OBSERVATIONS ON THE ORIGIN, DISTRIBUTION AND SIGNIFICANCE OF FUCHSIN BODIES, WITH SPECIAL STAINING TECHNIQUE.[1]

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Since the first description of fuchsin bodies by Fox (4) in 1858, an extensive literature upon the subject has been gradually accumulating and still, after fifty years, but little real progress has been made in the solution of their true pathological significance. Such widely divergent views are maintained by the leading workers that it is practically impossible for one to gain any clear conception of the subject from a review of the literature.

Though numerous opinions have, from time to time, been advanced to explain the origin and nature of fuchsin bodies, the general trend has been to narrow the question to two more general hypotheses.

I. Origin from cell granules.
   1. Plasma cells.
      a. Degeneration of "granuloplasm," (Unna (17)).
      b. Plasma cell granules, (Schridde (12), Fabian (2)).
   2. Origin from other granular cells, (leucocytes or *Mastzellen,* Lubarsch (7), Munter (8), and others).

II. Origin from red blood corpuscles, (Saltikow (11), Touton (16), Thorel (15), and others).

Detailed discussions of these hypotheses, with bibliography, may be found in several of the recent articles (3, 8). The object of this investigation has been to attempt to clear up some of the more fundamental questions which seem to have been a source of confusion. I refer, in particular, to the conception of what shall be considered a fuchsin body, the distribution and the relations of such bodies to other elements, and finally to the origin and significance of fuchsin bodies.

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The material for the present investigation comprises too extensive a list to publish in detail. It includes over two hundred distinct specimens representing nearly all the organs of the body and a great variety of pathological conditions as well as some normal tissues. The following list will give a general idea of the material used:

1. Tumors—benign and malignant	100
2. Inflammatory conditions—acute, chronic, abscesses, and organizing exudates	54
3. Vascular lesions—haemorrhages, thrombi, and infarcts.	16
4. Lesions of Spleen (7 types)	18
5. Lesions of lymph glands (6 types)	21
6. Lesions of liver (9 types)	9
7. Lesions of kidney (4 types)	6
8. Corpora lutea (ovary)	6
9. Goitres	3
10. Lesions of brain (3 types)	3
Total	236

This material was selected partly at random, and partly from lesions in which I felt sure of finding fuchsin bodies. The tissues were fixed by various methods, including Zenker's fluid, Orth's fluid, alcohol (95 per cent.), and formalin (10 per cent.). Paraffin and celloidin sections have been studied after staining with hematoxylin and eosin, van Gieson's stain, Weigert's fibrin stain, and Weigert's myelin sheath stain (Pal modification), as well as by a staining method which I have developed for this particular purpose. Of the staining methods mentioned above, the Weigert stains give by far the best results, though they are not adopted to routine work, while the other stains lack sharpness of definition and contrast. It is worthy of note that none of the stains recommended for fuchsin bodies is absolutely constant in reaction, unless it be hematoxylin and eosin.

The technique which I have employed for routine work meets some of these difficulties. It is relatively easy of application, gives exceedingly sharp contrast stain and, in my hands, is more constant in reaction than other methods.

Tissues are fixed in 10 per cent. formalin or 95 per cent. alcohol, formalin being preferable. Paraffin or celloidin sections are stained strongly in Delafield's hematoxylin. Stain five minutes in a 2 per cent. aqueous solution of acid fuchsin. Transfer to Lugol's solution for five to ten seconds. Wash quickly in water or 95 per cent. alcohol to remove iodine. Stain five to twenty seconds in a saturated aqueous solution of orange "G." Dehydrate with alcohol. Clear with any clearing reagent.

By this method, fuchsin bodies, red corpuscles (formalin fixed), and eosinophile granules stain a brilliant cherry red; nuclei, blue; cell protoplasm, buff to orange. No other type of hyaline ever takes the red stain and no other tissue element regularly takes this stain. Keratinized epitheleum, Mastzellen granules, and zymogen granules, occasionally stain red; fibrin stains red after alcohol fixation. All blood stained tissues stain red.

