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By Simon Flexner, M. D., *Fellow in Pathology.*

(*From the Pathological Laboratory of the Johns Hopkins University and Hospital.*)

presented by the author -

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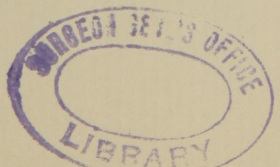
John McCready, colored, was admitted into the Johns Hopkins Hospital, in the service of Dr. Osler, on October 6th, 1891. About five weeks before his admission he was taken with a slight cough, and began to suffer from pain, especially on the left side of his chest, the pain being greatest on inspiration. At the time of his admission the cough had increased in severity and he suffered much from shortness of breath. His family history is negative. He had three brothers and four sisters still living. Beyond this nothing is known of it.

Status Presens.—It is observed that the patient tends to lie on the left side. He is a man of large frame and is fairly well nourished. His tongue is pale and covered with a brownish coat. Thorax:—The left side of the chest bulges outwards, and moves very little or not at all on expiration. The respirations are wheezy and 32 to the minute. On percussion the note is rather high-pitched and tympanitic throughout the right front; throughout the left front and axilla it is flat. Resonance is clear throughout the right back; flat throughout the left back. The vocal fremitus is absent over the left side. Respiration sounds at the left apex are distinct and tubular, while in the lower part of the left side they are nearly absent. The voice sounds are distinct and somewhat nasal. On the right side the voice sounds are clear, save an occasional sonorous râle. A hypodermic syringe was introduced into the left pleural cavity and some bloody fluid withdrawn. The pulse is 92 to the minute. The radial arteries are stiff, and the tension is not increased.

On October 9th the thorax was aspirated and 3500 cc. of reddish, somewhat turbid fluid were withdrawn. The patient expressed himself as much more comfortable after the aspiration, and resonance was now present to the 9th rib



before, and about half-way down behind. On the 12th he was aspirated again and 1900 cc. of sanguineous fluid removed. On the 22d, 2000 cc., and on November 7th 2300 cc. more were drawn off. The morphological elements of the fluid consisted of red blood corpuscles, polynuclear leucocytes, and large polynuclear and budding cells. On November 17th the patient was transferred to the surgical ward, service of Dr. Halsted, for operation.

The operation was performed under choloform narcosis. An incision 8 cm. in length was made over the 6th rib in the axillary line and 5 cm.of the rib removed. The thickened pleura was then incised, and a brownish or reddish, slightly turbid fluid poured out in a strong stream. The patient reacted favorably. There were several small nodules in the skin upon the side of the chest which had formed about the perforations made by the introduction of the aspirating needle. One of these nodules was excised at the time of the operation and it proved upon examination to be a carcinoma. The patient died on November 18th.

The autopsy was made a short time after death by Dr. Councilman. Anatomical diagnosis: Primary carcinoma of the tail of the pancreas extending into the retroperitoneal lymph glands, then through the lymphatics of the diaphragm. Secondary carcinoma of the pleura, lungs, liver, kidney, adrenal gland, intestines and lymphatic glands. Lymphangiectasis of the pleura and small intestine.

Exterior.—Body of a large man somewhat emaciated. On the left side commencing 2 cm. to the left and below the nipple and following along the 6th rib, is a linear incision 8 cm. long opening directly into the pleural cavity. There are several small nodules in the skin on this side of the chest.

Interior.—Diaphragm on the right side at the 5th intercostal space, on the left side at the 6th rib. The left side of the diaphragm feels thick and cartilaginous. The left pleural cavity contains air and a small amount of sanguineous fluid. The right lung is much distended and does not retract. The heart is pushed to the right side and lies mostly behind the sternum. The lung is free from adhesions. Over the entire pleural surface there are lines and patches of pigment, the latter having an average size of .5 cm. In the middle of them are white areas, which are not elevated above the margins of the pigment. Along the superior border of the lower lobe

there is a distinct retraction of the pleura, which is thickened here, and the thickening extends into the lung substance. At other places, between the lobes especially, are nodules of various sizes imbedded in the pleura. Many of these are very small, of grayish color, resembling somewhat the finest miliary tubercles. Others are larger, flat, with radiating masses of connective tissue going off from them and extending for a short distance over the surface.

