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## Original Articles.

### HYPERTROPHY AND HYPERPLASIA CONSEQUENT UPON LESIONS OF THE GENITALIA.*

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In presenting the subject of hypertrophy and hyperplasia incidental to lesions of the genitals, I shall not attempt to edify you with a wearisome resumé of all the work that has been done in this field. Some of this work has been composed of such illogical reasoning and so many inaccurate observations, illy assorted and crudely digested facts, that it constitutes a mass of pathological and clinical inaccuracies, useful, perhaps, for comparison and criticism, but absolutely useless to a body of clinicians of this day and generation. As far as the historical interest surrounding the pathological errors of the past is concerned, the classical contribution of R. W. Taylor has done the subject full justice. It has been mainly through the efforts of this author that the fanciful and absurd pathological conceptions of Huguier, published only a little more than four decades ago, have been dispelled and the errors of those who have followed Huguier—like sheep following the bell-wether over the fence,—illumined by the light of modern pathology. It was an unfortunate thing for pathology, that the essay of Huguier

* Read before the Chicago Medical Society, December 7th, 1891.

on esthiomène or lupus of the vulva[1] was ever published, for it was so generally accepted as law and gospel as to have been regarded as a classic until comparatively recent years.

Great men fell into the pathological trap set for them by Huguier and his contemporaries quite as readily as did the rank and file of the profession. The fact that the late Isaac E. Taylor adopted and taught the views of Huguier is very significant in this connection.[2]

R. W. Taylor has well stated the case when he says, regarding Huguier's brochure: "It is very probable that most of his cases were those of old syphilis, their etiology was wholly unexplored and the clinical history of the fanciful disease was given in the most positive manner, though based only upon crude and far-reaching assumptions. It seems wonderful that his lucubrations were entertained by educated men. Yet even to-day, though there are a few dissenters, there are very many believers in a morbid entity which they call lupus or the esthiomène of Huguier. I do not know in all medical history of an essay founded on gross error and pure assumption which had such influence for so many years in moulding medical opinion, not only in France but in other countries."[3]

The fact that the subject is still replete with error, or even a terra incognita to the majority of general practitioners, is my excuse for bringing it to the attention of the Society this evening. I do not hesitate to say, that in my opinion many specialists fail to grasp the principles of pathogenesis underlying the conditions which I propose to consider. In presenting these principles, I may be here and there somewhat heretical, but I trust that my facts may be none the less consistent.

Nearly, if not all the special work that has been done in the study of hyperplasia, chronic ulceration and hypertrophy of the genitals has been devoted to the study of these lesions in the female. It is my purpose to demonstrate that the lines of pathological parallelism between the male and female are closer than is generally supposed, as far as the lesions under consideration are concerned. The difference in degree and frequency is admitted, but even this is due to certain local anatomical and physiological peculiarities, the result of which is by no means conducive to the well-being of the female.

Beginning with the lesions observed in women, it is safe to say that Taylor's conclusions, as based upon hundreds of carefully studied and well observed cases, are not only comprehensive but with few, if

[1] P. C. Huguier, Mèmoire sur l'esthiomène ou dartre rongeante de la region vulvo-anale. Paris 1849.

[2] Lupus or esthiomène of the vulvo-anal region. Trans. Am. Gyn. Soc., 1882.

[3] R. W. Taylor. Chronic infiltration, inflammation, and ulceration of the external genitals of women. N. Y. Medical Journal, January 4th, 1890.

any, qualifications absolutely correct. I therefore take the liberty of presenting them verbatim.

"1. A large and perhaps the greater number of chronic deforming vulvar lesions are due to simple hyperplasia of the tissues induced by irritating causes, inflammation and traumatisms.

"2. Chronic chancroid is a cause in a certain proportion of cases.

"3. Many cases are due to essential and specific syphilitic infiltrations.

"4. Other cases are caused by the hard œdema which often complicates and surrounds the initial sclerosis and perhaps gummatous infiltration.

"5. Many cases are due to simple hyperplasia in old syphilitic subjects who suffer from chronic ulcerations of the vulva long after all specific lesions have departed.

"6. Some cases, also in old syphilitics, are due to simple hyperplasia without the existence of any concomitant ulcerative or infiltrative process and seem to be caused by conditions which usually in healthy persons only result in vulvar inflammation."

