stools, until ten weeks after the beginning of the disease; after this period special rules are provided for those who may still be bacillus carriers. As yet no such regulation exists in Boston or Massachusetts, but a knowledge of the presence or absence of typhoid bacilli in the stools would exert much influence upon the date recommended for the discharge of a patient. Such work would demand much time, but it would represent a high standard of preventive medicine.

CONCLUSIONS.

1. Our data agree with those of investigators having much larger series of cases, namely, that typhoid fever generally can be diagnosed in the first week by use of blood cultures, but that this method yields positive results in only about sixty per cent of the cases in the second week.

2. The typhoid bacilli are most easily obtained by blood cultures from the severest cases.

3. The typhoid bacilli were found in the relapse of typhoid fever in three individuals.

4. Typhoid fever is becoming more and more a disease to be treated in the larger public hospitals.

5. Isolation of typhoid fever patients in hospitals for the sake of other patients and particularly for the nursing staff is demanded.

6. Early diagnoses on entrance to the hospital and the detection of bacillus carriers before discharge are requisites in the present campaign against typhoid fever.

We wish to express our appreciation of the courtesy extended to us in our work by Dr. George B. Shattuck, Dr. John L. Ames and Dr. John Bartol who placed all their typhoid patients at our disposal, and to Dr. Francis H. Williams and Dr. Horace D. Arnold from whom we obtained special cases. The work would have been impossible without the co-operation of Drs. Rhea, Mabee and Bosworth of the Pathological Laboratory to whom we feel much indebted as well as to Dr. Adler for helpful suggestions.

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THE USE OF TUBERCULIN IN THE TREATMENT OF LOCALIZED TUBERCULOSIS EXCLUDING PULMONARY TUBERCULOSIS.*

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THE treatment of tuberculosis with the various products of the tubercle bacillus is nearly as old as the discovery of the specific cause of tuberculosis. A considerable mass of evidence has been collected concerning the therapeutic use of tuberculin in various ways. More recently, Trudeau and his associates at Saranac Lake have argued that the end to be attained was immunity against the tubercle bacillus. Some facts of animal experimentation also seem to favor this view. Those observers have reported a considerable series of cases of pulmonary tuberculosis showing the value of increasing doses of tuberculin. Sir A. E. Wright, of England, has utilized the theory of phagocytosis. He believes that in cases favorable for treatment, which are essentially localized tuberculosis, there is a deficient amount of opsonins, those substances in the blood which prepare the bacteria for ingestion by the leucocytes. According to his theory tuberculin acts by increasing the amount of opsonins, and the treatment should be controlled by the determination of the opsonic index.

It is not the purpose of this paper to discuss the theories of the action of tuberculin but to give the results obtained in a series of cases of localized tuberculosis. There were 25 cases, divided as follows: 9 cases of tuberculous adenitis, 4 cases of lupus vulgaris, 4 cases of tuberculosis of the genito-urinary tract, 3 cases of tuberculosis of the wrist, and 1 case each of tuberculosis of the knee, tuberculosis of the spine and pelvis, tuberculous sinus, tuberculous fistula in ano, and erythema induratum. As far as known no cases of pulmonary tuberculosis are included. In the early cases the opsonic index was determined as a routine, as a rule, twice a week. Of the cases included in this list, the opsonic indices were followed in 9 for varying lengths of time during the treatment. Seven were followed for over four months. Four cases (I, II, XI and XIII) showed an opsonic index of 1 or above, at two or more observations at the beginning of treatment. According to the rules laid down by Wright they were not satisfactory cases for treatment. However, they were not doing well at the time. Nevertheless, under treatment by tuberculin, 3 of the 4 showed a most satisfactory result. In 5 cases (X, XIV, XVIII, XIX and XXIII) the initial observations were distinctly below normal. All these 5 are classed as distinctly benefited. In none of the 9 cases was a marked tendency for the opsonic indices to follow any particular curves noticed. As a rule, it should be said, however, that if a case was doing badly the index was often low, but not invariably so. The clinical manifestations were markedly more accurate. At first, attempt was made to re-

* This work was assisted by a grant from the Proctor Fund for the Study of Chronic Disease.

inoculate at the time advised by Wright, that is when the opsonic curve was descending to normal. This was soon found to be impracticable, and for the last several months no opsonic indices have been determined in any of the cases under treatment. Cases which have been put under treatment since that time have apparently done as well as the others. The old cases have apparently done as well without the opsonic index as with it.

