Duhring (L. A.)

SUPPLEMENT

TO A CASE OF

INFLAMMATORY FUNGOID NEOPLASM

BY

LOUIS A. DUHRING, M.D.

PROFESSOR OF SKIN DISEASES IN THE HOSPITAL OF THE UNIVERSITY OF PENNSYLVANIA, DERMATOLOGIST TO THE PHILADELPHIA HOSPITAL, PHYSICIAN TO THE DISPENSARY FOR SKIN DISEASES, PHILADELPHIA, ETC.

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SUPPLEMENT TO A CASE OF INFLAMMATORY FUNGOID NEOPLASM.*

THE case of inflammatory fungoid neoplasm which I had the honor of bringing before the Association last year is of such importance that a few remarks supplementing that report must, I feel confident, prove interesting. I shall in no way retrace the ground of my former notes, assuming that the principal features of the disease, at least, will be readily recalled. The notes as they occur in the published account of the case (ARCHIVES OF DERMATOLOGY, January, 1879) are complete to October 1, 1878. I shall now proceed to give an account of the case from that date.

Through the month of October the symptoms, both general and local were, as before, variable. The forehead and popliteal space lesions continued to grow and soon began to be excoriated and crusted, discharging profusely. The forehead tumor now changed its shape by the neighboring smaller formation coalescing and merging into the central growth, which became, as it were, the focus. Various local remedies were from time to time employed, with a view of checking the secretion and modifying the odor, which had become very offensive; among these I may mention the fluid extracts of Grindelia robusta and Thuya, diluted in various proportions, both of which moderated the itching. The preparation of Thuya acted powerfully for a time upon the growths, causing them to discharge more freely, and later to contract and diminish appreciably in size, but it was soon observed that the effect was not permanent, and that the disease was continuing to assert itself in the face of all treatment.

Throughout the autumn the patient complained of occasional distinct attacks of weakness, malaise, loss of appetite, and other similar symptoms, in consequence of which she began to lose not only flesh, but her spirits, which before had never wavered, and gave up hope. Smaller lesions continued to come and go, while a number of the older and larger ones were slowly undergoing absorption and so disappearing. The face and leg tumors were now discharging a copious yellowish, greenish, puriform, bloody, exceedingly offensive fluid, which was poured forth from the forehead in such quantity as to necessitate repeated daily dressings. It was found that chlori-

* Read before the American Dermatological Association at its third annual meeting, at New York, August, 1879. For discussion thereon, see ARCHIVES OF DERMATOLOGY, October, 1879, page 386.

nated soda solution best served the purpose of suppressing the heavy and sickening odor, and that a thick layer of oxide of zinc ointment and cosmoline with carbolic acid was most grateful. Lotio nigra was also used at times with favorable result, and appeared to modify the amount of the secretion.

Towards the latter part of December it occurred to me that very small doses of corrosive sublimate might possibly act beneficially, although, remembering the disastrous results from arsenic and iodide of potassium, it was given tentatively and with some misgivings as to the effect. A prescription containing compound tincture of cinchona and one-sixty-fourth of a grain of the mercurial was ordered. Three or four doses only were taken when alarming symptoms of ptyalism began to manifest themselves. Several weeks passed before the mouth recovered, leaving the lower incisors and several other teeth in a precarious state. Ulceration occurred, which it seemed to me must be attributed to the disease rather than to the mercury. A few weeks after this the right tonsil became swollen and tender and covered with a whitish deposit, which was followed by ulceration and a most fetid, stringy discharge. These latter symptoms increased from day to day, the tonsil soon completely disappearing, and being succeeded in the course of a month by an ulcerated cavity about an inch in diameter and a half-inch in depth. The fetor was insufferable. This ulceration, although at first obscure as to its nature, was without question a symptom of the disease.

According to the notes recorded on December 1 she had lost about thirty pounds since September. She began to have a nightly fever, together with flushes of intense heat and burning in the palms and soles, followed by copious perspiration and general debility. These symptoms manifested themselves gradually and continued almost uncontrollable for a month. An attack of suppression of urine lasting thirty-six hours, followed by a violent outbreak of urticaria, similar to an experience six months previously, occurred during the latter part of November.

Jan. 1, 1879, found her failing appreciably in general health, and confined to bed. The cutaneous lesions up to this time were behaving most capriciously, as had been the case during the entire autumn; but apart from the steady increase in size of the forehead and popliteal space lesions there was nothing particular to note, and upon the whole the disease was considered as being unusually quiet.

