organs which seemed to be injured by the action of the protein were fixed in Helly's solution and then they were stained with hematoxylin and eosin, or with Giemsa, for microscopic study.

TABLE I

Rabbit No.	Type of protein	Number of injections	Amount of each injection	Interval between last injection and autopsy
			mg.	*days*
R 1536	304	3	20	7
R 1166	304	3	20	10
R 1734	Alkali-soluble	5	10	7
R 1803	Ma-100	5	20	11
R 1600	304	4	20, ip.	2
			10, iv.	
R 1105	304	6	20	2
R 1735	Alkali-soluble	10	10	6
R 1151	304	12	10	2
R 1153	Alkali-soluble	12	10	2
R 1112	304	7	14, ip.	5
			6, sc.	
R 1109	304	10	20	1
R 1104	304	12	20	3
R 1804	MA-100	13	20	21
R 1106	304	15	18, ip.	4
			6, sc.	
R 1102	304	20	20	7
R 1168	Alkali-soluble	25	10, ip.	2
			5, sc.	
			(5 injections)	
R 1608	304	36	10, iv.	2
		10	10, ip.	2
R 1211	304	48	10, iv.	Not dead

Induced Foci of Plasma Cells

At autopsy the omentum usually showed a hyperplastic reaction; it was thickened, had an increase of milk spots, as well as much new fibrous tissue and many new blood vessels. In several of the animals (R 1102, R 1168, R 1153, R 1735[1]) small white nodules were found

[1] These are serial numbers of the work of the department covering a term of years.

attached to the omentum, body wall, and large intestine. Often there was inflammation of the body wall, with a new growth of small vessels and a roughening of the whole surface.

The omenta of five normal rabbits (R 650, R 651, R 652, R 578, and R 879) were studied in comparison with those of the experimental animals. Plasma cells were found in only two of these and in rather small numbers. The greater part of each normal omentum, as seen in section, was made up of fat cells. The remainder of the cellular structure was made up of undifferentiated cells, small groups of lymphocytes, a few monocytes, and a network of mesothelial cells.

Table II indicates the organs in which plasma cells were found in the experimental animals. The omentum was the site of the greatest proliferation of these cells, although they were present in the liver, spleen, cecum, body wall, and scattered lymph nodes. Two animals which received intravenous injections also showed a few plasma cells in the bone marrow. In the omentum the plasma cells were found in the milk spots, about the blood vessels, and scattered through the connective tissue. Some omenta were so stimulated by the protein that the plasma cell was the predominating cell element (Fig. 5). Where they were so vastly increased in numbers, the lymphocytes were also increased. New lymph follicles with germinal centers could be made out where the irritation had been greatest. Plasma cells were not seen in these lymph follicles, although they often encroached on the borders of them. On the whole the two strains of cells were quite definitely segregated, but one animal (R 1168) had areas in the omentum in which plasma cells and lymphocytes were mixed. The lymphocytes, as a rule, lay in the spaces between the fat cells, and the plasma cells always in the diffuse connective tissue.

The white nodules noted on the omentum, body wall, and large intestines were made up of necrotic material. Many of the cellular elements were still recognizable in them as plasma cells and leucocytes. The tissue surrounding these nodules was usually made up of connective tissue cells, including many plasma cells. One such nodule was taken from the large intestine of R 1735; another from the large intestine of R 1153. In these could be seen three stages of the growth of new fibrous tissue. There were areas of degenerating plasma cells and leucocytes, areas of deposition of fibrin and slight hemorrhage,