Dr. Roger Kinnicutt and the writer made some comparative opsonic index determinations, using different preparations of bacteria, white corpuscles and sera. In all the cases of which I have record, 10 in number, the greatest difference was in hundredths, using 1 as the standard. There were observations on a number of cases which were not treated. In all cases, at least four indices were determined over a period of two weeks. Twenty-three cases, obviously tuberculous, presented a fluctuating index beyond 0.8 and 1.2. Four cases, with the clinical diagnosis of probably a non-tuberculous disease, presented similar fluctuations. One of these is Case XXIII, in whom, it seems to me, we have a therapeutic diagnosis. Another was a case of a knee which was treated by request with vaccines of the gonococcus without change. A guinea pig inoculated with tissue from that knee showed tuberculosis. Another, clinically, was a case of Hodgkin's disease, in whose sputum typical tubercle bacilli were subsequently found. The fourth was a patient with a mediastinal tumor who gave a positive tuberculin reaction. There were 5 cases of obvious tuberculosis, whose opsonic indices did not vary from normal limits. There were 3 cases in whom the clinical diagnosis of probable tuberculosis was made, whose opsonic indices did not vary from normal limits and who gave no tuberculin reaction. Five milligrams of old tuberculin were finally given in each case.

There were 3 cases of especial interest. The serum of an interne at the Massachusetts General Hospital was used on two occasions as control. Compared with my own serum his opsonic index was 0.6 and 0.65. The discrepancy was attributed to an error in technic. Two months later he had pulmonary hemorrhages. One case was seen in May, 1907, with a diagnosis of the tuberculous glands of the neck. Four different observations showed her opsonic index to range between 1.1 and 1.3. She was kept under observation but not inoculated, since at that time it was considered that she was manufacturing enough opsonins and ought to get well spontaneously. Her general condition improved. The glands of her neck became much smaller. She then passed from observation until February, 1908. At this time she presented enlarged glands in the left axilla, which were apparently about to break down. She has been started on tuberculin but has been under observation only two weeks. The third case was a case of acute tuberculous pleurisy. Clinically the case was steadily failing and a bad prognosis was given. The opsonic index was continually over 1.2. After a period of three weeks, improvement

set in and the disease was apparently arrested. The conclusions from the work on the opsonic index in connection with tuberculous disease are that the opsonic index has no value as a therapeutic indicator; that it may be of some value in diagnosis and prognosis, but it is certainly not reliable. Two observers will get approximately the same results.

In the cases about to be reported, no case has been under treatment less than four weeks. No case was taken unless it was doing poorly from the clinical point of view. In every case due attention was paid to the necessary doctrines of fresh air, food and general hygiene. Most of the cases, however, have continued their same mode of life without essential change. The diagnosis has been, of course, unfortunately clinical in nearly every case. Nevertheless, there seems to be doubt of diagnosis in no case. In every case the diagnosis was confirmed by at least one other observer.

The preparation used was tuberculin, B.E. The initial dose has varied from 1-10,000 to 1-1,000 of a milligram. The doses have been graded always to avoid any reaction, either constitutionally or in the local lesion. In only 2 cases has there been any increase of dosage over 1-1,000 mgm. The dosage has been increased only when the case seemed to be standing still. There are a few cases which have been under treatment for nearly a year which are still improving on a dosage of 1-1,000 mgm. and have shown no signs of immunity. As far as known there have been no rises in temperature. On several occasions there have been constitutional reactions of headache and malaise in the twelve hours following inoculations. Occasionally, fairly well-marked local reactions at the site of the tuberculous lesion were seen. The most marked example was in Case XIX. A dose of 1-4,000 mgm. caused, first, a marked increase in a local lesion, and then breaking down and discharge, all within two days. Any such reactions were regarded as indications to decrease the dose. The inoculations have been given subcutaneously, chiefly in the back and abdomen. There have been no untoward effects at the site of inoculation beyond a trifling discomfort in some apparently susceptible cases. As a routine, cases have been inoculated once a week until the disease was apparently arrested. There was observed in no case any objection on the part of patients to the inoculation.

There were nine cases of tuberculous glands:

CASE I. M., a young woman of twenty-three, gives a history of glands in the left axilla which were lanced in 1899, glands in the right axilla which were first noticed in December, 1903. Glands in the neck were noticed in 1904. She has had three extensive operations on left side of neck. She was first seen April 23, 1907, at which time she presented large, disfiguring masses of glands on both sides of the neck. She was recommended for operation, but at my request operation was postponed in favor of a trial with tuberculin. She was inoculated with 1-2,000 mgm. of tuberculin, and since that time has been inoculated practically

once a week and is now receiving 1-1,000 mgm. a week. At the present time she shows a slight fullness of the neck, but no visible glands. On palpation numerous hard small glands can be felt, none larger than a small cherry. There has been marked improvement of the general condition, but no gain in weight. At the present time she has been working for over two months. This case is regarded as arrested.