Regarding the influence of simple irritation in the production of deforming vulvar lesions, Taylor quite naturally takes up for consideration vegetations, caruncles, and simple hyperplastic tumors of the vulva, and has traced the successive gradations of pathological development from these minor growths to those enormous tumors occasionally seen, which are productive of so much deformity and mechanical discomfort. In the light of our clinical knowledge of the smaller growths which indicate the point of departure on the road to extreme degrees of hypertrophy and hyperplasia, it is not easy to understand how local conditions alone as believed by Taylor can cause the development of such growths. When we are confronted by the more formidable varieties of lesion, the query becomes still more pertinent: Are local circumstances of environment alone responsible for this condition? Is there not required some inherent predisposition? If not, why do not all patients with similar or worse local environment, present similar lesions?

How like the vegetable fungi is the development and even the physical appearance of the so-called venereal vegetations. Heat, moisture, filth, deprivation of light and air, and more or less continuous irritation are the essential conditions for the development of the mush-room-like genital vegetations. But whence comes the peculiar influence which develops them in one dirty patient rather than in any one of a dozen others? Why is it that a woman may develop from a comparatively slightly irritating discharge during pregnancy,—mayhap

without venereal infection—an enormous mass of vegetations while much less cleanly and perhaps gonorrhœally infected women with profuse and acrid discharges escape? Why will vegetations springing up in several women, under circumstances apparently identical, take such a dissimilar course; in the one, a few small and insignificant growths appearing, while in the other an enormous mass develops in an incredibly short time? It certainly must be admitted that the discharges of a pregnant woman have no specific property per se, yet it is during pregnancy, especially, that vulvar vegetations flourish and wax luxuriant. This, in face of the fact that women with serious uterine and vaginal discharges do not often become pregnant. If, then, there are no evidences of post-pregnant venereal infection we must necessarily admit that the presence of "venereal" vegetations in any given case is not a criterion of the acridity or specificity of the discharge.

Heat, moisture and darkness favor the development of vegetable fungi, but these conditions do not develop fungi. The seed must be sown or pre-exist in the soil, and the soil itself must be of proper quality. We must either admit a special bacterium in genital vegetations, or else advance something in the way of individual susceptibility of tissue and tendency to connective tissue proliferation, to explain the occurrence of these lesions in so small a proportion of cases of like conditions. Again, primary predisposition alone may not be a sufficient explanation. We must still explain the development of vegetations, caruncles, etc., in pregnant women in whom the local conditions are no worse than for months or even years before pregnancy occurred, yet in whom vegetations develop only after pregnancy, and almost immediately thereafter.

It is easy to understand how one may be led to believe that local causes are all-important in the causation of chronic deformities of the vulvo-vaginal and vulvo-anal region from observation of broken down prostitutes, but even these conditions occasionally occur in comparatively young women, and persist and prove fatal despite removal of sources of irritation and the best of treatment.

In seeking the cause of perverted tissue-growth, we must consider not only the excitant, be it bacterial, chemical or traumatic, that sets the process of pathological tissue-building in motion, but the inherent physiological power of development—through the medium of which all perversions of tissue growth must necessarily act. Independently of the potential power of proliferation and development possessed by the cell per se, there exists, to put it metaphorically, a master architect and general superintendent of construction somewhere in the nervous centers, exactly where we do not know, but in close relation at least to the great sympathetic system. The result of this

superintendency we recognize as the trophic or nutritive function of the nervous system. To consider whether there be a special trophic system or simply a specialization of function on the part of the sympathetic ganglia as a whole, which seems most probable, would be begging the question. As in the building of a house faulty construction may be in the direction of poor materials, lazy or incompetent workmen or poor architecture and superintendency, so in tissue building we may have faulty pabulum, excessive zeal or laziness and incompetency of cells, and faulty architecture or superintendency.

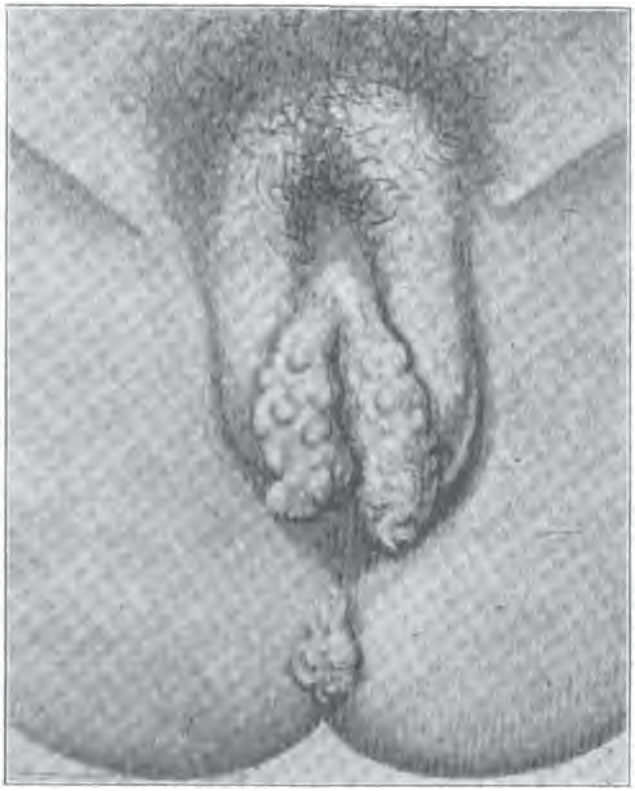

FIG. 1. Showing great hyperplasia of the clitoris and nymphæ. (After Taylor.)

Now, it is my humble opinion that we are drifting away from certain sound principles of medical philosophy, abstract perhaps, but still practical and logical, into too materialistic a view of pathological states, the focal point of which is the germ and its products; or to put it more succintly, a view which is chiefly founded on the local and tangible influences which tend to excite pathological conditions. The

influence of the nervous system, firstly in normal and secondly in abnormal conditions of tissue-building is forgotten.

As regards the various forms of genital hyperplasia and chronic induration, the microscope shows them to be composed of simple overgrowth of connective tissue with a varying amount of new vascular tissue. It is hardly necessary to call attention to the fact that we have here an excellent illustration of exaggerated repair, and that behind it we have the normal trophic impulse. Now, I cannot be convinced that this overgrowth is due to local causes alone; there is too great a disparity between the number of those in whom the supposed local causés exist, and those in whom these conditions actually develop. I believe, in brief, that the difference between those who do and those who do not develop these conditions under like circumstances lies in the direction of the nervous system. In other words, I believe that the essential cause is a tropho-neurosis. We have not far to look for analogies. Have we as yet received any satisfactory explanation of Keloid? And where can we find a prettier illustration of tropho-neurotic disturbances than in herpes zoster and its congeners, more particularly herpes progenitalis? If the illustration of herpes progenitalis be not accepted, I desire to call attention to menstrual herpes and the herpes of pregnancy. These latter conditions may be associated in your minds with the irritation of menstrual and utero-vaginal discharges; I have, however, observed menstrual herpes occurring regularly just before and during menstruation, and in pregnant women who have no discharges of any kind. I have met with two cases where the first and pathognomonic sign of pregnancy is herpes progenitalis, recurring in one case precisely at the usual menstrual epoch.[1] The serious nutritive results of herpes, or rather the nutritive perversion of which herpes is but a symptom, are well known. Those who are engaged in ophthalmic practice will at once recall the disastrous effects of herpes frontalis seu orbicularis when the eye is invaded. As a further illustration of a tropho-neurosis, I will call attention to Raynaud's disease. The cause of the tropho-neurosis may consist of a congenitally unstable equilibrium of trophic innervation, or of an acquired perversion due to constitutional causes or to local influences of a reflex character. There may or may not be a germ factor in the case. Obviously, when once the perverted tissue-building has begun, we may have at any time in the course of the affection intercurrent ulceration, suppuration or necrosis, dependent on the degree of tropho-neurotic disturbance, and the degree and kind of local irritation or infection, present. It will be observed that I give due credit to purely local conditions.

[1] I have expatiated more fully upon the subject of herpes progenitalis in a paper read before the North Texas State Med. Assoc. Dec. 15, 1890.