TABLE II

Organs in Which Plasma Cells Were Found

Rabbit No.	Omentum	Kidney	Liver	Spleen	Body wall	Peyer's patches Small intestines	Wall of large intestines	Bone marrow	Lung	Lymph nodes — Axillary	Submaxillary	Popliteal	Inguinal	Retroperitoneal	Tracheal	Mesenteric	Cecum
R 1112	++++	o	o	o	++++	o	++++	o	o	o		o	o	o		o	
R 1153	++++	o	+	o				o				o				o	
R 1105	++++	o	o	o	+++			o		o	++++		o		++	o	
R 1151	++++	o	o	o				o		o							
R 1106	++++		o	+	+++			o				o	+				
R 1104	++++	o	o	o		o		o		+		o	o			+	
R 1109	++++	o		o		o		o	o++++	+	+	+			+	+	
R 1536	++++		o	o			o	o	+	o						+	
R 1102	++++	o	o	o				o					o			o	
R 1600	++++	o	+	o									o			o	o
R 1734	++++	o	o	+				o		o	+		o			+	
R 1168	++++			+	++++	++	++++	o				L+ R o					
R 1735	++++	o	o	o				o	o	+	+	o	o	o	o	o	
R 1166	+++	o	o	o				o		o	+++	o				++	
R 1608	++++	o	o	o				+	o	o		o			o	+	
R 1803	++++	o	+	o		+		o	o	o		o	o			o	
R 1804	++++	o	+++	o		o		o		o			+	o		o	

(Liver column: "Parasites" noted for R 1151)

and areas of new fibrous tissue. About the base of the gland cells were many lymphocytes and many young plasma cells. One nodule from the body wall of R 1168 showed an infiltration of the plasma cells into the connective tissue between the muscle bundles. The lung of R 1536 contained an area of bronchopneumonia about which was a small amount of fibrous tissue. In this fibrous tissue and infiltrating into the pneumonic area were many plasma cells. There were also present small nodules of lymphocytes with germinal centers.

The animals which received the largest amounts of the protein over the longest periods of time (R 1102, R 1109, and R 1168) showed the greatest proliferation of plasma cells. These animals also revealed the greatest variety of stages in the life cycle of the plasma cell. The period elapsing between the last injection and the autopsy was a determining factor in the differentiation of the plasma cell. More true Russell body cells were found in the tissues of those animals, especially R 1804, in which this period was the longest. The largest numbers of degenerating plasma cells were not necessarily present in these animals, but time was probably not so much responsible for them as was crowding.

Histogenesis of Plasma Cells

Most of the plasma cells in both the stimulated tissues and the normal organs were of the typical Marshalkó variety. However, other plasma cells with definite characteristics of immaturity were always seen in or near all the groups of typical forms. There were also older degenerating cells, but these were rare except in the necrotic white nodules which were composed of them almost wholly.

The primitive mesenchymal cells and the young cells in the milk spots were the precursors of the plasma cells. Undifferentiated mesenchyme cells are normally present scattered diffusely in the connective tissues and lying along the blood vessels. The milk spots of the omentum are made up chiefly of relatively undifferentiated cells which have the potentiality of developing into monocytes or macrophages. These cells have been termed polyblasts by Maximow (11). Sabin et al. (1) have shown them to be transformed readily into monocytes after intraperitoneal injections of the tuberculo-phosphatide. Monocytes, lymphocytes, and cells which are more immature

than these so called polyblasts are also found in the milk spots. These young cells in the milk spots also are often called primitive cells. In stained sections they appear slightly younger than blast forms of lymphocytes and leucocytes.

Two primitive mesenchymal cells are shown in Fig. 1 (see arrows). These cells were characterized by large nuclei and little if any cytoplasm. The structure of the nuclei was a fine network with little chromatin. This stained light gray-blue and the nucleoli, which were small and usually two or three in number, stained red or purple. When the cytoplasm was discernible, it was of a slightly basophilic quality. The development of the primitive cells into the Marshalkó type plasma cells was a graded transitional process in which both the nuclei and cytoplasm changed in staining quality and structure. The fact that the young cells were of different ages could be readily made out. Those slightly older than the primitive cells showed slight condensations of chromatin near the nuclear membranes. The nucleoli of these cells were somewhat larger than those in the undifferentiated cells, and the cytoplasm showed beginning basophilia. The grade of basophilia of the cytoplasm and the amount of condensation of chromatin of the nuclei were indices of how far advanced from the primitive cell any one of these had become. Many of this type of cell are shown in Fig. 1. The photograph was taken from a section of body wall of R 1168. A portion of the section was composed almost entirely of young cells and there were also a few lymphocytes. The part shown was from a nodule in the body wall which was almost tumor-like in its cellular picture. Typical plasma cells were seen in groups and scattered throughout all parts of the tissue surrounding the nodule.