The left lung is much reduced in volume. A few old adhesions are present, and there are several teat-like projections from the surface. The size of the lung is $14 \times 9 \times 5$cm. On section it is observed to be dense, airless, and of a leathery consistence. The pleura is much thickened over the lung and presents a red and granular appearance, and band-like processes of intensely red granulation tissue extend over the thickened pleura. The parietal pleura is thickened, the average thickness being 5 mm. It is hemorrhagic, uneven, covered with elevations and depressions, and looks fibrous. On section it is seen to be composed of grayish tissue enclosing whitish or yellowish masses. The pleural side of the pericardial sac is covered with minute nodules. The inner layers are smooth.

The liver contained a single white nodule in the interior of the right lobe. The left kidney is the seat of a yellowish nodule which occupies a renculus of the organ, having the shape of an infarction, the apex being in the pyramid. At the apex of the nodule is an occluded vessel containing a distinct reddish thrombus. The outlines of the nodule are not very sharply separated from the neighboring tissues. The right kidney contained several smaller nodules. The right adrenal gland contains a tumor mass almost filling the gland.

The pancreas contains in its tail, at a distance of 9.5 cm. from the jejunum, a grayish tumor mass, distinctly nodular on the side next to the pancreas and measuring $6 \times 3.5 \times 2.5$cm. It occupies the entire circumference of the organ at its seat. A second and smaller tumor mass is situated nearer the head. The retroperitoneal glands near the pancreas are enlarged and converted into grayish tumor masses, and all the glands in this situation are involved, more or less, in cicatricial tissue which extends in the form of thick radiating masses into the under surface of the diaphragm and through it, and is continuous with similar tissue on the other side.

Beneath the mucous membrane of the intestines there are

a few whitish masses larger than follicles. Throughout the upper part of the small intestine there is a perfect lymph injection. The mesenteric glands are enlarged, tolerably soft, and from them a white, thin fluid can be squeezed.

Fresh frozen sections of the primary tumor and several of its metastases, including the nodules in the intestine, proved it to be a carcinoma of the glandular type. In the kidney metastasis the tumor cells contained many inclusions, readily distinguished by their bright refraction and their irregular size and form.

It is not difficult to follow the distribution of the carcinoma in this case. From the primary tumor in the tail of the pancreas the neighboring lymphatics became affected, the growth in the lymphatics then passing through the diaphragm into the left pleura. From the left pleura the right, which was far less involved, became affected, and the general infection must have taken place from the same source through the medium of the blood.

The involvement of the retroperitoneal glands and other neighboring structures in dense cicatricial tissue proceeding upwards to the under surface of the diaphragm doubtless explains the lymph injection of the intestine and the lymph congestion of the mesenteric glands. It is more than probable that the receptaculum chyli was compressed or occluded by this new growth of tissue.

The clear spaces in the pleura of the right side, which lay in the midst of collections of pigment, represented dilated lymphatic vessels filled with clear fluid. On slight magnification this was rendered perfectly evident, and the explanation is found in the obstruction offered to the passage of lymph along these channels, owing to the growth of the carcinoma within them or in their communicating branches.

We have had the opportunity of observing many instances of lymph injection of the lymphatic vessels of the peritoneal cavity and intestines. In most, if not all cases, of marked chronic passive congestion of the internal organs, whether due to lesion of the heart valves or arterio-sclerosis, which have come to autopsy here, this condition was seen. Sometimes it reached a high degree, and as there has recently appeared an account of a similar condition in the small intestine under the title "Ueber Chylangioma cavernosum" (Kruse, Virchow's Archiv, Band 125, S. 488), in which the author compares it with

the cavernous angiomata, we wish to indicate this mode of their production. The mucous membrane of the intestine may show a number of circumscribed, circular, elevated bladder-like projections, sometimes having a diameter of one centimetre, which are filled with a milky fluid. They may lie between the folds of the valvulae conniventes or on the summit of them (if in the small intestine), and we have recently made a histological examination of one of the latter kind.

A piece of the intestine including the vesicle was excised and hardened in sublimate. On section the mucous membrane of the intestine was intact, but just beneath it were several lymphatic vessels much dilated, separated by very thin septa, and filled with a granular material resulting from the coagulation of the fluid contents.

The microscopical examination of the hardened tissues from the primary growth and its metastases shows the carcinoma to partake of the glandular type, and indicates its origin as having been the ducts of the pancreas. In the primary tumor the growth is not everywhere typical as regards this fact, but the pleural metastases are essentially a reproduction of duct forms. The nodules on the pleura covering the lung consist of lumina lined by a single layer of low cylindrical or cuboidal epithelial cells. There are no nodules deep in the substance of the lungs; from the surface, however, there is a slight extension of the carcinoma into the lung substance along the thickened interlobular tissue. In the primary tumor some of the epithelial cells show the same cell inclusions which have already been mentioned in connection with the fresh frozen sections of the kidney metastasis. However, as it is our intention to dwell on them at some length in treating of the latter, they can be dismissed here.