In using this stain, the treatment with Lugol's solution may be omitted and

the section washed until it has a faint pink tint, then the usual method is followed. The red stain is not usually so brilliant after this procedure. Again better results are sometimes obtained when the iodine is completely removed with alcohol before staining with orange "G," while a saturated alcoholic solution of orange "G" gives improved results with some tissues. The process of differentiation constitutes the one, though slight, difficulty of the method.

This technique can be recommended for demonstrating blood elements in tissues after formalin fixation and it is an excellent fibrin stain after alcohol fixation. It is not applicable for any purpose after Zenker's or Orth's fluid.

By reference to the literature, one may see that the bodies described as fuchsin bodies, by various authors, and most commonly, though probably improperly, designated as "Russell's fuchsin bodies," do not agree in all particulars, and this has undoubtedly given rise to much confusion. In considering the various types of fuchsin bodies (if there be such), it might be well to state that there is one form in the description of which all authorities agree. These bodies are round or oval on section, varying in size from that of an eosinophile granule to two to three times the diameter of a red blood corpuscle. They are highly refractile, and sharply contoured, occurring singly or, more commonly, in clusters of variable numbers and variable sizes, both intra and extracellularly. They show a strong affinity for acid stains. Such, in brief, may be considered the typical fuchsin body.

In a recent paper Fick (3) considers only such bodies as are round or oval, sharply contoured, and staining yellow with van Gieson's stain as true fuchsin bodies. Unna (18), on the other hand, has described a variety of forms, including columnar, prismatic, cuboidal and other shapes. Likewise there has arisen some difference of opinion in regard to staining reaction.[2]

Some claim that the typical fuchsin body stains yellow with van Gieson's stain; others, that it stains orange; and still others, that it stains red, excluding all bodies not staining the typical color. The same is true with other staining methods. This seeming discrepancy is due, in part, to composition of stains used by different workers and, in part, to the nature of the body in question, as perhaps modified by fixation. Most authorities agree that van Gieson's method stains fuchsin bodies yellow. What then of those bodies typical in morphology and not in staining reaction? Under

[2] For discussion of this question see Fick, *loc. cit.*

the term "fuchsin body," is one to include only those typical in both morphology and staining reaction or is the type subject to variation in one or both respects? This is naturally the first question which presents itself. It can be answered only after studying fuchsin bodies from a great variety of conditions by various methods of fixation and carefully checking one method of staining against the others. This gives the first reason for the extensive list of material I have used for this work, and the second is that I have been unable to find any article which has considered the question from so broad a field.

Considering first the question of morphology, I have found that by far the most common type of fuchsin body, after all methods of fixation and staining, is the oval or rounded, sharply contoured form. In many cases, this is the only form present. In other specimens, however, I have observed hyaline bodies of irregular shapes, though staining typically by all methods, and associated with typical fuchsin bodies. Further, the groupings and distribution were identical with those of typical bodies and, in some instances, both types could be observed in a single group. In still other cases, I have observed definite hexagonal plates and prisms, similarly associated with the typical forms and in no wise to be distinguished from them except in point of morphology. In one case (chorio-epithelioma) these hexagonal plates and prisms were the predominant forms. The prisms varied from very minute crystals to bodies measuring forty micra in length and from twelve to fifteen micra in diameter. The hexagons were apparently cross sections of the prisms.

In a majority of the cases in which the morphologically atypical fuchsin bodies were observed, bodies could be found which might be grouped in a series of gradually increasing irregularity from those showing only slight degrees of irregularity to those with markedly irregular morphology. In such a series, so gradual are the transitions that one must either consider all forms as fuchsin bodies, or confine his term to those which show no irregularity whatever. The latter position seems, to me, manifestly unjustifiable and I feel confident in stating that it is possible for fuchsin bodies to exhibit an exceedingly wide range of morphological variations.

As regards staining reactions, extended experience with the stains usually employed for demonstrating fuchsin bodies has convinced me that we can, with certainty, differentiate the fuchsin body type of hyaline from all other hyaline formations. I consider this particularly true of the triple staining method which I have employed. Yet, in any section showing fuchsin bodies in abundance, it is rare to find them absolutely uniform in type and degree of staining reaction. Most commonly, certain bodies manifest a variation in intensity of staining, taking a fainter or heavier stain than the average body of approximately the same size. This is observed even in bodies of the same cluster or in the same cell. Again, there are bodies, morphologically of the fuchsin body type, which take in varying degrees a different type of stain. For example, with van Gieson's method, some bodies will stain constantly orange or pink, or, by my triple staining method, instead of the fuchsin stain, they will take the orange "G." At first, I have considered these variations as defects of the staining methods, but they have been so constant, even after repeatedly restaining the section and controlling one method by another, that I feel sure there are bodies which will constantly manifest these atypical reactions. The same types of variation are noted among the red blood corpuscles in the same specimen.