As the young forms matured, they fulfilled the criteria of the Marshalkó plasma cells. Young cells were seen which had one or all of the specified characters. Some had a distinctly basophilic cytoplasm with a clear area in its center. The chromatin in the nucleus was so condensed as to give the appearance of the cart-wheel nucleus, a *Radkern*, and in most of this type of cell the nucleoli were retained. The nuclei were either eccentric or central in position.

In groups of the young plasma cells some were found with mitotic figures; one such is shown in Fig. 1. Reproduction of the plasma cell in this early phase by mitosis, though not rare, was not very common.

As the cells matured, the nuclei became smaller and the chromatin more condensed, especially at the nuclear membrane. The condensation of the chromatin was in blocks which gave the characteristic cart-wheel nucleus. The basophilic quality of the cytoplasm became more pronounced. Most of this type of cell had eccentrically placed nuclei and clear areas in the centers of their cytoplasm. In these mature cells the nucleoli were lost. These cells are shown in Fig. 2. In this figure are seen typical plasma cells and also two or three cells which have one or more of the criteria of Marshalkó plasma cells, but which are too young to have them all. There are also areas such as that represented in Fig. 5, in which all the cells are of the mature type. The plasma cells proliferated by both mitosis and amitosis, and this latter fact is shown by the presence of two or three nuclei, or by large cells budding smaller ones.

Even in the mature plasma cells, gradations of morphological character were evident. Not only were some obviously younger than the typical Marshalkó variety, but there were also older ones. The cytoplasm of these latter had become spongy and somewhat granular. The spongy cytoplasm conformed to the description of granuloplasm by Unna. The nuclei of cells with granuloplasm were usually smaller than those of the less mature cells. The cytoplasm of the younger cells, whether of the pre-Marshalkó type or of the Marshalkó type, appeared homogeneous in contradistinction to the granuloplasm.

Following the development of granuloplasm, the plasma cells began to degenerate. Two types of degeneration occurred. Some cells, as they became senile, lost their basophilic appearance, the nuclei became pycnotic, and often vacuoles appeared in the cytoplasm. There developed in certain of these cells hyaline bodies with the same appearance and staining reactions as the true Russell body cells. Most of the cells undergoing degeneration of this first sort were packed closely together, and it is possible that crowding led to their degeneration. The other type of degeneration was into characteristic Russell body cells. Some of the plasma cells developed acidophilic granules and hyaline or crystalline bodies appeared later in the cytoplasm; each of these bodies seemed to be a segregated part of the latter. The nuclei were fragmented or pycnotic and usually were in the eccentric position. The true Russell body cells were found infrequently in any of the areas

which had been stimulated with the protein. The first type of degeneration was frequent wherever the plasma cells predominated in the tissues, as in the white nodules described above. True Russell body cells could be made out scattered through the matrix of aggregates of the sort. Fig. 3 shows degenerating plasma cells. A few of these contain acidophilic granules and hyaline bodies (Arrows A).

Supravital Studies

Supravital studies of plasma cells have been reported by Bloom (12), Forkner (13), Jackson *et al.* (14). Their descriptions are quite in agreement, except for the fact that Jackson did not find neutral red bodies in the cytoplasm constantly.

Omenta from normal rabbits and from rabbits injected with tuberculo-protein were examined with the supravital method. The stimulated omenta were studied first and the findings correlated with those of the fixed tissues. All omental spreads were fixed with methyl alcohol and stained with methylene blue and Giemsa after they had been studied by the supravital technique.