Sections made from the large wedge-shaped mass in the left kidney, in the direction of its long axis, reveal the tumor thrombus in an artery of considerable size. This thrombus does not fill the vessel entirely at the point of the sections, as there is, besides it, an organizing white thrombus present. The tumor has invaded the wall of the artery, penetrated it and passed into the parenchyma of the organ, and its ascent into the cortical portion of the kidney can be traced along the tubules. The normal epithelium of the tubules, which have been invaded by the tumor, has been displaced by the latter. Occasionally a tumor cell can be made out (apparently) in the

tufts of the glomeruli in the tumor area, but they were not observed in other places. Where the tumor spreads from the vessel into the parenchyma the intertubular tissue of the organ is much thickened. In the cortex of the kidney outside the tumor area the epithelium of the convoluted tubules is much degenerated, and casts are frequently observed in the tubules.

Stained sections of the kidney afforded an excellent opportunity for the study of the cell inclusions, the so-called "coccidia" of cancer. The autopsy was a very fresh one and the tissues were preserved in alcohol and Flemming's solution, and various staining agents were employed. We did not observe new forms of inclusions, perhaps, but were able to make out many of those described by others; and in a few instances we thought that the mode of their production was perceptible. In general it may be stated that we could find but few intranuclear forms, while intracellular forms were abundant. Nuclear figures were frequently observed. Some of these were quite typical, while others were markedly irregular in form, and in still others there was a wide diffusion of the chromatin throughout the cell with only the slightest suggestion of arrangement.

We observed hyaline, refractive, more or less globular bodies devoid of stained contents lying in cells, either close by or at a distance from their nuclei. Sometimes they were perfectly homogeneous and at others granular; sometimes they were to be distinguished from the rest of the cell body only by the difference in refraction, and again they lay in distinct vacuoles. Where vacuoles occurred they varied in extent from the merest and narrowest circle to a considerable cavity, surrounding the hyaline body and presenting a double-contoured aspect. Another set of these inclusions was similar, only they contained stained particles within them, at times only one, and again several. The stained particles were not all the same size, but there was considerable variation in this respect, and oftentimes they differed from one another in shape. There was, too, a difference in refraction in the stained particles. This was not so evident in haematoxylin as it was in safranine staining. Not a few instances occurred in which these homogeneous bodies, either with or without stained particles within them, lay directly in contact with the nuclei of carcinoma cells and even compressed these greatly. We were able to observe an interesting point in connection with the formation of these

bodies, inasmuch as we found, in a few instances, the remnants of a connection which had existed between the included "body" and the "host." They consisted of radially arranged fibril-like processes, very delicate but quite perceptible, which passed from one to the other. The cells of the tumor were often so closely united in the tubules that separate outlines could not be seen, and the impression of giant cell formation was obtained. In some of the large cells a considerable number of the inclusions were present, and much difference was remarked in their size and refraction, even in the same cell.

We have no difficulty in reconciling the appearances which we have described with those of many writers on the psorospermic origin of cancer and some other affections. Indeed, it is even possible to see in the variety of form and number some of the stages of development which they have depicted. We do not, however, regard these bodies as organisms, but rather interpret them as being degenerations occurring in cells and nuclei, affecting, as a rule, not the whole of these, but circumscribed portions. The observed differences in density, granulation and homogeneity may, perhaps, be accounted for on the supposition that they depend upon different degrees of one process, or represent different ages. The presence of stained particles within many of them, however, is not so easily understood in those instances where the nuclei of the cells are intact. It may be well to suggest the possibility of their being leucocytes which have wandered into the necrotic parts of cells, as leucocytes are known to enter dead cells in other cases. Some of the stained particles suggest the nuclei of polynuclear leucocytes, while in other cases it is possible to see in the irregular particles what correspond to fragments of nuclei, probably derived from those leucocytes which have perished after having entered the degenerated bodies.

The interest which the parasitic doctrine of carcinoma and some other tumor formations has provoked has suggested to us the advisability of offering a brief statement of the principal literature contributed to the subject.