Another interesting group of bodies, which I have not seen described elsewhere, are those with "basophilic" or "polychromatophilic" reactions. It is manifestly a misnomer to speak of these as fuchsin bodies. Still, they have some properties in common. They are morphologically identical with fuchsin bodies, very refractile, show identical distribution and groupings, and even occur in plasma cells along with perfectly typical fuchsin bodies. With hematoxylin and eosin, van Gieson's stain, and with "hematoxylin —acid fuchsin—orange G," they invariably stain blue or purple. I have observed these in only a few specimens and am undecided as to their correct interpretation. They are, however, not the nuclear fragments so often seen in necrotic areas and can be easily distinguished from such. In one specimen of hypernephroma, these "polychromatophile" hyaline droplets were very numerous and constituted the predominant type.

That the term "fuchsin body" is a misnomer for all these bodies with atypical staining reactions is evident, yet, it seems highly probable that many of them are closely related to typical fuchsin bodies. They are possibly of like origin and have suffered some change, either physical, or chemical, which is responsible for their atypical staining reactions.

Before leaving this phase of the question I wish to emphasize the occurrence of cells, with granules of a "fuchsinophilic" nature, in association with fuchsin bodies.[3]

The occurrence of such cells has been frequently pointed out. It is not constant, but frequent, and the point which has impressed me most forcibly is that in many conditions where one would expect to find fuchsin bodies in abundance, we may find only a few, and those usually small, while the section may be crowded with cells with granules of a fuchsinophilic character. The cells may be, in some cases, largely polymorphonuclear, though they are as commonly mononuclear cells of various types, principally of the plasma cell type. The cell granules vary in size from those as small as neutrophile granules to granules larger than those of the eosinophile of the blood, gradually shading into definite fuchsin bodies. The gradation in size and the identity in staining reaction is such that it is difficult to draw a line of separation between cells with fuchsinophile granules and fuchsin bodies. This difficulty is increased when both granules and fuchsin bodies exist in cells of the same class.

Therefore, as regards both morphology and staining reactions of fuchsin bodies, we undoubtedly have variations from the typical, and these are of such a nature as to render it very difficult to establish sharp lines of demarcation. There is the typical group, easily identified; there are bodies, morphologically atypical, but recognizable by staining reaction and association with typical bodies; there is a third group, atypical in staining reaction but typical in mor-

[3] These cells are usually referred to as eosinophile cells. I use the term "fuchsinophilic" to avoid confusion with the true eosinophile cell, as I do not consider it certain whether or not these cells are identical with true eosinophiles. I am inclined to doubt that many of them are identical with these cells. Some are probably Mastzellen, the granules of which will occasionally stain by my method.

phology and grouping. The significance of these two possible atypical groups will be considered later.

Leaving this phase of the question for the present, I will consider briefly the distributions and relations of fuchsin bodies. The literature contains numerous monographs on the occurrence of fuchsin bodies in tumors, gastric conditions, rhinoscleroma, as well as a number of other conditions, where this question is considered in detail, and I shall discuss only such points as appear to have some direct bearing on our interpretation of the fuchsin body.

The first point to be noted is that there is no single pathological condition, or no class of conditions, in which fuchsin bodies occur exclusively. Reference to the appended list of material will serve to show how widespread this occurrence is. The distribution of fuchsin bodies in tissues has been the subject of much discussion. Early observers described them in cells of granulation tissue. To a certain extent, this observation has received abundant confirmation, in so far that it is in granulation tissue and "granulation tissue areas" of tumors and other pathological conditions, if not actually in the connective tissue cells that these bodies occur most abundantly. Particularly is this true of areas rich in plasma cells. Within such areas, fuchsin bodies occur singly or in clusters; some are extracellular, while many of the plasma cells are filled with droplets of various sizes. The relation to plasma cells is so marked that, while all recognize it, some have advanced the idea that fuchsin bodies never occur except in relation to plasma cells.

However, other competent observers have described them in association with numerous cell types. For example, Klien (5) has described fuchsin bodies in connective tissue cells, Lubarsch (7) in association with *Mastzellen* and polymorphonuclear leucocytes, Sternberg (14) and Munter (8) in polymorphonuclear leucocytes, Konstantinowitsch (6) in endothelial cells, Askanazy (1) as hyaline metamorphosis of lymphocytes, and still others might be mentioned. Saltikow (11), Touton (16), Thorel (15), and others have described fuchsin bodies within the lumina of blood vessels.

I have been able to confirm most of these observation and, while the occurrence of fuchsin bodies within cells other than plasma cells is comparatively rare, there is no question but that perfectly

typical fuchsin bodies do occur in other types of cells. In the series of specimens I have studied, I have found typical fuchsin bodies in the following types of cells: plasma cells, most numerously; connective tissue cells, large mononuclear cells; more rarely, in cells of epithelial tumors, of adrenal tumors, of round cell sarcomata, and of endotheliomata; in liver cells in four cases; in stratified squamous epithelium in two specimens; in epithelium of kidney tubules in one case; in polymorphonuclear leucocytes in one case. Further, this series includes several sections in which no plasma cell areas were to be found, namely, one section from kidney and one from liver. I have also carefully avoided including in this list the group of fuchsinophilic cell inclusions so frequent in tumor cells and necrobiotic cells of all types.[4]

There has been much discussion as to the occurrence of intravascular fuchsin bodies. Several observers have described forms resembling hyaline thrombi, but whether or not these bodies are to be classed as fuchsin bodies, and in some cases, whether or not they are really intracapillary are disputed questions. This type of body is shown best in gastro-intestinal material; gastric polyps furnish particularly good examples. In sections from such conditions, I have noted large hyaline masses completely filling capillaries which are possibly true hyaline thrombi; again, hyaline masses similarly situated showed lines marking off individual bodies of various sizes composing the mass, and finally, clusters of perfectly discrete fuchsin bodies, typical in every respect, filled small capillary vessels. These capillaries are frequently so situated that their contents may have been subjected to the post-mortem action of certain ferments, notably gastric juice; this observation suggests the possibilities that these bodies are artifacts.

As has been pointed out, the areas in which fuchsin bodies occur most numerously are granulation tissue areas, rich in plasma cells, and they are equally rich in newly formed capillaries. Cross sections of such capillaries frequently present the "signet-ring" appearance. When such capillaries contain hyaline thrombi or

[4] The cellular and nuclear inclusions referred to were included in the Russell (10) description and are still considered by many as belonging to the general class of "fuchsin bodies." I have omitted them to avoid discussing the type of body to which I refer in this connection.

fuchsin bodies, they are very difficult to distinguish from plasma cells containing fuchsin bodies and a nucleus crowded far eccentrically. I have observed even large vessels containing numerous fuchsin bodies. This has been noticed, particularly after alcohol fixation, where one of two conditions existed: (1) either the red blood corpuscles were laked and showed only as shadows; or (2) more frequently, no red blood corpuscles could be made out as the contents of the vessel were more or less fused and shrunken to one side of the vessel wall, while the free edge of the mass showed pseudopodia and nodular projections, some of which were very bulbous at the extremity and suggested constriction; in the open space were numerous perfectly typical fuchsin bodies. The tissue immediately about such areas stains strongly with the same stain as the fuchsin bodies, while at a little distance, the field is filled with typical intra- and extracellular fuchsin bodies. This appearance marks the smaller vessels and their course can frequently be traced through the tissues by this halo of fuchsin bodies, and what I call "blood staining" of the tissues.

If, as has been claimed, the fuchsin body is the result of a degenerative process in the plasma cell, these cells, in areas rich in fuchsin bodies, should show some evidence of degeneration other than the mere presence of fuchsin bodies, unless plasma cell degeneration is always indicatd by such formations. This we know is not the case. It has been my experience that the plasma cells in fuchsin body areas are remarkably well preserved, as a rule, while in areas showing degenerative changes and necrobiotic cells, fuchsin bodies are exceedingly rare. For example, necrotic areas of tumors and infarcts or abscesses seldom show typical fuchsin bodies, while the active periphery of such areas may show them in abundance.