The plasma cells appeared round or oval, when stained supravitally, or they took on peculiar configurations when pressed by other cells. The cytoplasm was a yellowish gray and, in the spreads, the mitochondria were not seen unless a small amount of a 1:10,000 solution of Janus green was added. Mitochondria did not always stand out even after this treatment. When demonstrable, they were either scattered throughout the cytoplasm, or were grouped in the center of it. Neutral red bodies were rare. Occasionally, in very large cells, a thinning in the center of the cytoplasm represented the clear area so characteristic in fixed staining. The mitochondria were usually numerous, some cells having as many as 30 or 40 of them. They varied in size and in shape and were usually smaller than those in young lymphocytes. They took the forms of small rods or round dots, though the rod-shaped mitochondria were more frequently seen.

The nuclei of these cells were usually about the same shade of gray as the cytoplasm. This made them difficult to see, though the heaping up of the chromatin was often distinctive. If the cells were young enough, nucleoli stood out as small pearls. Differentiation of young cells from older ones was difficult to make out, because the charac-

teristics of age were not marked in preparations made by this technique, except in the case of the Russell body cell.

Russell body cells were found in the tissues of three of the experimental animals. The cytoplasm of these cells appeared as gray as the cytoplasm of the younger cells. Some of the Russell body cells had from three to five cytoplasmic lobulations; others had lobulations which entirely filled the cells. Each lobulation seemed to be a segregated part of the protoplasm, and was smooth and non-granular. The nuclei were always eccentric in position and usually smaller than those of the less mature cells. The cells with the larger number of lobulations had no mitochondria, and the nuclei were so small that they could not be seen or else possibly were directed away from the microscope.

The cells described here as plasma cells were found singly and in groups throughout all stimulated omenta and were usually beneath the surface, so that they were difficult to bring into focus. They were most numerous along the blood vessels and in the milk spots. Lymphocytes were also seen, but as already mentioned, they were rarely in the groups of plasma cells.

The two animals which received intravenous injections of the protein developed as many as 4 per cent plasma cells in the peripheral blood stream on several occasions. Here they had the same tinctorial properties as in the omental spreads, but they usually contained from five to eight neutral red bodies grouped in the center of the cytoplasm. Maximow (11) has previously shown that the clear area is the site of the centrosome, and it is not therefore peculiar that there was a grouping of the vacuoles stained with neutral red around this space. The mitochondria stained more brightly and were seen with less difficulty than in the omental spreads. They were usually scattered throughout the cytoplasm. The nucleus often was very indistinct, being of about the same shade of gray as the cytoplasm.

Unstimulated omenta also contained cells which were recognized as plasma cells. In these omenta they were found rarely, although one animal (R 1606) had many of them.

By the supravital technique, plasma cells were differentiated from lymphocytes by their darker gray cytoplasm, eccentric nuclei, and the variations in size, staining quality, and distribution of mitochondria.

In the young lymphocytes the nuclei were usually large and the mitochondria stained with ease and were grouped about the periphery of the nucleus. The nucleus of the young lymphocyte stood out plainly, while that of the plasma cell was usually indistinct.

The plasma cells in these same omental spreads, when stained with methylene blue and Giemsa, were for the most part of the Marshalkó type. The cytoplasm of many of them had a tendency to be granular. Russell body cells had the same appearance as in tissues stained with hematoxylin and eosin. The nuclei of the typical plasma cell showed an unaltered chromatin arrangement, but stained light pink. As by the supravital technique, these cells were grouped about blood vessels, in the milk spots and scattered throughout the connective tissue stroma. In some parts of each omentum many lymphocytes were found, but only rarely amongst the plasma cells.

Some omenta showed increases in the number of fibroblasts and clasmatocytes. In these, often, the fibroblasts were seen with their fibrils about single plasma cells. This peculiar relationship is shown in Fig. 4.