Feb. 1.—The condition had by this date become distressing in the extreme. Sleepless nights, malaise, debility, inability to eat, alternate constipation and diarrhœa, capricious appetite,—oftener absent than present,—itching chiefly in the form of severe paroxysms, may all be mentioned as having been conspicuous symptoms; to which must also be added the horrible state of the head and leg, where the disease seemed now to be principally expressing itself, characterized by steady growth, augmented discharge and fetor. Internal treatment, consisting of supporting diet; stimu-

lants, which the patient, however, bore only to a very moderate extent; a preparation of bark and dilute nitric acid, and other similar remedies, were employed from time to time as she felt able to take them, her exceedingly variable condition rendering continuous treatment of any kind out of the question.

Feb. 19.—Within the last month the glands of the parotid and submaxillary regions have begun to enlarge, forming firm subcutaneous, deep-seated, diffuse swellings. They have of late been slowly but steadily increasing in size. A week ago she was seized suddenly with violent neuralgic pains in her arms, extending from the shoulders to the ends of the fingers. The pain was intense, causing her to cry aloud, and lasted about three hours. The arms were left in a helpless state, and without motion. The next day, at the same hour, the pains recurred, but were relieved in a measure by the application of chloroform. The following day there was no recurrence, but the day after they again attacked the arms, but less severely. The limbs have since been helpless, but show some signs of gradual recovery.

For the last week another new symptom, consisting of distinct attacks of gaping, yawning, and hiccuping, has appeared, coming on every afternoon at about the same time and continuing an hour or more. There has also been daily vomiting of a greenish, watery fluid, otherwise the general condition has changed but little within the past three weeks. The flushing still continues, coming on once or oftener every day. The glandular engorgements of the face and neck are enlarging, and cause much disfigurement, the skin covering them being tense and purplish in color. The integument generally is yellowish, soft, and flabby, and exhibits a cachectic hue, similar to such as is often noted in carcinoma. The pulse is weak, and from 120 to 140 to the minute. The tumor of the forehead has grown immensely within the month, and is so bulky, discharges so much, and is so offensive that the patient desires an operation at any risk. In appearance it resembles closely a huge roasted tomato.*

Feb. 21.—To-day the tumor was removed successfully with the galvano-cautery loop, Dr. F. F. Maury rendering valuable assistance in the procedure. Drs. J. Solis Cohen, Van Harlingen, Praeger, and Benning were also present. The instrument was that manufactured by the New York Galvano-Faradic Company, three cells being employed; the loop was of platinum wire. This was slipped over the tumor, the patient being under the influence of ether, and a red-hot heat obtained, when the wire was slowly and gradually tightened. Thirteen minutes were occupied in traversing the base and in removing the growth. The operation proceeded without complication and absolutely without hemorrhage. A wound two and a half inches in diameter remained, which displayed the frontal bone. The tumor of the popliteal space was subsequently removed by the same means; likewise without hemorrhage.

* The condition of the tumor at this date is shown in the accompanying portrait.

Feb. 28.—No unpleasant effects followed the operation. The wounds at once began to granulate abundantly and to close, but it was found that the periosteum upon the frontal bone had been destroyed and that repair would not go beyond a certain point. The general symptoms, however, did not improve. The gapes and hiccup still came on every afternoon, and the stomach rejected absolutely everything. Intense flushing of the whole body, especially of the back, also was present with regularity every day.

March 7.—There have been repeated attacks in the course of the day of vomiting of dark bloody material. The flushing continued until yesterday, when in its place cold extremities followed by heavy perspiration manifested itself. The nights are sleepless, even under the influence of morphia, which she has for some time been taking by the stomach in ¼-gr. and ½-gr. doses. The patient exhibits a marked disposition to be decidedly better or worse from day to day. For the past week a nasty, thick, tenacious, greenish, offensive accumulation in the form of a plug has daily, and often twice daily, discharged itself with difficulty from the nasal passages. The arms are still helpless, and the hands œdematous; the legs and feet are generally cold, swollen, and likewise œdematous. The urine for the past six weeks has been variable as to quantity, but generally thick and red, with an abundant brick-dust deposit. No albumen.

March 18.—She is entirely helpless, not being able to move her arms, and at times not even the lower extremities; yet some days she possesses considerable motion of the arms, and is able even to carry one hand to her face. While she is failing rapidly from week to week, she nevertheless rallies most remarkably. The wounds are healed except over the forehead, where the bone was injured. The leg wound is entirely well. The nurse states that the disease has showed itself in the form of a swollen tumor about the size and shape of an olive, on one of the labia of the vulva. But the patient objects to an examination, stating that it is only one of many and like those elsewhere. Three days ago she was seized with a most voracious appetite, which lasted several days. Notwithstanding that absolutely nothing remained on the stomach—not even the smallest quantity of fluid—she craved both food and drink of any kind.