CASE II. S., a young woman of twenty, first noted "lumps" in both sides of the neck and both axillæ in November, 1905. She was first seen in May, 1907. At that time she presented numerous disfiguring masses of glands on both sides of the neck and in the left axilla. Operation had been advised, but declined. The initial dose was 1-3,000 mgm. She has received inoculations weekly up to the present time. For the past three months dosage has been 1-1,000 mgm. Present appearance: axillary glands are barely palpable. Small kernels are felt in both sides of the neck. There may be some visible fullness of the neck. There has been marked improvement of general condition with a gain in weight of ten pounds. This case is regarded as arrested.

CASE III. C., a girl aged fifteen, noticed a "lump" in the right side of her neck in May, 1906. Tonsillectomy July, 1907. Oct. 15, 1907, a fluctuating mass was incised in the region of the lump before noticed. There was considerable induration and a persistent sinus which showed no tendency to heal. She was first inoculated Dec. 12, 1907. At that time there was a sinus leading to a mass on the right side of neck, size of small apple. She received weekly inoculations, increasing from 1-4,000 mgm. to 1-1,000 mgm. In three weeks the sinus was closed. At the present date she presents only a slight induration about the scar of the incision and no palpable glands. There was no change in general condition. This case is regarded as arrested.

CASE IV. C. S., a girl of eighteen, noticed a mass over the left clavicle, beginning in August, 1907, which steadily increased to size of a grape-fruit. There were no other palpable glands, and as she presented hoarseness and evidence of a mediastinal tumor it was thought advisable to operate. Operation, Dec. 28, 1907, and a few drams of tuberculous pus evacuated. She drained profusely for about a week and then stopped. The sinus persisted. On Jan. 17, 1908, she was inoculated with 1-3,000 mgm. of tuberculin. The discharge immediately again became profuse. She has had inoculations weekly since then. At the present time she is getting 1-2,000 mgm. There is a profuse discharge from the operation wound and a constant diminution in the size of the mass of tuberculous glands. This case is regarded as hopeful inasmuch as after the cessation of the discharge apparently a profuse discharge of necrotic material has been kept up by the use of tuberculin with a steady diminution in the size of the glands. The girl always appeared rugged, has remained at work, and shows no change in general condition.

CASE V. R., a young girl of ten, noticed glands in both sides of neck about one year ago. Incision for "cold abscess" of neck in October, 1907. Tonsils and adenoids removed November, 1907. The tonsils on section showed no evidence of tuberculosis. She was first seen Dec. 14, 1907, when she presented numerous small glands in both sides of neck and two masses of glands the size of large walnuts in right side of neck, with a sluggish sinus leading to the upper one. She was given 1-4,000 mgm. and has been inoculated weekly with dosage increasing to 1-2,000 mgm. up to the present time. There has been marked diminution in the size of the glands. None are larger than small cherries. The sinus is practically closed. There has been a very marked improvement in the general con-

dition with a gain in weight of twelve pounds in ten weeks. The weight before that time had been stationary for six months. This case seems to have been greatly benefited, with very good prospects of arresting the disease.

CASE VI. Sa., a man about thirty-five, presented in November, 1907, very large masses of glands in both sides of neck. The glands were somewhat tender. He refused to come for treatment except at two weeks' intervals. He was inoculated with 1-1,000 mgm. every two weeks for three months. At the end of the time the glands had diminished one half. The man kept at work and there was little change in his general condition. There seemed to have been some improvement in the condition of his neck and might suggest a hopeful prognosis if the man would consent to regular weekly inoculations.

CASE VII. F., a young woman of thirty, noticed glands in the left side of her neck six years ago. She had two radical operations five years ago. There was some little discharge from operation wounds. She took a long vacation and was apparently perfectly well for three years, although she could always feel small "lumps" in her neck. About one year ago she began to have pain in left side of neck with increased size of glands. An abscess was opened on Oct. 7, 1907, which left a discharging sinus. On Oct. 19, she presented a few small glands in left side of neck and a discharging sinus, leading to a small indurated mass about half-way up the sterno-mastoid muscle. She was started on 1-2,000 mgm. which was increased slowly at weekly inoculations to 1-1,000 mgm. The sinus healed in two weeks. On the week of Jan. 17, 1908, there was some little pain in the neck, but was immediately relieved when four to five drops of pus discharged spontaneously. There has been no discharge since. At the present time no glands are palpable. There is only very slight induration about the operation wounds. There has been marked improvement in general condition, but no particular gain in weight. Of some interest is the fact that her catamenia, irregular for the past seven years and absent all last summer, has been practically regular since the inoculations began. This case is regarded as arrested.