Lack of Relationship of Plasma Cells and Lymphocytes

In many aspects plasma cells and lymphocytes resemble each other. Plasma cells are found where lymphocytes develop, and the stimulating effect of the tuberculo-protein causes many young lymphocytes and new lymph follicles, as well as plasma cells, to be formed. The plasma cells are found almost always in the connective tissues; even when found in the lymph nodes they are in the connective tissue cords. They are a constant element in the submaxillary lymph nodes and occasionally may be present in any other of the lymphoid structures (Table II). In the submaxillary nodes they are usually present in rather large numbers, while in other nodes they are few in number.

As a rule, plasma cells are absent from the popliteal and inguinal nodes. Because of this, and the fact that lymphocytes have been termed the precursors of plasma cells, these nodes were subjected to direct stimulation or irritation by the protein. To effect this stimulation of the inguinal nodes, two animals were injected subcutaneously in the groin. Another animal was given injections of the protein into its left foot pad so that the material would drain through the popliteal node.

R 1106 received fifteen injections of the material in the right groin, each of 6 mg. in 2 cc. of fluid. R 1112 received five similar injections in the right groin. R 1168 was given five injections of 5 mg. each in its left foot pad. When these animals were autopsied, supravital studies of the regional lymph nodes showed no plasma cells. The inguinal nodes of R 1106 were very much enlarged and contained epithelioid cells, but those of the other animals were not enlarged and were free from abnormal components.

The fixed sections of the right inguinal nodes of R 1106 contained few plasma cells, and there were a few scattered plasma cells in the left popliteal nodes of R 1168. The other regional nodes or those which were subjected to the irritation of the protein were free from plasma cells.

Young plasma cells differ much from young lymphocytes in their morphology. The nuclei of young plasma cells are denser in chromatin; they simulate the nuclei of the older cells, but are larger and usually contain nucleoli. The primitive cells, of course, are so undifferentiated that they have no specializing criteria. Primitive cells which form plasma cells are much like those that form lymphocytes. The cytoplasm of the youngest differentiated cells of the plasma cell series is usually basophilic, although not so markedly as that of older cells. Young lymphocytes appear much like the young plasma cells, although their nuclei are centrally placed, and often bean-shaped. The chromatin in the nuclei of the young cells of the lymphocyte series is usually in thread-like formations, not condensed near the nuclear membranes. The cytoplasm of these cells is slightly less basophilic than that of the plasma cells. Mitotic figures are more frequently seen in groups of young lymphocytes than in plasma cells.

Young lymphocytes are best seen in or near the germinal centers of the lymph nodes. The mesenteric nodes contain many more young forms than do other nodes, and they are abundant in the sinuses. Where these young cells are found there are no plasma cells of the Marshalkó type.

There is no difficulty in discriminating Marshalkó plasma cells and the degenerating forms from lymphocytes of all types. It has been a rule to reserve the name plasma cell for these mature forms. However, many workers have included abnormal types of cells in this category. This should not be done unless these cells have one or several of the characters of true plasma cells, and show by proximity that they are developing into more mature typical forms. The differential

characters of the young cells of the lymphocytic and plasma cell series are definite though not marked. This, together with the fact that few plasma cells developed in organs rich in lymphocytes after direct stimulation of those organs, makes it clear that plasma cells are not derived from lymphocytes. With a separation of the young cells into two classes the maturation cycle of the plasma cell is complete.

SUMMARY AND CONCLUSIONS

As result of finding numerous plasma cells in the omenta of rabbits injected with tuberculo-protein, a method to induce the production of large numbers of these cells has been discovered. The tissues in which they were pronouncedly increased were the subserosal connective tissues of the omentum, body wall, and intestinal wall.

The precursor of the plasma cells is a primitive connective tissue cell. As this cell develops into the typical Marshalkó plasma cell there is a progressive increase in the basophilia of the cytoplasm, the nucleus becomes eccentric, a condensation of the chromatin occurs near the nuclear membrane, and there is a loss of the nucleoli. At the time when the nucleus assumes the eccentric position, the clear area appears in the center of the cytoplasm. The early cells are capable of reproducing themselves by mitosis, while the typical mature cells divide by amitosis.