In 1887 and 1888 a number of articles appeared on the ætiology of carcinoma and sarcoma, in which the authors affirmed that they had separated from these structures certain bacteria which they regarded as the cause of the respective diseases. Scheurlen [1] made a series of bacteriological examinations of primary and secondary carcinomata, and succeeded in isol-

ating in a fair proportion of cases certain bacilli considered by him as peculiar to these growths. Rappin[2] studied five carcinomata, eight epitheliomata and three sarcomata, and separated diplococci from them. Schill[3] obtained from carcinomata, bodies which he described as polar-staining organisms, and from sarcomata similar but shorter forms. Freire[4] claimed to have first described the organisms of Scheurlen, and Francke[5] confirmed Scheurlen's observations and in addition described a bacillus which he obtained from sarcomata.

At the present time it is not considered that any one of these organisms is the cause of either sarcoma or carcinoma. The bacillus of Scheurlen is now known to be a common saprophyte, often found on the healthy skin and quite common on the nipples of healthy women and young girls.[6] The cocci of Rappin belong to the pyogenic micro-cocci, and the polar staining bodies of Schill may not be micro-organisms at all.

The theory of the parasitic origin of cancer received a new impetus in very recent times on account of the description of certain bodies, regarded as peculiar and believed to be parasitic in nature, contained within the epithelial elements of the growths. In a comparatively short space of time numerous observers have contributed the results of their investigations of this interesting subject. The study of these intra-cellular bodies has taken a wide scope, and tissues from various sources have been examined. These bodies which occupy the tissue cells themselves, at one time the nuclei and at others the cell bodies, though some describe them as occasionally free, are not of bacterial nature. So far as any classification of them has been attempted, assuming for the moment that they are living things, they have been referred to the animal parasites, to the sporozoa.

It is stated that the first observations on the nature of these bodies were made by Neisser[7] in his contribution to Molluscum Contagiosum, but we have found that Virchow[8] described them long before and suggested the possibility of their being psorosperms. Neisser was able to study these bodies only upon microscopical sections, as culture and inoculation experiments gave negative results. He found the fresh tissues to afford the best view of the bodies, which he describes as clear and highly refractive, and he distinguishes between the spore and more highly developed stages. Neisser found them in

the greatest number in the affected tissue; but he also found them in the depth of the inter-papillary processes of epithelium adjoining, in the uninjured epithelial cells.

Pfeiffer[9] described in two cases of general carcinosis and in one case of sarcoma of the breast, certain bodies which he compared to the organisms which were shown by Pasteur to be the cause of the malady of the silkworm, and he regards them as belonging to the sporozoa. Darier[10] then observed similar bodies, believed to be coccidia, in a form of cutaneous affection to which he gave the name "Psorospermose folliculaire végétante," and Darier and Wickham[11] attributed the development of Paget's disease of the nipple to a special form of coccidia which invades the epidermis.

Malassez and Albarran[12] found certain peculiar bodies in two cases of epithelioma of the jaw which they regarded as parasites, having striking analogies with the coccidia occurring, at times, in the liver of the rabbit. Vincent[13] found similar parasitic bodies in flat-celled epitheliomata.

About this time several contributions were made which have particular interest, inasmuch as these bodies are described very fully. Thoma[14] examined carcinomata from the intestine, stomach and mamma. He found in the nuclei of the epithelial cells certain bodies, which in form, size and combinations were in such remarkable contrast to the other forms of cells as found in human beings that he considered they may well be regarded as parasites. They are unicellular bodies, 4 to 15 mm. in diameter, which are rendered more apparent by staining, and consist of protoplasm and possess nuclei and sometimes nucleoli. In form they are irregularly rounded, oftener oval; sometimes, however, they appear fusiform. In general they are quite refractive; they lie in the nuclei of epithelial cells in groups of 4 to 6, whereby the staining capacity of the nuclei is lost and these assume a hollow and bladder-like form. In other instances, immediately adjoining the nuclei, vacuoles are formed, in which similar bodies lie, or the vacuoles may contain a number of ball-like, strongly refractive objects, which may be thought of as encapsulated coccidia. Thoma does not, however, commit himself finally as to the nature of these bodies.

Sjöbring[15] endeavored to follow the life history of the supposed parasite and he describes several stages in its development. He finds a free extra-cellular form, an intra-cellular

form and spore forms. He has also seen irregular forms which he thinks may indicate an active or motile stage, but he has never succeeded in observing the bodies (sarcodes) entering the nuclei of cells, although they are seen lying against and within the nuclei.

Steinhaus[16] examined a melanotic sarcoma, and the liver from a case of cirrhosis. In the sarcoma there were bodies such as other authors describe, occupying the nuclei of the cells and reaching so great a size as to reduce the original nucleus to a mere rudiment. Somewhat similar bodies occurred in the liver cells. He concedes that they may be degeneration products, but also thinks they may be parasites. Similar forms to these are, he says, described by Danilewski[17] in Polymitis malariæ, and, moreover, he regards certain forms present in his specimens as corresponding with the Karyophagus which occupies the cells of the intestine of the salamander. Later Steinhaus[18] has examined thirty cancers from different sources, in which he sometimes found the bodies and at others not; but he still considers that they may be of parasitic nature. His last communication[19] refers to an epithelioma of the plantar surface of the foot, from the study of which he concludes that the bodies described in skin cancers as foreign to them and regarded by some as parasitic, are probably not such, but are to be interpreted as hornified cells enclosed in vacuoles.

Van Heukelom[20] extended his investigations so as to include cancers of the skin, stomach, œsophagus and mamma, of the lips, mouth, intestine, rectum and kidneys, and a carcinomatous papillary cystadenoma. The metastatic growths were also examined. Those occurring in the axillary glands in carcinoma of the breast, in the liver in carcinoma of the stomach, and in the lungs following carcinoma of the stomach and pancreas. He studied nearly 200 tumors in all, and he was able to confirm the results of Sjöbring and Thoma.

Russell's[21] "fuchsin bodies" are probably closely allied to the forms already described. By means of a special and peculiar method of staining* this observer was enabled to

*The sections remain in a saturated solution of fuchsin in 2 per cent watery solution of carbolic acid for 10 minutes or longer; then they are washed in water and placed in absolute alcohol for half a minute. They are then counter-stained in a 1 per cent solution of iodine-green in 2 per cent aqueous solution of carbolic acid, where they rest for 5 minutes. Remove from this, dehydrate quickly in absolute alcohol, pass through oil and mount in balsam.

make out certain bodies, occurring in groups of 2 to 20, which lay among the round cells at the edge of the advancing tumor, in the stroma of the cancer, and in the alveoli themselves. Out of 45 carcinomata examined he found the fuchsin bodies in 43. Yet he also observed them in a large-cell sarcoma, gumma of the dura mater, tuberculosis of the knee-joint, and in syphilis of the larynx.

On the other hand, Shattock and Ballance[22] view the "fuchsin bodies" of Russell as altered cells, and they have demonstrated them in the lung in glanders, in an unorganized thrombus of the femoral artery, a diphtheritic tonsil, and in tuberculous lymphatic glands. Piffard[23] regards the molluscum bodies as being rete cells which have undergone keratoid degeneration. Schütz[24] sees in them only altered cells, either red blood corpuscles or leucocytes, and Macallum[25] states that they may be at one time simple masses of chromatin, and at others simply leucocytes. Török and Tommasoli[26] made use of the warm chamber to determine whether or not any change and increase took place in these bodies, and they were convinced that they remained unaltered under these conditions. Transplantations from individual to individual were negative, and hens could not be infected. The effect of various caustic and injurious chemical reagents was far less marked on the molluscum bodies than on living coccidia. In this respect the former resembled colloid material, and the authors regard them as products of cell-degeneration, perhaps, not unlike this material. Klebs[27] planted pieces of carcinomata from the mamma and penis into the abdomen of white rats. Not only was he unsuccessful in causing infection of them, but the hyaline, parasite-like bodies neither increased in number nor underwent any further development. Borrel[28] has found bodies similar to those described as parasites in carcinoma, in simple inflammatory conditions of the skin, and he regards them here, as in carcinomata, as being peculiar kinds of cell degeneration and necrobiosis. Pilliet[29] examined the thymus glands of fœtuses and still-born infants at term, and found these bodies in Hassal's corpuscles. He also encountered them in the prepuce of newly-born males where agglutination to the glans existed. Moreover, he was able to make out a marked difference in the resistance of these bodies to chemical agents as compared with the coccidium oviforme as found in the liver of the rabbit. Duplay and Cazin[30] have

examined sixty epithelial cancers with especial reference to these supposed parasitic elements. They regarded it as an indispensable link in the chain of evidence that these bodies are of parasitic nature, that they exhibit the principal features of the evolution of the coccidia. They failed to find evidence of such changes as these organisms present, and hence they concluded that the peculiar bodies are of a degenerative character, and they consider that they result not only from cells but from mitoses. Cornil[31] and Hansemann[32] had already indicated the latter mode of origin in some cases.

Ribbert[33] made an extensive study of the cell-inclusions in carcinomata, employing for it skin and gland cancers, and, in particular, a cancer of the bladder which was especially rich in them. He used both fresh and hardened materials and a variety of staining agents. According to his investigations they are more numerous in the older than in the young portions, and the middle zone of the alveoli contains more than other parts. He looks upon the inclusions which have been described in the old literature as well as the new (see below) as degenerated and metamorphosed cells. The metamorphoses occur most commonly in those situations where the so-called "pearls," are formed. The central cell usually suffers and it becomes surrounded by 2, 3, more seldom 4 or 5 adjoining cells. Or the transformed cell may become entirely surrounded by a second, but this can only occur if the enclosed cell is smaller than enveloping one. It must be remarked in this connection that in these cases the inclusion is an apparent one only, for the included cell often occupies a depression only in the host, although in section it appears as if it were completely surrounded by protoplasm. What next happens is a reduction in volume of the enclosed cell resulting from a thickening of the protoplasm, which becomes more or less cloudy and opaque. As the surrounding cell or cells do not suffer any alteration, a vacuole is formed around the central cell. Finally the central cell loses its granular appearance, becoming more and more homogeneous, and then hyaline. The nucleus behaves in different ways. In many instances it becomes gradually more indistinct and finally fuses with the hyaline protoplasm. In others it becomes homogeneous, but shows a tendency to take coloring agents, and hence is demonstrable for a long time. The end of the

process is the production of homogeneous, mostly round bodies which lie in vacuoles. They lie excentrically, or according as the section passes, nearer the center of the cell; and for the reason just stated the vacuole may, at times, appear entirely empty. As a rule, the homogeneous bodies are smaller than the epithelial cells, but they may be larger, if it happen that very large epithelial cells or giant cells suffer metamorphosis. The shape of the transformed bodies varies considerably, being round, oval or irregular. Some of the hyaline bodies contain secondary vacuoles within them, and leucocytes are found in the degenerated cells.

Another appearance is obtained when a single cell contains multiple inclusions, suggesting what Sjöbring has described as spore-cysts. On account of the number of the inclusions they could not be considered as having formed in an ordinary epithelial cell, but they must have occurred in large epithelial or giant cells. The mode of their production was not so clear, nor could it be followed as in the previous instance. These latter forms occurred in a cancer of the bladder, and they lay within the protoplasm of the cell, and, in some cases at least, represented metamorphosed nuclei of polynucleated cells. Ribbert also observed changes in karyokinetic figures which led to inclusions, and, finally, he has seen vacuoles produced by the shriveling of the nucleus, the remaining chromatin particle representing the nucleolus or simply conglutinated chromatin. Even though the process of the production of these inclusions cannot be followed in the last case as it was in the first, yet if the one is admitted to be due to cell metamorphosis, the other will not be held to have a totally different origin.

Ribbert states in conclusion that the results of the foregoing investigations, when taken together, do not permit the acceptance of the idea of the parasitic nature of the bodies included within the cell protoplasm, or lying outside of it in carcinoma, but he regards as more probable the belief that they are degenerated epithelial cells.

In a paper just presented by Kosinski [38] the author gives the results of his study of a "colloid" carcinoma of the liver secondary to a colloid carcinoma of the stomach, in which he has followed the mucoid metamorphosis of the epithelial cells. He found that the mucoid change may sometimes be very circumscribed, affecting a limited portion of the cell body or

only the nucleus of the cell. Many of the appearances described by others as parasites are simulated, in his opinion, by the pictures obtained in these degenerated cells. He describes, and figures also, the presence of leucocytes in the degenerated portions of the cells. Kosinski points out that these altered tissues are markedly meta-chromatic, staining orange with safranin and violet with toluidine-blue. It is a matter of historical interest to know that some of these cell-inclusions were observed by Virchow[34] as early as 1847, although he regarded them as indicating a form of endogenous cell division. And, also, that he described in the follicles of the nail-bed similar bodies, and stated that they occurred whenever a growth of epithelium remained for a long time.[35] In conclusion we would give the titles of two reviews which have recently appeared on the subject of carcinoma, one by Stroebe,[36] "Neuere Arbeiten über Histogenese und Aetiologie des Carcinoms," the other by Cazin,[37] "La théorie parasitaire de cancer," to which we would refer for the recent literature touching other aspects of the subject than the one we have treated.

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