CASE VIII. Ri., a woman of forty, has noticed some glands in the neck the size of English walnuts for a number of years. She has always been nervous but otherwise in good health. On Nov. 22, 1907, she presented a few small glands, the largest on the right side the size of an English walnut. Throat is negative. She was given 1-4,000 mgm. tuberculin which has been increased at weekly inoculations to 1-2,000 mgm. The glands are somewhat smaller but the marked change has been in the great improvement in the general condition of the patient. She is able to do her work more easily. She has no annoying symptoms from her glands which formerly troubled her and made her nervous. This case is classed as benefited.

CASE IX. B., a young woman of thirty, noticed a little over a year ago a "lump" in the right side of her neck which steadily grew larger. Ten months ago a large abscess was evacuated. The wound healed in two weeks, but below the scar a sinus has formed which from time to time has discharged a little. On Feb. 1, 1908, she presented a discharging sinus in her neck on the right side which led to an irregular mass the size of a small peach. She was given 1-4,000 mgm. and at weekly inoculations the doses have been increased to 1-1,500 mgm. After five inoculations the mass is hardly noticeable. The sinus discharged rather freely at first and is not yet healed. This case is classed as distinctly benefited in four weeks' time. Favorable outcome seems reasonable.

There were four cases of lupus vulgaris:

CASE X. Mar., a woman of forty, has had extensive and increasing lupus of both sides of the face for the past seventeen years. She has faithfully been under treatment for ten years. This treatment has consisted of various caustics, x-ray, etc., without effect. She was first seen on March 12, 1907. At that time she presented many red, active, confluent, lupus patches over both sides of face, and left side of neck. These patches were raised in some instances one quarter of an inch. She has received weekly inoculations beginning at 1-2,000 mgm., increased to 1-750 mgm. at the present time. The present condition is that the left side of her face, which was most involved, seems quiescent. There has been very marked improvement in the appearance of her face. The lesions are no longer confluent, raised and red, and are much fewer. An occasional single nodule appears. The color is a dark red. The scarring is very smooth and soft. Curiously, on the right side of the face, which was least involved, the result has not been so good, but the very marked improvement of the appearance of the face leaves no doubt of the great benefit derived from the tuberculin treatment. Whether this obstinate case will be ultimately cured is still an open question.

CASE XI. E., a young woman of thirty, has had an extensive lupus of the nose and adjacent part of face and mucous membranes of the nose and mouth for eleven years. Under the most efficient treatment available the disease had steadily progressed. She was first seen in May, 1907. She was given 1-2,000 mgm. tuberculin, and was inoculated at weekly intervals for eight weeks with marked improvement. She was better than she had been at any time for ten years. Inasmuch as she lived so far from Boston she was given some tuberculin with instructions for inoculations by the local doctor. Improvement continued for a month. After that time the inoculations were given very irregularly, often two weeks going by without an inoculation. With the irregularity of the inoculations, improvement ceased, and after two months, treatment was abandoned. This case was not benefited, but the improvement with regular inoculations and the cessation of that improvement when the inoculations became irregular, seem to suggest a possible reason for the failure.

CASE XII. H. L., a boy nine years old, had lupus of the wrist in 1901 and which began on the neck in 1902. Since 1904 he has been under treatment for Pott's disease. He was first seen April 23, 1907. At that time he had a few lupus nodules in an extensive white scar of neck and chin. Over an area, 6 x 3 in., on the right wrist was a crusted lupus lesion. He was inoculated at weekly intervals from April 24 to Aug. 17. The dose was increased from 1-2,000 mgm. to 1-1,000 mgm. On Aug. 17 he showed no lupus nodules and presented a smooth, white scar both on wrist and chin. He was given 1-1,000 mgm. at about two weeks' intervals from Aug. 17 to Oct. 25. At that time there was no recurrence. He disappeared from observation until Dec. 7. At that time a few new lupus nodules were starting on his wrist. He was re-inoculated, but has reported only at very irregular intervals since. At the present time he has numerous, new crusting lupus lesions in the scars of his neck and wrist. The boy lives among the most unfavorable environments. This case is one presenting a recurrence which it seems possible might have been averted had the boy reported regularly for inoculation. It certainly shows importance of close observation of cases and the necessity in some cases of continuing the inoculations after the disease is apparently arrested to avert recurrence.

CASE XIII. C. B., a boy eleven years old, has had an increasing patch of lupus vulgaris on his left cheek

for seven years. This patch had slowly spread, despite the usual efficient treatment. He was first seen on April 23, 1907, when he presented a circular patch on his cheek about four inches in diameter. There were numerous red, active, new lesions. He was inoculated weekly from April 23 to July 28. The dosage was increased from 1-3,000 to 1-1,500 mgm. On July 28 the patch presented for the most part a smooth scar with only a small rim of ulcerated tissue on one half the circle. The physician in charge of the skin department stated that he was better than at any time during the four years he has been under observation. It was thought advisable to remove the small remaining rim of diseased tissue with curette and cautery. The boy then reported not oftener than once in six weeks. He was seen on Feb. 8, 1908, when his lesion was entirely healed. Inoculations every two weeks had been urged upon the boy but he had not reported for them. Tuberculin seems to have had some part in the arrest of this disease. This case is in notable contrast to the preceding case, as this boy went without inoculations without recurrence. It should be stated, however, that the boy has better home surroundings; his general condition is far better and he shows no other lesions of tuberculosis.