Her mind, which has heretofore been in a perfect state of preservation, has lately begun to fail, especially her memory. The swellings of the face and neck have steadily increased in size, but they vary from day to day, and moreover show a decided tendency to change from morning to night, being swollen half as large again in the morning, and decreasing in size by afternoon. They have lately been painful. The swelling is now so enormous that the mouth can scarcely be opened. The tumor on the back of the scalp is now the size of a small orange, but flat and lobulated, soft and boggy, and for some time has been discharging an ounce or more daily of a bloody, puriform, fetid fluid. It is, moreover, excoriated and fungoid, being in a similar state to that of the forehead at the date of

operation. No new lesions of any size are noted over the general surface. The growth on the arm near the axilla has likewise now attained a greater size, being as large as a goose-egg; and the axillary glands still remain free, slight engorgement only being present.

April 6.—The tumors on the side of the face, those over the parotid and submaxillary region, have been growing perceptibly from week to week. The face is now so disfigured as to be barely recognizable, the swellings protruding so as to render the shape of the head somewhat square. One tumor on the side of the neck has recently opened, exhibiting a vegetating, fungoid appearance, and is still discharging freely. The vomiting continues constantly, as a rule every ten or twenty minutes, the fluid being offensive and varying from a bloody to a greenish color.

May 1.—Patient has been failing rapidly within the last month. The retching and vomiting are constant, day and night, often but a few drops of fluid being ejected; other times larger quantities, the matter, as before, varying in character. Nothing worthy of mention has remained on the stomach now for some weeks, while during the last fortnight scarcely anything has passed her lips. There has been constant diarrhœa of late, the discharges being bloody and blackish. She is much emaciated, and, as before, entirely helpless. The eyes have lately become closed by the densely infiltrated eyelids, which are the seat of flat tumors. A few new small growths, mostly flat, have come here and there, and many of the older ones have gone, the trunk exhibiting chiefly the remains, in the shape of diffuse infiltrations and pigmentations, of the former lesions.

May 5.—Patient to-day expired from exhaustion, being conscious to the last.

AUTOPSY.

Autopsy made twenty-four hours after death, by Dr. Morris Longstreth, Pathologist to the Pennsylvania Hospital. Body markedly emaciated, slight rigidity. No posterior discoloration. Skin of general surface, apart from the lesions and a few petechiæ on back of hands, is soft and pliable and natural in color. Scattered over the surface are variously sized and shaped, for the most part sharply defined, flat or raised, reddish, more or less crusted cutaneous lesions; on the forehead to the right of the median line the cranium is bare in the form of a rounded area, three-quarters of an inch in diameter; the skin around is firmly adherent to the tissues beneath, and is not thickened or infiltrated. At the root of the nose extending to the right eyebrow and involving the same is an irregularly-rounded, uneven, firm, fungoid, dark-reddish mass, covered with a dark-red, blackish crust, about two inches in diameter and raised a half-inch. A similar tumor exists on the back of the head just above the occiput, which is distinctly fissured and lobulated and soft.

Commencing on a line with the right ear, occupying the lower temporal, the parotid, and the submaxillary regions, from the cheek to the sterno-cleido-mastoid muscle, is a firm, lobulated, subcutaneous

swollen mass covered with slightly movable, reddish, infiltrated skin. At the upper portion of the growth there is a superficial, quarter-dollar-sized ulcer, which is covered with a brownish crust. A similar enlargement but smaller exists on the opposite side of the face at a corresponding point. In the right posterior supra-clavicular region are three hazelnut-sized subcutaneous nodules, freely movable beneath the skin. Two smaller ones are found in the same region on the other side of the neck. No enlarged post-cervical glands. Upon the inner side of the right arm near the axilla is a large, hen's egg-sized, firm, fleshy, reddish-brown, excoriated and crusted, movable tumor. Much to our surprise the tumor of the labium of the vulva has entirely disappeared; nor can so much as a trace of it be found. The abdomen is flat. Upon incision a half-inch of subcutaneous fat is noted down the median line. Intestines are not distended. Omentum is supplied with a small amount of fat, and is adherent to left side with a single cord-like band. The color of small intestines is dark-red on surface: little or no serum present. The surface of the intestines has in places a finely granular look, and is dry. The abdominal organs occupy their normal position. The right costal junction is prominent,—more so than the left.

The pleural cavities are very dry, and except a few old adhesions on either side are normal. The left heart is moderately contracted; right relaxed. Blackish clots are found in right auricle and ventricle: the left ventricle is empty. The tricuspid and pulmonary valves are normal. The mitral orifice is also normal in size; the anterior leaflet is thickened but smooth. The aortic leaflets are also thickened at several points along their line of junction, and at one point there is a slight calcareous deposit. Coronary arteries and aorta normal. The color of the heart-muscle is pale; the tissue is friable; the walls are of normal thickness; cavities of normal size.

The lungs are everywhere crepitant. There is a slight amount of fibroid thickening at their apices beneath the pleural adhesions. No nodules are anywhere to be felt or seen in the lung-substance. The glands at root of lungs are not enlarged but are deeply pigmented; no enlarged glands can be felt from the pleural sac.

The spleen is of usual size, with a slight fibrous depression at one border; otherwise normal. Supra-renal bodies small and firm; surface covered with yellowish-gray nodules. Kidneys show no marked evidence of disease; they are small; moderately firm; surface smooth; substance congested, especially pyramidal portion; capsule moderately adherent, leaving on removal a fairly smooth surface; have a slightly urinous odor; cortex is of normal thickness.

The liver is small; deeply notched on its right border; bile-duct patulous; gall-bladder very much enlarged, containing thick, dark-greenish bile, and a single olive-sized, rounded gall-stone. The surface of the liver has a mottled, yellowish-white color; on section the mottling is very distinct; fibrous tissue increased, and very resistant to finger. There are no nodules present.

The stomach contains a greenish-black, thin fluid; stomach-walls moderately softened, especially towards the cardiac end, apparently by post-mortem changes. The vessels are full of blood, giving the surface a dark color. The submucous connective tissue is not increased in amount. Pancreas normal. Uterus normal and ovaries contracted.

A small amount of urine is found in the bladder. Its internal surface appears at first sight as though ulcerated, but on close examination distinct lesions are seen. They are flat, variously sized, mostly ovalish, firmly-seated, with broad bases, dark-reddish, slightly raised, soft but organized patches, covered with mucous membrane. One of the lesions rises to the height of a half-inch, and is the size and shape of an almond. There are no enlarged glands about the bladder. None of the mesenteric glands are increased in size.

The mucous membrane of the intestines is everywhere stained dark-red, but nowhere is there any thickening. The lower end of the ileum and the head of the colon show no enlargement of Peyer's patches nor of the solitary glands; nor is there any enlargement of the retro-perineal glands.

MICROSCOPICAL EXAMINATION.

Specimens for microscopical examination were removed as follows:

An ovalish, large olive-sized piece of integument, containing in its centre an almond-sized, ovalish, sharply-defined, well-formed, slightly-elevated, reddish tumor (a recent growth), surrounded with healthy skin,—from the front of the right leg to the left side of the tibia.

A finger-nail-sized piece of integument from an old abdominal patch which had almost disappeared by absorption.

A subcutaneous enlarged cervical gland from supra-clavicular region.

A portion of enlarged parotid gland.

A section of heart from left ventricle.

Two sections from the liver; one from the surface, the other from a deep-seated part of the organ.

A piece from the stomach, including mucous membrane and muscular coat; also a section from the bladder, embracing apparently healthy tissue as well as the patch.

The specimens, as before, were frozen and cut with the microtome, and examined in an indifferent fluid.

The tumor of the leg exhibited precisely the same structure as was found in connection with other similar cutaneous lesions, as described in the former report. The transitional line between the border of the growth and apparently healthy skin was very imperfectly defined under the microscope. Nowhere could a sharp line of demarcation be found. Numerous cellular elements, more or less disseminated, were observed to exist in tissue which to the naked eye appeared sound.

The piece removed from the old abdominal lesion still showed abundant traces of disease in the form of cellular infiltration, far more than would be expected from the external appearance to the naked eye. When this portion of integument was excised it was thought likely that nothing beyond a general thickening together with a deposition of pigment would be observed. An unusual amount of pigment was, however, not discernible with the microscope.

The capsule of the cervical gland was thickened as is ordinarily the case in hyperplastic glands. The glands were crowded with the same sort of cells as were found in the skin and other parts, constituting a very dense uniform infiltration.

The tubuli and acini of the parotid gland were seen in some places presenting normal appearances, the cells lining which showed no marked changes; at other points the acini seemed compressed. The greater part of the mass was uniformly infiltrated with cells identical with those existing in the cervical gland, skin, and elsewhere. This infiltration extended close up to the acini and tubuli, and at the surface was found in the adipose tissue.

Nothing markedly abnormal was found about the heart. The muscular tissue, however, was fatty; and corpuscular elements were unusually numerous in the connective tissue and some were also discovered between the bands of muscular tissue.

The cells of the liver were undergoing fatty atrophy, and there was a slight increase of connective tissue in the portal canals. There was no evidence of corpuscular infiltration either in the connective tissue or in the liver cells; nor were there anywhere aggregations of new cells.

No positive organic change in the stomach, except a slight fatty atrophy in the walls of the tubuli, could be detected. There were no infiltrations.

In the bladder, the lesion which has been referred to and described, was seen to be a somewhat circumscribed infiltration, manifestly of the same general character as those found on the cutaneous surface. The formation was thickest and densest towards the epithelial structure, and exhibited a disposition to form about the free surface. The cells were compactly arranged in trabeculæ as on the skin, and in the densest portions were fused. The epithelium on the free surface of the lesion was absent, the border displaying a frayed condition, from which the cells had apparently been washed out. In the submucous connective tissue and between the muscular bands the cells were found in abundance, especially beneath the circumscribed swelling. Beyond the borders of this swelling they also existed, but in fewer numbers.*

From the foregoing notes of the autopsy we observe that certain

* In the light of the results of the microscopical examination, it is to be regretted that portions of perfectly healthy tissue from various regions of the integument, as well as portions from all the internal organs and glands, were not removed and examined.

glandular structures were involved in the morbid process, a point of interest in considering the pathology of the disease. The nature of this alteration, however, is capable of more than one explanation. We have, moreover, seen that of the internal organs the bladder alone exhibited positive signs of disease. That the formation on the internal surface of this organ was of the same character as those on the integumentary surface can, I think, admit of no question; and its occurrence here goes to show the tendency of the disease to attack free surfaces rather than deep-seated tissues. This observation is also corroborated by the lesions which were noted to occur in the mouth and vagina. The character of the growth of the parotid glands, as stated, may be differently construed,—that is, as being due either to simple inflammatory changes, giving rise to simple hyperplasy, or, on the other hand, to a direct involvement of these glandular structures by the same morbid process as existed on the skin, mucous membrane, and wall of the bladder. I strongly incline to the latter view. The clinical features certainly point to this conclusion, while their microscopic appearances likewise leave no doubt in my mind as to the identity of the process at work in all of the structures invaded.

The notes of the case have been so fully recorded that but little remains to be remarked upon. The symptoms throughout the course of the disease were so peculiar that it was deemed a matter of importance that they should be noted *in extenso*. They certainly are of the greatest interest. Such an array of curious symptoms cannot, it seems to me, be regarded as peculiar to the case but rather as characteristic of the disease. I know of no disease where similar objective and subjective symptoms are encountered; certainly not in the recognized forms of sarcoma, as we know this disease and as it is described by authorities, nor in the several varieties of carcinoma, the only known maladies which one would be inclined to call to mind.

A point of great interest exists in the action of the morbid process to the influence of internal remedies. As will be recalled, among the numerous and varied medicines employed in the early stages of the disease with the hope of arresting or modifying the process, there was not one which exerted the least beneficial effect; on the contrary, with but few exceptions, they all aggravated the condition, and some of them in a very positive degree. Thus, small doses of iodide of potassium, mercury, and arsenic produced almost immediate and decided exacerbations, which in the case of iodide of potassium was alarming. Concerning local remedies, it was found that beyond modifying certain symptoms, such as itching and the amount of discharge, they were entirely powerless.

It will be remembered that five operations for the removal of the tumors were performed on four different occasions. The vitality and vascularity of the disease was at these times plainly established by the disposition to hemorrhage, which, in the case of the operations upon the face, was only arrested after the liberal use of ligatures.

The disposition for the wounds to heal kindly and readily (when the tumor and its base had been completely extirpated) was remarkable; and the more so as in no instance was there subsequently any tendency to repullulation. The apparently healthy character of the granulations of the several wounds, the rapid process of healing, and the final result—scarcely a trace of the incision being afterwards discernible on the face—are, moreover, all worthy of remark. At no period in the course of the disease was it noted that the lesions followed local irritation; they rather appeared to be entirely arbitrary as to their points of election, and consequently were generally distributed, with, however, preference for the head and trunk.

Of the nature of the disease unfortunately but little positive knowledge can be offered, for the process seems to be *sui generis*, regarding the matter as a whole and including all points, clinical as well as pathological. The inflammatory symptoms in the early stages of the disease are perhaps capable of being variously interpreted, but I cannot regard them other than as secondary to the disease proper. The profound impression on the system produced by the process, so plainly manifest latterly, without doubt insidiously began its work of disturbance very soon. Symptoms, some of which were regarded as insignificant at the time, occurred earlier even than the history shows, and differed only in degree from those that followed. The disease, as exemplified in the tumors, is unquestionably a new growth, allied in its pathology to sarcoma, but different from what we have heretofore recognized as sarcoma; very different from the forms of this disease as described (either clinically or pathologically) by authorities. Therefore, if we place this case among the sarcomata, as Dr. Heitzmann suggests,* the subject of sarcoma must be allowed a broader definition than obtains to-day; for there are many points which are difficult or impossible to reconcile with our present views of sarcoma. Indeed, it seems to me that rather than relegate the disease to that already confused group, it is wiser to allow it to remain for the present as unclassified. One case is insufficient to determine the question. In time the disease will doubtless find its place, and I venture to predict it will be no uncertain one.

Since presenting the case to the Association at the last annual meeting, Dr. Piffard has been kind enough to send me a photograph of his patient supposed to be suffering from the same disease,—the same case to which reference was made in the discussion at the last meeting. From a study of these photographs, together with the history and the statement that the patient had died, I have no hesitation in regarding the case as exhibiting the same disease as that under consideration. I am at present, therefore, familiar with four cases, all of which bore very similar clinical features.

Dr. Longstreth, who has been much interested in the case with me, at my request has kindly expressed his views as to the nature of the disease, which I take pleasure in presenting.

* See ARCHIVES OF DERMATOLOGY, January, 1879, page 19.

REMARKS BY DR. LONGSTRETH.

The striking phenomena of this unclassed and unnamed disease, found in this patient, viewed in an anatomico-pathological aspect, are the adherence, more or less close, of the lesions to the epithelial surfaces of the body,* the vast amount of material concentrated, and the absence of infection of other structures or organs of the body (by means of metastasis or transplantation).

The characteristic of the lesion appears to be the crowding of the connective tissue of the skin with cellular or corpuscular elements. Considered in respect to their form, the cells have nothing characteristic of any new formation or growth, merely resembling those of granulation tissue; in respect to their arrangement the cells do not present anything characteristic of a tumor growth. There is this statement to be made concerning the arrangement or massing of the cells, which seems to me to be conclusive (so far as it is possible to be conclusive) of the pathology of the lesion. The cells are arranged in more or less straight lines (at least this is true of the newly-formed lesions), and this arrangement is the same as I have found in a variety of inflammatory changes, marked by a similar abundant appearance of new cellular or corpuscular elements. As illustrations of this condition, I may refer to what is seen within the alveoli of the lung in croupous pneumonia, examined in the early stage of red hepatization; the exudation-cells are pressed close together in the meshwork of the fibrinous net, and, in the height of this stage of the disease, these cells are seen arranged in straight lines conformable in direction to the fibrous mesh, the cells, as it were, are strung in lines along the fibrin spanning the alveoli. The appearance of a Peyer's patch, when it has just reached the stage of most marked enlargement, presents a striated arrangement of the cellular elements very strikingly similar to that seen in the lung and in the lesions of this skin. The explanation of this arrangement of cells is to be found in the changes brought about in the normal tissue by the distention caused by the influx of the new elements. The distending force of the cells stretch out, elongate, and render straight the connective tissue and other fibres, which under normal conditions have a tortuous arrangement. The cells naturally are confined within the

* "Epithelial surfaces" means a tissue or organ covered with epithelium, and of course includes the subjacent tissue or elements which have a histological connection with such a surface. For example, in respect to the skin the term is applied to the cutis and subcutaneous cellular tissue; it includes, therefore, three histologically connected parts, namely, the subcutaneous cellular tissue, the derma, and the epidermis. [See Stricker's Manual of Histology, chap. 26.] In respect to the mucous membrane, the term "epithelial surfaces" includes every structure or form of tissue met with from the surface down to the parts beneath, which are histologically disconnected with such a surface, that is,—from the surface to the fibrous sheath of the muscular layer. The term "epithelial surfaces," as it is used, does not refer, as was incorrectly stated or supposed in the discussion of Dr. Duhring's communication, to a component part of such "epithelial surfaces," namely, to the epithelium or epidermis alone.—M. L.

limits formed by the fibres, and thus present a distinct striation. The arrangement of the cells, in relation to one another, is not a characteristic of pneumonia or of typhoid fever; neither is it a characteristic of this disease, but it is an essential feature of the process by which the lesions of this skin were produced, and closely allies the processes of these morbid changes to each other.

The presence of the cellular or corpuscular elements in the tissues beneath the skin is comparable to the condition found in the surroundings of every inflammatory or other centre of infiltration, and the presence of these cellular elements in the adipose, muscular, arterial, or nervous tissues must not be viewed as a tendency of these tissues to degenerate into or to be involved in this lesion,—certainly not in the same sense as in the cancerous invasion of adjacent tissues. The muscular and fibrous coats of the intestine in typhoid fever beneath an involved Peyer's patch, and the alveolar walls of the lung in pneumonia, show similar dissemination of cells as is found here in the tissues beneath the involved skin.

The second characteristic, viz., the amount of new material present in the lesion, has a twofold aspect of importance. In a clinical aspect, we have the malignant course of the disease and the cachectic appearance presented by the patient; in an anatomico-pathological aspect, we would expect to find systemic infection by metastasis.

Malignancy, used as a clinical expression, means that the disease or the lesion leads to death, and the degree of malignancy is more or less proportioned to the extent of the disease or lesion and of the accompanying blood alterations. The malignant course of the disease in this patient is to be accounted for by the vast amount of cellular constituents used in forming the lesions and the consequent alterations in the blood due to the withdrawal of the corpuscular elements from its current.

Cachexia, or the cachectic look of patients suffering from malignant disease, is a change by no means invariable or uniform. The cause of the cachexia is "the alteration or corruption of the blood and fluids" of the body, "bringing with it emaciation with anæmia and hydræmia, increased by ulceration and its consequences (loss of blood and fluids), as well as previous occupation of organs important in the new formation of blood; cachexia may be absent if the malignant growth is small, firm, and remains confined to its original seat or place of origin." [Samuel, *Hanb. d. allg. Path.*, etc., iii. abth., s. 602, u. iv. abth., s. 903.]

It would seem *a priori* that the change of color, as well as the other phenomena of cachexia, must be due to a blood change rather than to a general tissue change (except so far as general tissue changes necessarily accompany blood alterations), and that the blood change must be one especially affecting its corpuscular elements or the proportion which the white corpuscles bear to the red. It seems *a priori* probable, also, that if it be true, as Samuel says, that in small, firm, non-metastatic tumors cachexia is *not* present, and conversely that in soft, cell-rich, malignant growths, giving rise to metastatic

knots, cachexia *is* present, in the one case the blood would be rich in corpuscular elements (derived from the cell-growth of the tumor, its immature cells or nuclei), and in the other case would be poor in such cells; and also that such corpuscular elements are the cause, at least in part, of the altered appearance of the cachectic patient.

I have a very few observations in which a marked cachectic appearance was coincident with an increase of corpuscular elements in the blood, resembling white corpuscles. In the case here referred to the autopsy proved the existence of a malignant growth, rich in cells, and I have no doubt that nuclei or immature cells of the new growth found their way into the blood-current and gave rise to the increase in number of so-called white blood-corpuscles counted in the blood during life. The cachectic appearance of this patient similarly may have been due to the existence of altered corpuscular proportions of the blood. The rapid increase and the equally rapid diminution of the lesions, and the lymphatic gland enlargement (which had also rapid rises and falls), show conclusively that the blood must have been not only the source of this vast amount of misplaced material composing the skin lesions, but also the recipient of it after the absorption of the lesion and the subsidence of the gland enlargement.

The vast amount of material in the lesions, viewed from a purely anatomico-pathological aspect, would lead us to expect, if this disease were a sarcoma, to find metastatic knots in other parts of the body. A sarcomatous tumor, so succulent, so rich in cells, and with cells so mobile, would almost certainly have had such a result.

In respect to the third one of the characteristic phenomena of this disease, viz., the absence of infection of other organs of the body by metastasis, something still remains to be said. The lesion of the urinary bladder is not to be regarded as a metastatic formation but as an exhibition of the tendency of the morbid process to develop and manifest itself on and about a free "epithelial surface." It is an outburst of the disease at a new surface point, just as occurred on the cutaneous surface at so many points; surely these skin lesions are not to be spoken of as metastatically related to one another. The occurrence of the lesion of the bladder does not follow the rule concerning the infection of distant organs. The process of metastasis consists in the absorption, by lymphatic agency, of the cells or nuclei of a morbid growth, the transferrence of these bodies to the blood, and the deposit of the wandering new-growth elements in the tissue or capillary net of a distant organ where the development and new formation of a tumor, resembling the original, takes place; or the new-growth elements enter directly the blood-vessels, usually a vein, and are carried with the blood-current to a distant point; in the latter case the name of metastasis by embolism is given to the process. The point of selection for the development of the metastatic knot depends largely on mechanical grounds; the embolic mass is carried onwards until it reaches a vessel (usually a capillary, for these masses are, of course, very minute) whose calibre does not allow of its passage; here it rests and develops. The histogenetic

relations of tissues influence also the selection of the point of development. Mammary gland tumors are developed by metastasis, in the liver, partly because the two organs are histogenetically related, both being glandular epithelial organs, partly also because the blood-vessel capillary net of the liver is quite the finest in the body. Sarcomata of the bones, being histogenetically related to other bones, have their metastatic knots appearing in bone at distant parts; but not invariably, because the wandering elements of these tumors are in large masses and abundant, and, consequently, are liable to be strained out, so to speak, by any narrow-calibred capillary net through which they pass and develop in tissues not related to bones histologically.

Concerning the lesion of the parotid gland, the explanation is not so clear and definite as in respect to the bladder. It is possible to suppose that the invasion of this organ was a fortuitous occurrence resulting from the involvement of the surrounding parts and of the skin overlying it. It is well also to remember in this connection that the parotid gland is an epithelial structure, and that its tubules are to be included in the list of "epithelial surfaces." Whatever may be the explanation of its involvement, it is clear that it is not an instance of metastasis.

It may be well to mention that the enlargement of the lymphatics did not uniformly occur in glands seated near large lesions (for example, the axillary glands), and that the microscopic picture presented by them was that of a hyperplasia. It was not the picture seen in glands situated near malignant growths, but rather that accompanying inflammation or a similar irritation.

In conclusion, attention must be fixed on the fact that the appearances, both microscopical and clinical, indicated the disease to be one produced by an infiltration of the tissue; the relations of the corpuscular elements to the tissue in which they are placed are the same as those found in other diseases in which an infiltration is unquestioned; the rapid rise and fall of the tumors, so called, show the nature of the disease to be of this character. No one ever saw a malignant growth, not even a sarcoma, rise in a night and disappear by the end of a week. The size and the structure of its cells does not throw one morbid growth into one class, and another morbid growth into another; this method of classification was dispensed with, I supposed, when we refused to take scrapings of a tumor and call it cancer, because the microscope showed irregular-shaped cells. There is nothing in the structure, relations, or the mode of production of this disease, which resembles sarcoma. A sarcomatous tumor is decided to be such, not because its cells are spindle-shaped or round, but because the growth, made up of spindle or round cells as a whole, has a certain relation to the tissue in which it is placed. A disease of the intestine is decided to be typhoid fever or tubercle, not according to the kind of cells found, but according to the position of the cells and the relation they bear to the tissue in which they are placed. As already explained, the disease cannot be

regarded as one occurring in a connective-tissue structure, and therefore we should not be inclined, from its apparent seat beneath the epithelium, to place it among sarcoma; it occurs in an "epithelial surface," and the connective-tissue part of this surface has its histological *descent*, not from the same blastodermic layer as the connective-tissue organs of the body, viz., the middle, but from the outer or epithelial layer.

Again, particular stress must be placed on the vast amount of material required in the construction of the lesions. Whether the material has its origin in the blood or in the tissue there is no means of deciding, and, therefore, whether there was a dyscrasia present is undecided. What is probable is that the corpuscular material in the lesions was transferred to the blood on the subsidence of a swelling (we have no observations of the blood in the later stages of the disease to decide this point), and that the cachexia and malignancy (closely connected conditions) are the results of the vast amount of the corpuscular material being thus thrown into the blood-current, attacking and destroying its normal structure.

And again, let us remember the absence of infection of other organs, which, with such monstrous lesions, composed of such highly succulent material, is incompatible with the supposition of a sarcomatous growth.

I do not mean to say that this disease is a simple inflammation; it may have to be placed in an intermediate district between inflammation and new morbid growths or tumors; I do not think it should be placed among sarcomata, until that division of new growths receives the revision it so much needs and is recast. Better let it be unnamed and unclassified than be placed and become fixed wrongly.