The mature plasma cells often have muddy, spongy cytoplasm which contains acidophilic or hyaline granules as the cells grow old or begin to degenerate. The cells with granules or hyaline bodies usually have pycnotic or fragmented nuclei. These cells are the final stage reached by some plasma cells. Others, when degenerating, show vacuoles and signs of senility. Those with the granules and hyaline bodies are the so called Russell body cells.

Plasma cells developed in greatest numbers after our largest injections of tuberculo-protein. The differentiation into young, mature, and senile forms was most clearly recognizable when some days had been allowed to elapse after the last large injection of the stimulating agent.

A description of the plasma cell as viewed supravitally has been given. The cells are met in the blood stream as well as in the tissues. They are characterized by their deep yellowish gray cytoplasm, in-

distinct eccentrically placed nuclei, and large numbers of mito-chondria.

The plasma cells differ from lymphocytes, in that they did not develop in large numbers after direct stimulation of the lymph nodes with tuberculo-protein. The young plasma cells also differ in mor-phology from the young lymphocytes. When plasma cells were found in the lymph nodes they were in the connective tissue cords.

The plasma cell is a definite entity, having a maturation cycle. It is stimulated to great proliferation by certain toxic irritants.

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EXPLANATION OF PLATES

PLATE 30

FIG. 1. Section from body wall of Rabbit R 1168 which received twenty-five intraperitoneal injections of 10 mg. each of alkali-soluble protein. It shows many young plasma cells; two are primitive connective tissue cells (Arrows), many have eccentrically placed nuclei, and the chromatin of most of the nuclei shows a begin-ning condensation near the nuclear membrane. Hematoxylin and eosin. × 1,000.

FIG. 2. Section from omentum of Rabbit R 1102 which received twenty intra-peritoneal injections of 20 mg. each of 304 protein. It shows plasma cells of the typical Marshalkó variety. The arrow points to a cell assuming the characters of the mature form. Hematoxylin and eosin. × 1,000.

FIG. 3. Section from the wall of the large intestine of Rabbit R 1153 which received twelve intraperitoneal injections of 10 mg. each of alkali-soluble protein.

It shows degenerating plasma cells, including some cells which contain Russell bodies. Arrows labeled A point to almost typical Russell body cells, while Arrows B indicate cells with acidophilic granules. These cells are less mature than the typical Russell body type. Hematoxylin and eosin. × 1,000.

FIG. 4. Omental spread taken from Rabbit R 1166 which received three intraperitoneal injections of 20 mg. each of 304 protein. It shows four plasma cells, one of which has about it the fibrils of a fibroblast. It was first studied in supravital neutral red and Janus green, then fixed in methyl alcohol and stained with methylene blue and Giemsa. × 1,000.

PLATE 31

FIG. 5. Section of omentum of Rabbit R 1102 which received twenty intraperitoneal injections of 20 mg. each of 304 protein. It shows a focus of typical plasma cells of the mature form. Hematoxylin and eosin. × 1,000.
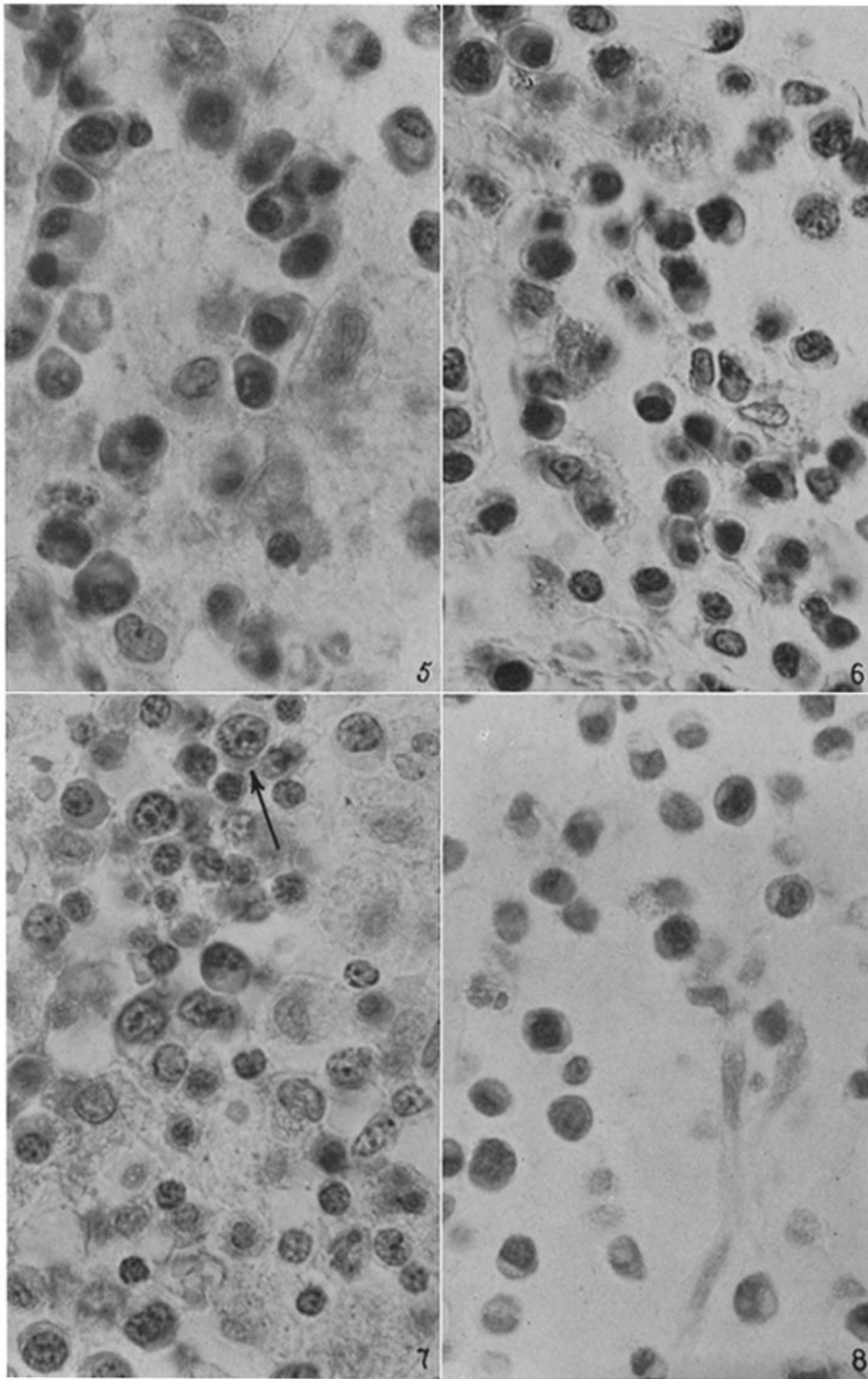
FIG. 6. Section of omentum of Rabbit R 1168 which received twenty-five intraperitoneal injections of 10 mg. each of alkali-soluble protein. This figure shows plasma cells in several of the phases of maturation. One cell in the lower right corner is budding a smaller cell, a mitotic figure is present above the center to the left, and there are several young cells scattered through the figure. Hematoxylin and eosin. × 1,000.

FIG. 7. A portion of the same section shown in Fig. 1. It has many young plasma cells, one (Arrow) just beginning to differentiate from the primitive type. In the background are young connective tissue cells and clasmatocytes. Two large pale clasmatocytes are plainly seen near the upper right border. Hematoxylin and eosin. × 1,000.