There were four cases of tuberculosis of the genito-urinary system:

CASE XIV. G. P., a man of thirty-three, has had pain and frequency of micturition since October, 1906. Since March, 1907, his urine has been cloudy and at times has contained clots. No other symptoms. The man is athletic and has worked hard. Rectal examination is negative. Urine contained pus, blood and tubercle bacilli. A guinea pig inoculated with the urinary sediment showed tuberculosis. Inoculations were begun on Nov. 25, 1907. The dosage was slowly increased at weekly intervals from 1-10,000 mgm. to 1-1,000 mgm., which he is now receiving. There has been little change in the local condition. The frequency is about the same. Pus and tubercle bacilli remain in the urine. There has been considerable improvement in the general condition. For some time previous to the inoculations his weight has been steady at 155. Without any other change, he now weighs 160, his best weight. He says he feels better than for years. This case is classed as doubtfully benefited. This case is a patient of Dr. Wilder Tileston, to whom I am indebted for notes of the case and permission to include it in this series.

CASE XV. L., a young man twenty-one years of age, has noticed increasing frequency of micturition for the past year. When first seen on Oct. 31, 1907, he got up five times at night to urinate and urinated every one and a half hours during the day. There was considerable pain on micturition. His urine contained much pus. A guinea pig inoculated with the urinary sediment died of tuberculosis. On examination, his external genitals are normal. There is a nodule in the right lobe of the prostate. The right kidney is palpable and large, somewhat tender. On cystoscopic examination an injected bladder was found but no ulcers. He was not considered a case for surgical interference. Beginning with 1-4,000 mgm. the dosage has been increased on weekly inoculations to 1-1,000 mgm. At the present time he gets up either once or twice at night to urinate, and urinates during the day every two to three hours. There has been no pain on micturition after the first three weeks of treatment. There has been a gain of weight of about ten pounds. The man has kept at work. He says himself that he feels vastly better than at any time for two years. His comfort is apparently insured by stopping the frequency of mic-

turition. His urine still contains the same amount of pus. This case seems benefited. The most conspicuous change has been the improvement in general condition.

CASE XVI. La., a young man of twenty, four years ago, had frequent and painful micturition with pus in the urine. For the last three years the pus has continued in the urine, but the frequency and pain have not been so marked. On cystoscopic examination the bladder seemed normal and pus was seen coming out of the left ureter. At that time, September, 1907, the testicles and prostate were normal. On Sept. 10, 1907, a tuberculous left kidney was removed. The wound healed slowly. Beginning Oct. 17 he received weekly inoculations of tuberculin, the dose being increased from 1-3,000 to 1-1,500 mgm. The wound rapidly healed, but perhaps a more important feature than the tuberculin was the removal of several silk sutures. However, there was a gain of ten pounds in weight. The man is now at his maximum weight and working every day. He has no urinary symptoms. There is still microscopic pus in the urine and a few tubercle bacilli. On Feb. 7, 1908, his left testicle, which became swollen immediately after the operation before the tuberculin was given, again became swollen. His dosage was immediately cut from 1-1,500 mgm. to 1-3,000 mgm. At the present time the testicle is rapidly growing smaller. It cannot be definitely stated that this case was benefited by tuberculin. It seems probable that the use of rather large doses (1-1,500 mgm.) stirred up the process in the testicle. There has been, however, a marked improvement in the general condition.

CASE XVII. Ma., a man of thirty-three years old, gives a history for the past six years of backache, and frequent, painful micturition, and pus in the urine. In August, 1906, a perinephritic abscess was drained, which left a persistent sinus. Since that time his frequency and pain in micturition increased and he no longer had control of his urine. He lost weight and was unable to do steady work. Cystoscopic examination showed a small injected bladder without ulcers. Testicles and rectal examination were negative. Tuberculin reaction was positive. Nov. 22, 1907, his left kidney was removed. Pathologically, it showed typical appearance of tuberculosis. After the operation the frequency and lack of control of the urine persisted, and on Jan. 13, when first seen, he presented a large sluggish wound in his kidney region. Beginning with 1-4,000 mgm. he has received weekly inoculations up to 1-1,000 mgm. At the present time the wound has healed. He still has some lack of control of urine at night, but is able to hold his urine three or four hours in the daytime. There is no pain. The urine still contains pus and tubercle bacilli. The most marked change has been in the general appearance. In a little over six weeks he has gained fifteen pounds, and he is now doing a full day's work as painter. He states that after the inauguration of the inoculations of tuberculin he began to feel generally better and now is better than he has been for six years. While the local condition is apparently the same, there seems no doubt that the man's general physical condition has markedly improved.