In classes 2, 4, and 5 in Taylor's conclusions we have lesions which are, in my opinion, still more closely associated with tropho-neurotic disturbances than are the simpler genital lesions, and differing from the latter in the fact that there is a tendency to tissue necrosis which results in more or less extensive ulceration, and oftentimes sloughing. As far as chancroid is concerned, there is, even in the primary chancroidal infection, no tendency per se to extensive destruction of tissue; the process is self limited. It is probable that phagedæna, sloughing, and serpiginous ulceration of a chronic character are not due to the primary infection, but to local or constitutional conditions predisposing to tissue destruction or to secondary infections. After eliminating all local causes of severity or malignancy, there still remains a certain proportion in which profound destruction of tissue results. In some of these a true cachexia exists as explanatory of the severity of the process, syphilis being very apt to lead to a severe type of chancroid. In others, however, healthy, robust patients will be attacked by phagedæna and perhaps serpiginous ulceration, while other patients of apparently less robust physique will contract simple chancroid from the same source of infection. This I have known to occur even among cleanly patients in private practice. The key-note to the situation I believe to be a tropho neurosis in the one class, which does not exist in the other. If this be true of acute chancroid, how much more powerful must the element of tropho-neurosis be in the so-called chronic chancroid, a condition which should not be termed chancroid at all, and which consists of chronic post-chancroidal ulceration, the starting point of which is a virulent infection to be sure, but the perpetuation of which depends upon so-called idiosyncrasy. Would not the term tropho-neurosis, theoretical though it may appear, be a welcome substitute for idiosyncrasy in these cases? In the battle between the cells of the infected area and the poison of the infection, the cells conquer after a short period; the power of the virus is exhausted and simple ulceration takes the place of a virulent process; in other words, the product of the evolution of infection undergoes involution under the modifying influence of the cells of the affected part. This, under normal circumstances and in the majority of individuals. Have we nothing better than the term "idiosyncrasy" to account for the cells giving up the fight in some less fortunate patients?

The relation of syphilis to hypertrophic and ulcerative chronic lesions of the female genitalia is, in my opinion, of the utmost importance. Dr. Hyde has dwelt with especial emphasis on the intimate association of syphilis with these lesions.[5] Dr. Taylor takes exception to the etiological prominence accorded syphilis by Dr. Hyde, but it

[5] Journ. Cutaneous and Venereal Dis.

seems certain that the conclusions of the latter are sound as far as his own cases are concerned. Taylor's word of caution is, however, timely, as it is quite common for the practitioner to attribute every lesion of the genitalia, whether simple or severe, to syphilis, if a history of that disease be elicited, no matter how remote the infection may have been. Leaving out of consideration the essential and specific syphilomata, there are certain cases, and these are by no means a minority, in which the relation of the syphilis is indirect, i. e., we have processes resulting from simple irritation, traumatism or chancroidal infection, upon a syphilitic foundation on the one hand or a tropho-neurotic foundation produced by syphilis on the other. As an additional factor, alcoholism is apt to be quite prominent. It has been my fortune to see a number of cases of chronic ulcerative vulvar lesions, and it has so happened that, as far as I can recall the cases, they have all been patients who had passed through a more or less severe course of syphilis. As most of the cases I have seen have been hospital patients, and most of the old timers seen in hospital practice are syphilitic, this may not count for much but it is worthy of note.

Another point which is worthy of consideration is that these cases are usually dosed with mercury at varying intervals and in varying amounts. I have seen many cases of chronic ulcerative processes not only about the genitalia, but elsewhere, that have been made worse by if indeed their chronicity was not dependent upon the abuse of this drug, which brings up the practical point that in these cases of chronic ulceration and hyperplasia of the female genitals, we must be careful not to treat the syphilis too vigorously, even if a clear history of that disease exists; on the contrary, we must treat the patient and her ulcerative process rather than a constitutional infection which as an entity may no longer exist.

I have been led to regard the severe ulcerative and hyperplastic affections of the genitalia coming on at a late period in syphilitic patients in the same light as other sequelar lesions. Their true character I believe to be tropho-neurotic. I presented this view of the late lesions of syphilis in extenso in a paper before the Southern Surgical and Gynæcological Association, in 1889, a copy of which I recently sent to each member of this Society. Time will not permit me to expatiate upon this subject this evening.

The source of the tropho-neurosis in syphilis is rather complex and can be arranged in several factors. First, The effect of the syphilitic infection on the nervous system during the active period. This gives rise to tropho-neurotic disturbances both immediate and remote. Second, The effect of mercury, either from special intolerance or excessive and injudicious administration. Third, Alcoholism. Fourth,

Vicious environment, with all that it implies. Fifth, Malnutrition from privation. Underlying all, may be a special fault of nervous structure with resultant instability of nutritive equilibrium under all forms of pathogenesis.