FIG. 8. Section of the same material as Fig. 5, but from a less cellular part. It shows scattered plasma cells, some more mature than others, and several long fibroblasts. Hematoxylin and eosin. ×1,000.
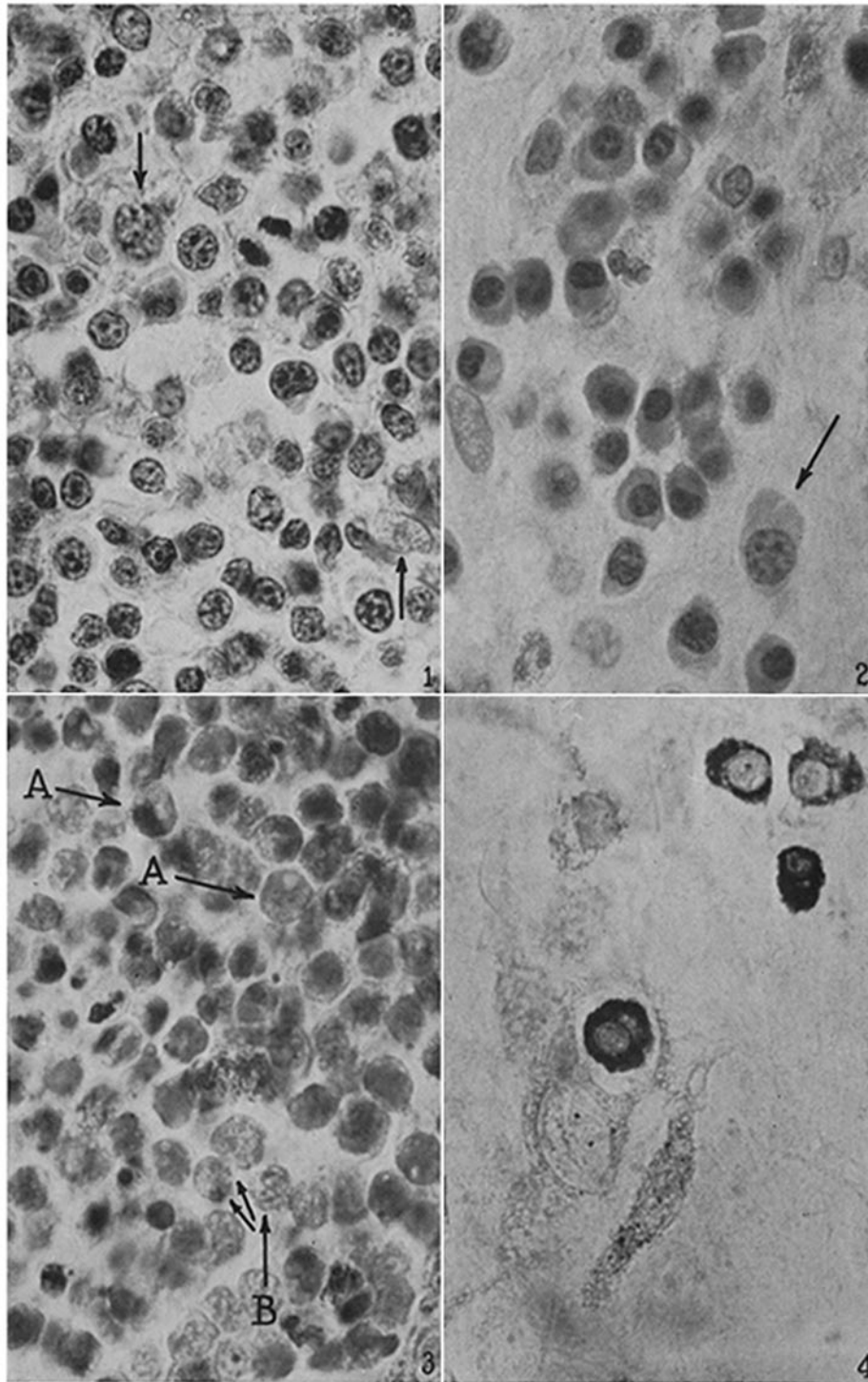
(Miller: Histogenesis of plasma cells)

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