There were three cases of tuberculosis of the wrist:

CASE XVIII. Ch., a woman of forty-five, had had a painless swelling on the back of the right wrist for over a year. This swelling was removed at operation in March, 1907, and the mass proved to be tuberculous. She was first seen May 14, 1907. At that time she presented a clean scar with a considerable mass of indurated tissue about it. This mass had been in-

creasing for the past three weeks with an increase of pain. She was given six inoculations of 1-1,000 mgm. at weekly intervals. At the end of that time there was no pain in the wrist, no induration, the motion was free. She was then discharged to go into the country. She was again seen in January, 1908, and had no symptoms or signs of recurrence. This case is regarded as probably arrested, although there might be some room for doubt as to the nature of the induration and pain coming on several weeks after the operation.

CASE XIX. G., a young girl of ten, gave a history of injury to the right wrist in December, 1906. This was soon followed by a painless swelling over the fourth and fifth metacarpal bones. She was treated by plaster fixation and Bier's hyperemia for two months without change. She was first seen April 8, 1907. At that time she presented a painless fluctuating mass the size of a golf ball on the back of her hand. On April 12 she was given 1-4,000 of tuberculin. The lesion promptly became larger, broke down within the next forty-eight hours. There were apparently well-marked constitutional symptoms also. The inoculations were kept up at ten-day intervals, the dosage being increased to 1-2,000 mgm. On June 21, the splint was omitted but the child did not keep the hand quiet. The induration of the back of the hand persisted. The splint was re-applied July 26. From that time on improvement was rapid. The splint was again omitted on Sept. 20. At that time there was present only a smooth scar on the back of the hand and considerable diffuse induration. She was then given inoculations at two weeks' intervals until Nov. 22, 1907. At that time very little difference between the two hands was noticeable. There was no deficiency in motion. Unfortunately, none of several x-ray plates were satisfactory. There were no inoculations after Nov. 22. The child was again seen two months later and the condition remained the same. This case is regarded as arrested.

CASE XX. M. M., a woman forty years old, who had pain and swelling in both wrists in January, 1906. Operation in September, 1906, when considerable tuberculous material was excised from the anterior surface of both wrists. Tuberculin test was positive. She went into the country for six months. Considerable swelling still remained in both wrists but no pain. She started in work but the pain and swelling in the wrists increased. She was first seen Dec. 5, 1907. At that time she presented two clean scars in both wrists. In the left wrist there was a little swelling but no pain. There was fair motion of the left hand. The right wrist was markedly swollen. There was considerable pain, increased on motion and some swelling of the thenar eminence. There was marked limitation in motion of all the fingers. She has been inoculated at weekly intervals, the dosage being increased from 1-4,000 mgm. to 1-1,000 mgm. at the present time. There is now no swelling of the left wrist. The motion and strength of the left hand are apparently normal. The right wrist is still considerably swollen, although less so than at the inauguration of treatment. There is much less pain in the right wrist than at the beginning of treatment. There is marked improvement of the general condition, despite the fact that she does hard work in domestic service. This case is classed as doubtfully benefited.

There was one case of fistula in ano:

CASE XXI. Bu., a man of fifty, has had a fistula on either side of the anus for four years. Has had several abscesses and several operations, including radical ones, for the cure of fistula, but the fistulae have never been healed. He was first seen Oct. 20, 1907,

when he presented large wounds on either side of the anus. Beginning with 1-2,000 mgm. of tuberculin he has had weekly inoculations and now is getting 1-1,000 mgm. The fistula has closed on one side and is apparently healing in well on the other. There have been no untoward symptoms since the beginning of the treatment. Again in this case there has been marked improvement of the general condition.

There was one case of persistent sinus after operation for tuberculous peritonitis:

CASE XXII. B. G., a young woman of nineteen years, had an operation for tuberculous peritonitis six months ago, which left a persistent sinus. Beginning Feb. 6, 1908, she received tuberculin weekly beginning with 1-10,000 mgm. and increasing 1-10,000 every week. The environment of this case was changed for the better. Her general condition has been much improved. There has been marked gain in weight and strength. The discharge from the sinus is now spasmodic and averages much less. This case has been doubtfully benefited by the tuberculin.