While there is thus no relation between fuchsin bodies and degenerations, and while perusal of the literature shows that conflicting results have been obtained by those who have employed an iron reaction (3, 11), the distribution of fuchsin bodies in various tissues shows a very definite relation to blood vessels and to red blood corpuscles and to pigments derived from them. The presence of some type of hematogenous pigment is practically constant, though relationship between such pigment and the fuchsin bodies is

not always traceable. Hematin occurs so commonly in all sections that, as a rule, its presence is of no significance. There are cases, however, in which it is so closely associated with fuchsin bodies, that its presence can not be disregarded. In the case of chorio-epithelioma, previously referred to, I have been observing the progress of certain changes with reference to hematin and fuchsin bodies. The specimen was fixed in alcohol and all red blood corpuscles were laked. When first studied, there was an abundance of typical fuchsin bodies and crystalline forms, especially within and about some large vascular spaces; there were very few hematin masses. At present, after two years preservation in alcohol, there are fewer typical fuchsin bodies, and the areas previously occupied by them are filled with irregular fuchsinophilic masses and masses of hematin. Likewise, many of the fuchsin bodies show clumps of hematin about them and imbedded in them while some of the hematin masses show the form and grouping of fuchsin bodies.

Hematoidin and hemosiderin have both been observed in association with fuchsin bodies. Neither of these have I found to be constant though both are frequent findings, particularly hemosiderin.

The first point I wish to emphasize is the distribution of fuchsin bodies in chronic abscess formation. This condition is well illustrated by one specimen in my series from an abscess of the broad ligament.

The history of the case indicated a duration of eight years. The material was fixed in formalin. In describing the condition found in the wall of this abscess, we might regard the section as divided into three zones, from within outward: (1) zone of pus, (2) granulation tissue rich in plasma cells, (3) zone of hyaline connective tissue with a few foci of plasma cells. The zone of pus showed only an occasional fuchsin body, or cluster, and exceedingly few red blood corpuscles. The granulation tissue zone was crowded with fuchsin bodies of all types. There were large solitary bodies, clusters of large and small bodies, and both extra- and intracellular bodies of the granular type. There were also a number of hemaglobin-stained plasma cells. Numbers of these bodies showed atypical staining. Very few extravascular red blood corpuscles could be distinguished. Corpuscles in the vessels, though staining sharply, showed no distinct outlines but a decided tendency to fusion. Cross sections of some capillaries contained hyaline thrombi. There was an unmistakable parallelism between distribution of capillaries and fuchsin bodies. At the border line between Zones 2 and 3, fuchsin bodies were relatively few, except in vascular foci. Again in the plasma cell areas of Zone 3, there were a few fuchsin bodies. As the fuchsin bodies decrease from within outward, hematoidin and hemosi-

derin increased. The outer foci of plasma cells showed rich intra- and extracellular deposits of these pigments. A few plasma cells were observed containing both fuchsin body and pigment. The red blood corpuscles in the outer zone were more discrete.

The points to be particularly noted here are:

1. Absence of fuchsin bodies in areas of pus formation.
2. Absence of fuchsin bodies from inactive scar tissue.
3. Presence of large numbers of fuchsin bodies in active granulation tissue showing: (*a*) intravascular autolysis of red blood corpuscles; (*b*) absence of demonstrable extravascular red blood corpuscles; (*c*) parallelism in distribution of capillaries and fuchsin bodies.
4. Association of fuchsin bodies with hematogenous pigment.

My series of vascular lesions, including hemorrhages, thrombi, and infarcts, have shown some important pictures. Areas of hemorrhage, when large, or when fresh, are usually negative, except about the periphery. Smaller areas, showing organization, will show cells containing red blood corpuscles, some typical fuchsin bodies, as a rule, and cells with fuchsinophilic granules as well as cells containing variable amounts of pigment.

In a ruptured tubal pregnancy in which the walls of the tube contained diffuse extravasation of blood, the following condition was found.

There had evidently been oozing of blood for some time, as there was a well-marked phagocytic and plasma cell reaction with abundant production of iron-containing pigment. Most of the red blood corpuscles were well preserved. There were only a few typical fuchsin bodies, though atypical forms were numerous. Many of the large mononuclear and plasma cells showed fuchsinophilic granules. Cells of identical character, containing finely granular hemosiderin, were still more numerous. In addition, there were clusters of globular pigment masses and, associated with these, globular bodies of various sizes taking different degrees of the fuchsin stain.

A section from the wall of an old aneurysm, with a large thrombus mass, showed a quite similar condition.

The wall of the aneurysm was infiltrated with lymphocytes and plasma cells. Portions of the wall near the thrombus showed numerous fuchsin bodies, mostly irregular in form. Further out, these bodies gradually decreased and were replaced by hemosiderin. The pigment in the inner layers (as were the fuchsin bodies) was largely within the plasma cells, while further out it was deposited in irregular masses. This was the first case in which I was able to demonstrate both fuchsin bodies and hemosiderin in the same cell.

Fuchsin bodies have been but little studied in such conditions as the above and I should like to point out in this condition:

1. The occurrence of fuchsin bodies in or about areas of red blood corpuscle destruction.

2. The relation between the distribution of hemosiderin and fuchsin bodies, with reference to thrombus or area of hemorrhage.

3. The identity in the cell types containing fuchsin body and pigment, particularly plasma cells.

It is well to note here an exception to the staining results mentioned with the method I have suggested. The canalized fibrin in material I have used, though formalin fixed, stained intensely with fuchsin. There were, likewise, minute and large globular masses of highly refractile nature within the meshes of the fibrin that also took an intense fuchsin stain. I consider it not improbable that the latter were of the same nature as true fuchsin bodies, and that the fibrin was permeated with hemoglobin, as numbers of the red blood corpuscles were laked and did not stain.

The intimate association of fuchsin bodies with plasma cells led me to study lymphoid tissues. Unfortunately, most of the tissue available for this study was fixed in Zenker's fluid and the staining method relied on for other observations could not be employed. Hematoxylin and eosin and van Gieson's stains showed fuchsin bodies to be relatively frequent in these tissues. I have demonstrated them in acute and chronic lymphadenitis, lymphatic hyperplasia, and in glands of tuberculosis, typhoid, and Hodgkin's disease. In one case of tuberculosis, formalin fixed and stained as usual, there were a large number of medium-sized bodies almost entirely confined to cells of the plasma cell group. Cells of the same type with fuchsinophilic granules were also numerous. Both types of bodies were irregularly distributed throughout the section. Though fuchsin bodies were demonstrated in numerous sections from the spleen, one specimen from a case of pernicious anemia showed an unusually large number of typical intra- and extracellular bodies. There was a high percentage of "granular cells" in the specimen; many were of a type which might have come from the blood stream in such a condition, though there was an unusually large number of the type of relatively large lymphocytes and plasma

cells with typical cogwheel nucleus. The pigment deposits were comparatively slight. Irregular fuchsinophilic masses and even an occasional typical, globular form could be noted, associated with these deposits of pigment. It is of interest to note that both the kidney and liver from this case showed fuchsin bodies in the tubular epithelium and liver cells, respectively. They were mostly small, granular forms but some larger than a red blood cell.

The observations on lymphoid tissues from the gastro-intestinal tract agree closely with the findings in the lymph gland and spleen. Cells containing red blood corpuscles have been carefully excluded in all these specimens. Three specimens from the liver, besides the one above noted, showed fuchsin bodies in liver cells. Two of these were cancer metastases with abundant pigment deposits, the third, biliary cirrhosis. This section also showed pigmentation.

My study of these tissues has shed but little light upon the subject. The only points to be made out with certainty are as follows:

1. Fuchsin bodies are relatively frequent in lymphoid tissues in a variety of conditions.

2. Fuchsinophilic granular cells are numerous, although the conditions under which they occur make it difficult to distinguish them from true eosinophiles.

3. There is evidence of association with pigment production.

4. Lastly, fuchsin bodies occur in tubular epithelium and liver parenchyma in association with pigmentation.

As previously indicated, fuchsin bodies frequently occur in areas which have been subjected to the post-mortem action of certain ferments, such as the gastric juice, and wherever the red blood corpuscles show evidence of such action, the number of fuchsin bodies is correspondingly increased. Further, I have noted carefully the effects of fixation on the number and type of fuchsin bodies and have observed the associated changes in other elements which might give some clue as to the origin of fuchsin bodies. The results are briefly that within certain limits the number and type of fuchsin bodies may be decidedly influenced by fixation. As a rule, the number of typical bodies is inversely proportional and granular forms are influenced to a less extent. Fixation by

dilute alcohol, or by a small amount of stronger alcohol, or by fluids containing bichromate gives the largest number of typical fuchsin bodies and causes laking of the red blood corpuscles, or autolytic changes with fusion of the corpuscular mass, where larger pieces of tissue are used. After rapid fixation with 10 per cent. formalin there are few typical fuchsin bodies, but, instead, forms resembling fragmented red blood corpuscles and many granular forms. The degree of preservation of nuclei of cells has a decided relation to fuchsinophilic cellular or nuclear inclusions; otherwise the changes in red blood corpuscles are the only constant tissue changes that seem to have any relation to the number and type of fuchsin bodies present.

Thus far, I have attempted to show that the fuchsin body represents a type subject to variation in morphology, and staining reactions, and that in addition to the forms generally recognized as typical, there are, at least, two varieties which might be regarded as atypical: those atypical in morphology, and those atypical in staining reactions.

This broader conception of the so-called fuchsin body seems essential to any explanation of the phenomena observed in a comprehensive study of these bodies. Further, such a conception clears up a great many of the seeming contradictions which exist in the literature and are undoubtedly traceable to differences in type of fuchsin body studied by various workers.

The occurrence of fuchsin bodies in cells other than plasma cells, the occurrence in and near blood vessels, the association with hematogenous pigments, and the identity of staining reactions of fuchsin bodies and red blood corpuscles are points deserving especial emphasis.

The cellular and vascular relations of fuchsin bodies have been the subjects of greatest controversy. That no single type of tissue cell, or, of necessity, any tissue cell whatsoever can be held accountable for the production of these bodies, is evident to any one who will extend the material for his investigation over a sufficiently wide field. That cells of the plasma cell type are most commonly associated with fuchsin bodies is quite evident, but it is equally evident that fuchsin bodies occur in areas free from plasma cells and even

within blood vessels in the absence of any cell save those from the blood stream.

The staining reactions are, to say the least, strongly suggestive of a relation to red blood corpuscles. Every stain that I have employed has shown an identity in staining reaction between fuchsin bodies and red blood corpuscles. The only exception is where the red blood corpuscles have been laked and do not stain at all. Eosinophile granules are the only other structures sharing this identity of staining.

The association with hematogenous pigments, particularly where fuchsin bodies and iron-containing pigment are demonstrable in the same cell, furnishes some of the strongest evidence of a possible origin of fuchsin bodies from red blood corpuscles. While thus the relation of fuchsin bodies to red blood corpuscles is apparent, certain features (alcohol fixation) suggest the possibility that these bodies are artifacts. That they are artifacts only in part, I feel sure, as fuchsin bodies are present in the tissues even after the best possible fixation and where the red blood cells show perfect fixation. According to my observations, as I have previously pointed out, the bodies in such specimens are predominantly types which are granular or resemble fragments of red blood corpuscles. It appears that these must constitute the fundamental types, and that other types found in sections are derived from these. Mere alteration in form or coalescence of granules might give rise to the larger and oval or rounded forms. This tendency would be aided by slow fixation, as in alcohol. The theory of coalescence of granules is in harmony with the views of Schridde (12) and Fabian (2), though I believe my interpretation of the nature of these granules would hardly coincide with theirs (13). While, as I have before stated, these granules are often indistinguishable from eosinophile granules, yet I believe they are undoubtedly derived from the red blood corpuscles. It might be recalled that the conditions in which fuchsin bodies occur are, in the main, conditions in which there is local or general destruction of red blood corpuscles.