Does not this view of the etiology of the class of genital lesions under consideration explain the lesions described in Taylor's sixth class, of old syphilitics, in which simple hyperplasia "seems to be produced by conditions which usually in healthy persons only result in vulvar

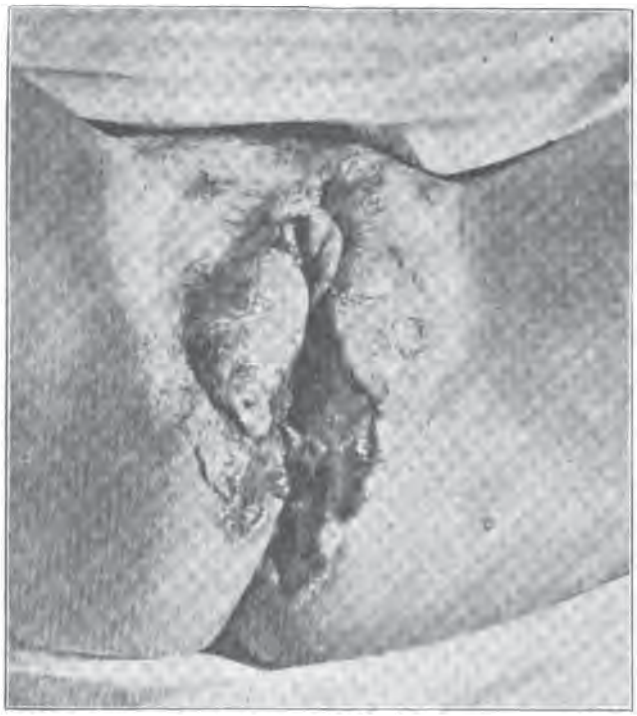

FIG. 2. Showing great destruction of hypertrophied vulva and perinæum in an old syphilitic. (After Taylor.)

inflammation?" If so, we have only to consider that the supervention of ulceration and infiltration depends upon the degree of the trophoneurotic disturbance, and we can apply the same explanation to several of the other classes of these peculiar lesions. Aside from the trophoneurotic element in the causal influence of syphilis upon the development of chronic deforming vulvar lesions, there is a special effect which may result from the primary lesion which may be developed at either an early or later period. This special effect is included by Taylor under the head of "cases caused by the hard œdema which often complicates

and surrounds the initial sclerosis and perhaps gummatous infiltration." This indurating œdema is an important element not only in syphilitic cases, but may be a factor even in non-syphilitic lesions in subjects who have previously suffered from syphilis. Taylor lays especial stress upon its occurrence in the primary stage of syphilis, and states that it is the sole appanage of syphilis. This I believe to be true. As Taylor further shows, and as I have several times observed, cases occur in which a chancroid, or simple inflammation, may set up this peculiar condition months after the primary lesion has disappeared. Thus, I have seen one case in which indurating œdema followed a chancroid nearly a year after syphilitic infection. I am inclined to believe that some of the so-called chronic chancroids owe their chronicity to the fact that the infection has occured upon a syphilized base. The explanation is not difficult. The immediate damage to the multitudinous capillary lymphatic supply of these parts by the primary lesion is well recognized. That this damage may be permanent is not to be denied. With looseness of structure, obstructed lymphatic drainage, dependent position and more or less constant irritation, traumatic and chemical, it is by no means surprising that œdema should finally merge into connective tissue hyperplasia and firm induration. That slight causes produce œdema of the genitals, primarily, is known by every one whose experience ranges over even a dozen or so of cases of venereal lesions in male or female.

It would be a work of supererogation for me to attempt a minute description of the peculiar indurating œdema of syphilis. Taylor's monograph is a classic on this subject. The point which I desire to make in connection with this form of lesion is that while later on the element of tropho-neurosis may be superimposed, or may even exist primarily, the chief factor in the condition is of a mechanical character and relates to the lymphatic vessels and glands. Taylor dwells in this connection, on the active influence of the syphilitic diathesis in cases of late indurating œdema excited by traumatism, and shows the enormous hypertrophy of the vulvar tissues incidental to this peculiar œdema. The term diathesis is in this connection a little obscure. We should have some explanation of a local character, of the peculiar results of trauma and local irritation in a syphilized as compared with a non-syphilized patient. Is not the keynote of the pathological situation sounded by Taylor in the remark that "syphilitic inguinal adenopathy is observed as a rule in these cases?" The greater degree of lymphatic involvement in these cases as compared with ordinary syphilitics in the latter periods of the disease is to me an all-sufficient explanation of indurating œdema. With depots clogged and roads obstructed it is not remarkable that pathological goods should

accummulate in the factory, i. e., the genital lesion and its immediate environment. The possible irritating effects of pathogenic organisms must of course be considered in connection with the determination of the disease, and especially with its perpetuation if ulceration exists.

The analogy between the male and female types of chronic deforming and ulcerative chronic lesions of the genitalia is especially marked in cases of indurating œdema. That this may be extensive is shown by a case reported by Sturgis,[6] a reproduction of which I will later exhibit. I have seen a number of less marked cases of a similar character, and while I have seen a few in which indurating œdema followed a concealed chancroid in which there was no history of syphilis and no subsequent symptoms of the disease, it has been my fortune to .observe that in nearly all cases there has been antecedent syphilitic infection, or the œdema has been directly dependent on a chancre or a mixed sore. I am inclined to believe that while chronic ulceration is less often seen in the male, the comparative infrequency is due to local anatomical and physiological peculiarities, and the relatively greater facility of management of such conditions in the male. Many cases of condylomata, gummy ulcer and recurrent induration in the male might be transformed into chronic deforming lesions similar to those seen in the female, if local environment were favorable.

That the lines of pathological parallelism are sometimes quite closely drawn was shown by two very interesting cases observed during my term of service at the New York Charity Hospital. One of these was a young woman with so called lupoid of the vulva in whom the ulcerative hyperplastic process involved the entire vulva, the glands of the groin, and femoral regions in one continuous hyperplastic sluggish mass bathed in scanty ichorous pus. The condition was painless but the cachexia profound. This case proved resistant to treatment and finally died after many months invalidism.

The other case was that of a man under middle age who had a precisely similar condition, involving the entire penis, anterior portion of the scrotum and the inguinal and femoral glands. This case was in the hospital for four years and was treated in every conceivable way without effect. He finally drifted into a homeopathic hospital and died, after having achieved a tremendous reputation as a pathological curiosity and a perpetual clinic. This man was a robust person originally, who had been syphilized. The local infection which finally destroyed life was, in all probability, in no wise different in these two cases from that in thousands of other cases of chancroid, but observe the difference in results. Surely there must

[6]Journal Cutan. and Ven. Dis.

be some special condition behind such cases. This I have already expatiated upon.

The possibility of these cases having been tuberculous may suggest itself at this point. Although I saw these cases before the question of the tubercle bacillus had assumed very definite proportions, and consequently cannot speak authoritatively, I do not believe they were tubercular in character. Neither case developed tubercle elsewhere and both cases were of long duration. It is probable that some few cases of so-called esthiomène have been of a tuberculous nature. There is a form of local ulcer occasionally seen which begins as rounded, dark-red or purplish tubercles, finally forming ulcers with a fungous, granulating surface, free purulent secretion, and hard everted borders. Taylor has seen three cases of this kind, and following Hardy and Bazin, classifies them as "*scrofulide tuberculeuse ulcéreuse.*" These cases, however, he observed before the advent of the bacillus tuberculosis. In one case pulmonary phthisis existed. Taylor concludes from his observations, "That vulvar ulcers, not hyperplasiæ or hypertrophies, may be very rarely caused by tuberculous infection and that they should be included in our classification. If it is hereafter established beyond all question that lupus and tuberculosis are wholly identical in their nature and clinical history, we shall then have to admit that there is a lupus of the external female genitals. In the meantime we can content ourselves with the thought that what has heretofore been considered as lupus on these parts is not lupus at all." There is a peculiar form of chronic vulvar lesion described in former times as oozing tumor, and cases of which were reported by Duncan, as lupus and hemorrhagic lupus, which are of interest. Taylor attributes the so called hemorrhagic condition to the excoriation of coapted hypertrophic surfaces, and the consequent exudation of serum or sero-sauguinolent fluid. I observed one case in the New York Charity Hospital which was quite typically hemorrhagic. The woman had been syphilized, and contracted chancroid which became chronic. Pregnancy occurred and soon afterward the labia became enormously swollen and painful. Hemorrhage from the affected part soon began and the pain was relieved, but the parts settled down in a state of obstinate chronicity. The hemorrhage persisted constantly. Notwithstanding the fact that confinement occurred in the venereal ward which was filled with the worst class of cases, and despite the local condition which so favored septicæmia, the woman not only convalesced satisfactorily, but her local lesion entirely healed in a few weeks. The relation of the pregnancy to the hemorrhagic condition of the lesion is obvious. The child of this woman, by the way, subsequently died of meningeal hemorrhage of distinctively syphilitic origin.

There is much more that might be said upon this interesting subject, but I have already occupied too much time. I will therefore trust to my charts to fill in the defects in my paper.

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[*For Discussion see Society Proceedings.*]