There was one case of erythema induratum:

CASE XXIII. O'D., a young woman of twenty-five years of age, has had psoriasis for years. When a child she had some "scrofulous glands" of which she now has only the clean scars on both sides of her neck. For a number of years on both legs she has had varying sized lesions of erythema induratum which have ulcerated and formed scars. In that time her legs have never been free from ulcers. In the winter time the lesions are more numerous. She has had various treatments, including active specific treatment. There was some doubt concerning the diagnosis of this case, and Dr. Roger Kinnicutt observed her opsonic index for the tubercle bacillus from April 3 to Aug. 10. I am indebted to him for his notes and his permission to include the first part of this case. The first four determinations of the opsonic index showed an index well below normal. She was then given tuberculin, starting in with 1-2,000 mgm. For several weeks there was no special change. Since that time the improvement has been steady. She now requires inoculation of 1-750 mgm. every seven days. On two occasions she has gone without inoculation for nine or ten days and very promptly on the eighth or ninth day new lesions have appeared. The last appearance of a new lesion was on Feb. 24, when she had been nine days without inoculation. Before that time she had been two months without any lesion, a thing which she does not remember to have happened since the onset of this disease. It is to be remembered also that she has more lesions in the winter time. This case is to be classed as distinctly benefited. It is of considerable interest, however, to note that the inoculations apparently have got to be kept up, although she has been under treatment for ten months, and at one time the disease seemed arrested. The psoriasis was unaffected.

There was one case of tuberculosis of the knee:

CASE XXIV. J. B., a girl twenty-four years old, seven years ago had an excision of the right knee joint for tuberculosis. About Jan. 1, 1907, the left knee became swollen and somewhat painful on motion. There was no limitation in motion. She did not improve under best of general hygienic and local treatment. About Dec. 15, 1907, she had some pain localized to two red areas on the outside of the knee. On Jan. 9, 1908, she was given 1-10,000 mgm. She has had weekly inoculations to the present time, the dosage

being increased 1-10,000 mgm. at each inoculation up to 1-1,000 mgm. On Jan. 25, she presented a sausage-shaped swelling along the outside of the knee joint, which distinctly fluctuated and which apparently was outside of the knee joint. The swelling was incised on Jan. 31, and pus evacuated. After the evacuation of the pus, the knee joint itself was very little swollen and not at all painful on motion. There has been some constant discharge from the incision but no swelling of the knee joint. Under precisely the same conditions as before tuberculin was given she has gained seven pounds in weight. Before that time her weight had been stationary for three months. It is problematical how much the tuberculin had to do with the change in the picture. It seems possible that the formation of this localized abscess was hastened by its use. The general condition and the local condition, which had been at a standstill for several months, are now certainly better. This case is classed as doubtfully benefited.

There was one case of tuberculous spinal and pelvic caries:

CASE XXV. V., a woman twenty-nine years old, had, one and a half years ago, a left ilio-psoas abscess which was opened in March, 1907. She was in a plaster cast for some time. This ilio-psoas abscess has continued to drain. She presented a rigid back, but no knuckle. She came under observation Oct. 2, 1907, and was running a continuous temperature. She received 1-3,000 mgm. on Nov. 3, which was increased, by weekly inoculations to 1-1,000 mgm. on Nov. 24. The temperature came down. The discharge increased, but on Dec. 1, 1907, a fluctuating mass appeared over the crest of the right ilium, which increased in size with variations in temperature. The abscess was opened on Jan. 2, 1908. At that time apparently bare pelvic bone was felt. The temperature still showed wide excursions. On Jan. 16, 1908, she was again given tuberculin, this time with the initial dose of 1-10,000 mgm., which was increased at weekly inoculations 1-10,000 mgm. to 1-1,000 mgm. Since the second inauguration of tuberculin the temperature has drifted to normal and there has been some improvement in the general condition. The history of this case suggests the possibility that the tuberculin stirred up increased suppuration as evidenced by the formation of the second abscess. There seemed to be some slight improvement in the general condition. On the whole it cannot be said that this case received any benefit from the inoculations of tuberculin.

Of course, too short a time has elapsed to draw any permanent conclusions from the results as seen in this very small series of cases. Many of the cases are still under treatment. Experience also has shown the fallacy of definitely designating any case of tuberculosis as cured, no matter how long the interval of quiescence. The following conclusions, however, seem justified. Of 25 cases of tuberculosis localized elsewhere than in the lungs, treated with tuberculin, B. E., 6 cases were classed as arrested; 12 as distinctly benefited; 5 as doubtfully benefited; and 2 as uninfluenced by tuberculin. The most striking feature is that practically all of the cases showed a marked gain in a general condition, thus enabling them better to combat the local disease. The local condition was certainly markedly benefited in the cases of tuberculous glands and lupus. In the cases of genito-urinary

tuberculosis, while there was some amelioration of the local disease, on the whole there did not seem to be much change. The use of tuberculin apparently has to be continued over a long period of time. It does not prevent relapse. While the opsonic index may be of some value in diagnosis and prognosis, it seems to be of no value as a therapeutic indicator. The dosage should be small. The initial dose is from 1-10,000 to 1-4,000 mgm. On few occasions is it necessary to give over 1-1,000 mgm. Any marked reactions are to be carefully avoided. The best interval of inoculation apparently is one week. Regularity of inoculations is essential. The routine use of tuberculin is simple and should be accompanied by no discomfort on the part of the patient. In no case apparently was any lasting injury caused by the use of tuberculin. That it may be harmful if used incautiously seems certain. That it is a potent factor for good in selected cases of localized tuberculosis seems also certain.