It seems certain that hemoglobin is one factor concerned in fuchsin body formation. Whether this is the sole factor, or in what form it exists, will require further work to determine abso-

lutely. In those instances in which the fuchsin bodies have a definite crystalline form they correspond closely with the parahemoglobin of Nencki (9). As previously shown for intravascular fuchsin bodies, autolysis with fusion of red blood corpuscles may give rise to fuchsin bodies, in which case the entire corpuscle is concerned in such formations. I have reason to believe that in some cases the pigment nucleus has been split off, and the fuchsin body represents mainly or solely the "globin." This material might enter plasma cells and other cells by diffuse staining of cells or simple diffusion. Plasma cells stained by hemoglobin are not uncommon, in fact, plasma cells seem to have an especial affinity for hemoglobin and I consider this of significance. It will be noted that the hematogenous pigments are found abundantly in the same classes of cells in tumors, chronic inflammatory tissues, spleen, lymph glands and other organs.

Our knowledge of hemosiderin, its mode of formation, its chemical and physical constitution, is too slight to permit of any positive assumption on these points. According to Neumann (19), it may be formed both intra- and extracellularly, but only under the influence of living cells. But little is known concerning the possible transitional stages from hemoglobin to hemosiderin. However, in such organs as the spleen, where abundant deposits of hemosiderin are present, fragments of red blood corpuscles, granules and droplets of blood coloring matter are very common in association with this pigment. These "hematogenous droplets" show varying degrees of affinity for such stains as eosin, as well as gradations in iron-reaction. The fuchsin body in the plasma cell seems to bear an identical relation to the hematogenous pigments in these cells; this relation is particularly obvious when both fuchsin body and pigment can be observed in the same cell. As I have pointed out, there is a striking parallelism in certain instances between the distribution of fuchsin bodies and hemosiderin.

From this and similar evidence it seems probable that the fuchsin body with its atypical groups may represent intermediate products in the formation of hemosiderin from hemoglobin by plasma cells and allied cell groups. It can not be claimed that all fuchsin bodies represent factors in such a process. Undoubtedly, a number of

such bodies are artifacts due to post-mortem action of certain enzymes or to mode of fixation.

Finally, I may seem to hold the view that all fuchsin bodies have their origin from red blood corpuscles. This, however, does not represent my opinion. While believing firmly that fuchsin bodies may and do arise from red blood corpuscles, I have been unable to convince myself that this is, or is not, the sole source of such bodies. Changes in nuclear material, which I have purposely avoided discussing in this paper, seem to demand closer study than has been accorded them in this connection, and I have been unable to exclude such changes as a second possible source of fuchsin bodies.

SUMMARY.

In summarizing the results of this work I feel justified in drawing the following conclusions:

1. The fuchsin body represents a type of body subject to wide variations in morphology and in staining reaction.

2. Though more frequently associated with plasma cells than with any other cell type, these bodies may and do occur in a great variety of cells.

3. Further, certain sections show unmistakable fuchsin bodies within blood vessels; some of these bodies are true hyaline thrombi, while others are due to autolytic changes in the red blood corpuscles.

4. Fuchsin bodies are most numerous in granulation tissue and lymphoid areas. In the former, they follow closely the distribution of capillaries and show a parallel with the changes in the extra- and intravascular red blood corpuscles.

5. The number and type of fuchsin bodies in tissues can be influenced by methods of fixation, the number of typical bodies being inversely proportional to the rapidity and degree of fixation of the red blood cells.

6. The type of body found after the best fixation is not, as a rule, what is considered the typical form, but an irregular fragmentary type or the fuchsinophilic granular form.

7. The identity in staining reaction, the constant association with changes in red blood corpuscles, the relation to distribution of capillaries in granulation tissues, the occurrence in hemorrhagic lesions

associated with pigment, the intravascular occurrence, and, finally, the close relation to pigment deposits, all indicate conclusively that fuchsin bodies arise from red blood corpuscles.

8. No theory of origin from plasma cells, or other granular cells, offers an adequate explanation for the origin of fuchsin bodies, nor can any theory prove adequate which does not take into account the red blood corpuscles.

9. The peculiar association of plasma cells with fuchsin bodies and hemosiderin seems explainable on the assumption that the plasma cell in such instances is the active factor in a metabolic process, the fuchsin body representing a stage in the metabolism of hemoglobin by an intracellular enzyme, and hemosiderin, one of the products of the process.

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