HODGKIN'S DISEASE WITH EOSINOPHILIA: REPORT OF A CASE WITH AUTOPSY.

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THE presence of eosinophiles in the glands of Hodgkin's disease, or pseudo-leukemia, has been observed in a number of cases since 1892, when Goldmann first called attention to their presence. Some of these cases showed eosinophiles in other organs, but their presence in marked excess in the blood has almost never been so striking that they have been a clinical as well as a pathological factor.

The following case of Hodgkin's disease at the Worcester City Hospital, in the service of Dr. Ray W. Greene (whom I wish to thank for his permission to report the case), presented such a very unusual and marked eosinophilia, both in the blood and in several of the organs, that there exists sufficient excuse for reporting it.

Clinical history: D. S., fifteen years old, born in Worcester, Mass., of Swedish parents, entered the Worcester City Hospital on March 18, 1907.

Family history: Negative, except that his father was insane for five years, and one brother was in the hospital about the same time with osteomyelitis of the femur.

Previous history: He was always sickly, working ten hours a day for the last year.

Present illness: Before entrance he had been ill about four months, but three months before this some swellings began to appear on both sides of his neck and in his groins. These never gave him any trouble, but have been constantly present. About the second week in December, 1906, he felt tired and run down, with a backache which at that time he complained of as low down in the lumbar region. Up to two weeks before entrance he was up and about the house most of the time. Then followed one week of severe diarrhea, he having six or seven movements of the bowels a day. At the same time there developed a swelling of his face and legs, and occasional nausea and vomiting. For

four months dating from November he had a cough, coming on insidiously, with expectoration. During this time he had a few attacks of dyspnea. At first he had some pain in his chest, but there was none later on. His appetite was fair, but he slept poorly.

Physical examination showed a rather poorly developed and poorly nourished boy, the skin and mucous membranes pale, marked edema of face and legs, considerable loss of subcutaneous tissue, and pupils of equal size and reacting alike. In the cervical, axillary and inguinal regions (especially in the right inguinal region) there were enlarged lymphatic glands of various sizes, from about half a centimeter to about two and a half centimeters in the longest diameter, some being in chains.

The apex of his heart was in the fifth intercostal space, about one and a half centimeters outside the nipple line. The right border was at the right edge of the sternum. No murmurs were heard.

His lungs showed dullness on percussion at both bases, with numerous fine moist râles, and on the right side there were diminished respiratory sounds, but normal fremitus. His breathing was rapid, though not labored, both sides of the chest moving freely and apparently equally.

The liver dullness extended from the sixth rib to about three centimeters below the costal margin, giving resistance on palpation, but the lower edge was not felt.

The abdomen was full and tympanitic, except in the flanks, where it was thought that shifting dullness could be made out. The kidneys and spleen were not palpable. The knee jerks reacted equally.

Sputum examination showed no tubercle bacilli.

A blood examination showed: hemoglobin 40%, white cells 49,000, red cells 1,470,000. (These red cells were not counted directly, but were estimated by comparing the relative number of white and red cells in a hundred microscopic fields.) A differential count of 500 white cells showed:

		Absolute number per cmm.
Polymorphonuclear neutrophiles,	27.4%	13,426
Small lymphocytes,	.6%	294
Medium sized lymphocytes,	2.6%	1,274
Large lymphocytes,	.6%	294
Transitionals,	.6%	294
Eosinophiles,	68.2%	33,418
		49,000

The red cells showed considerable poikilocytosis, and some achromia. There was some, but not a general, increase in the size of the cells, some macrocytes and some microcytes. One normoblast was seen, or 98 per cubic millimeter.

A differential count of 200 white cells of the same specimen by Dr. J. B. Manning (to whom I am also indebted for the three white counts) showed:

Polymorphonuclear neutrophiles,	27%
Small lymphocytes,	3%
Eosinophiles,	70%

During this count one blast was seen.

March 19. A systolic murmur was heard at the apex and base of the heart, but only when the patient held his breath.

March 20. The chest was full of fine and medium sized and coarse râles with prolonged expiration giving rise to dyspnea. The urine was of normal color, acid reaction; albumin and sugar were absent. A differential count of 500 white blood cells showed: