

ciated with rheumatism or rheumatoid conditions has not only cleared up the cystitis, but has also relieved the rheumatoid symptoms promptly in a small series of cases with us. *B. coli* vaccine should always be prepared directly from the patient's organism and should be used in small doses. The initial dose should not be more than 25,000,000, cautiously increased.

Tuberculin.—No final judgment of the value of any agent used in the treatment of tuberculosis can be made unless its practice has been followed for many years. I am, therefore, only hazarding an opinion of the value of tuberculin from our limited observation. I believe that tuberculin in proper doses is a valuable addition to standard methods of treatment. Its use, however, is associated with dangers which make extreme caution necessary in its exhibition. Wright's method, which calls for an extremely small dose at weekly intervals, seems to eliminate all dangers of over dosage.

I hope that the time is not far distant when local laboratories will properly develop the field of vaccine therapy. The observer in this field requires an accurate and extensive knowledge of the small group of organisms which play a part in most infectious processes. With this mental equipment a knowledge of the technic of vaccine production and therapy can be quickly developed. There is no reason why autogenous vaccines cannot be produced in the larger hospitals and medical centers of the community. I look forward to the day when an equipment in this direction will be expected of the local pathologist and bacteriologist.

Vaccine therapy is in its infancy. It is but a step in progress toward the specific therapy of infectious processes for which the medical world has been anxiously waiting. I trust that I have made clear my reasons for believing that, through the new viewpoint it has opened, a way to the solution of these problems may be made possible.

Original Articles.

TYPES OF GRAVES' DISEASE.

BY J. G. MUMFORD, M.D., BOSTON.

THE types of Graves' disease are so various, and the special symptoms, or lack of symptoms, so puzzling, that it is well for a student of the subject frequently to compare cases, especially that he may bring home to himself the possible and serious outcome of conditions which often appear trivial and more often are obscure. Frequently it happens that the frank, acute cases, with the classical symptoms, are cured by any treatment, and by no treatment even. Sometimes it occurs that a case apparently trifling, perhaps running an easy, chronic course, suddenly becomes worse and dies in spite of all treatment.

Here are two dissimilar cases, a typical case and an atypical case, both of which occurred in my practice, both of which caused me the greatest anxiety and taught me new lessons regarding the nature of this interesting ailment.

Case I was that of Mrs. A. S., a woman of forty-two. She had behind her a long surgical history, — operations for salpingitis, for retroperitoneal cyst, for ovaritis, — but in spite of these serious diseases and operations, which occupied many years of her younger life, she came out strong and vigorous. At the age of thirty-seven, however, she consulted her physician for what appeared to be a trifling heart lesion, for she found herself troubled with occasional dyspnea on exertion. Her physician discovered a slight mitral leak and some dilatation of the heart. Careful treatment and prolonged rest resulted in no benefit; gradually there developed further a constant distressing dyspepsia, pain and nausea after eating and a state of continual apprehension. These symptoms persisted for two years, when there developed further a mild, bilateral tremor of the fingers. At this stage she consulted me, on the advice of her physician, and I was able to suggest the diagnosis of exophthalmic goiter. Even so, the diagnosis was by no means assured, for no enlargement of the thyroid was evident, nor were there marked eye symptoms, while the heart rate rarely went above 80. We continued to treat her as a cardiac case only — bearing in mind the possibility of Graves' disease — for another year, when within a month there developed a series of characteristic symptoms: the thyroid gland became enlarged, with a typical thrill; the eyes gradually became prominent, with lagging of both lids and widening of the palpebral fissure; and tachycardia became pronounced, the rate of the heart ranging between 110 and 130.

Here was a case which, in spite of its gradual onset, seemed suitable for immediate and vigorous medical treatment. Accordingly, we instituted the use of hydrobromate of quinin, neutral, in 5-gr. capsules, three times a day, and continued the medication without intermission for fifteen months. During the early months of treatment the patient experienced great relief; her apprehension vanished, her thyroid tumor became somewhat smaller, the heart action became slower and her general sense of improvement marked. Such was her state twelve months after the beginning of the quinin treatment. She was not well, however, and her condition of instability became especially apparent at that time through the accident of a serious grief; a favorite sister became ill, and, after a month's extreme suffering, died, under the constant watchfulness of our patient. The strain and anxiety of this experience renewed at once, and markedly, the exophthalmic symptoms. Within a very few weeks, from the state of quiescence I have described, all her discomforts reappeared; the eyes became prominent and anxious, with their associated abnormal lid phenomena; her tachycardia returned; the heart became irregular; dyspnea became extreme; she was troubled with a constant diarrhea and distaste for food; profuse sweating became pronounced; the tremor returned in force; and the right lobe of the thyroid rapidly doubled in size.

Now the case presented all of the typical

symptoms of acute Graves' disease and demanded, apparently, most energetic treatment. Fortunately, during the whole of this period she had been under constant medical care and I had seen her myself once a month for more than a year. The hydrobromate of quinin appeared to be no longer useful, and, in view of the rapid development of her acute symptoms, it seemed wise to me to undertake a radical operation; at the same time, in view of her alarming psychic state, I made every attempt to bring her to the operation in a calm frame of mind. I believe firmly in the value of Crile's suggestion regarding psychic influences in acute Graves' disease, and in the importance of bringing the patient to operation practically without her knowledge. In the present case I followed the plan which I always institute in similar acute cases. The probability of our doing an operation was explained to the patient and her consent to it was secured, as well as the consent of her relatives, but the exact time of the operation was not set, nor was the operation explained to her as inevitable. I sent her to a quiet private hospital, confined her to her room, with a congenial nurse, and kept her there, resting and closely observed, for ten days. She spent her time in bed. I was able to relieve the sleeplessness from which she suffered by the liberal use of bromide of strontium, and, through the inhalation of various volatile oils and colognes, to suggest to her the possibility of improvement. During those ten days she was treated every morning by inhaling either nitrous oxid, eucalyptus, alcohol, spirits of camphor, ether or cologne, all in small, harmless amounts and freely mixed with air. In this way she acquired the idea of taking inhalations without the slightest terror or distress.

The principle of this treatment, as enunciated by Crile, rests on the following proposition: We know that the acute phenomena of Graves' disease are due to the abundant outpouring of the thyroid gland secretion into the lymphatics and so into the general circulation; we know that this outpouring can be increased by such stimuli as fear, anxiety and even mirth, but fear and anxiety are especially deleterious. Clinical evidence shows that the ordinary preparation for operation and the giving of ether have, through the stimulus of fear, more than once killed a patient, from the sudden resulting outpouring of thyroid intoxicants, without any operation having been done. If, then, we can bring the patient to the operation, can produce anesthesia and can operate without altering the equanimity of the patient's mental attitude, we are convinced that we then operate under the most favorable conditions.

I followed this method with the patient under discussion. On the morning set apart for the operation she realized no change in the ordinary routine. She was, indeed, given a hypodermic of morphia, but she had been given hypodermics of sterilized water daily, so that a hypodermic of morphia impressed her mind not at all. An hour after the hypodermic, when she was in a calm and untroubled state, I myself, as had been my

custom, entered her room and proceeded with the anesthetic, giving her first a few whiffs of cologne, then an abundant inhalation of nitrous oxid, with a little oxygen, and then, when consciousness was gone, had the anesthesia carried on by ether. This was more than a year ago. My present custom is to carry the patient through the operation with nitrous oxid and oxygen, as I am convinced that thus her resistance can be kept nearest to its normal. The patient was carried, anesthetized, to the operating room, and these interesting facts were noted. Before taking her anesthetic her pulse had been 110; when completely anesthetized her pulse was 112; during the removal of the gland her pulse varied between 100 and 110; half an hour after her return to her room, and while recovering from the anesthetic, her pulse reached 120, but three hours later it had fallen to 90.

This is in notable contrast with the ordinary experience of bringing a terrified patient to the operation, when during that operation we note a steadily rising pulse and a condition often of great gravity before the recovery from ether.

The operation itself in the present case was a simple one; it consisted in removing the left lobe of the thyroid, stripping the posterior capsule after the method of C. H. Mayo, in the removal of the isthmus and the removal of about one third of the right lobe.

After the operation, and with the patient's recovery from ether, all acute interest in the case ceased; though one was struck, as one always is in satisfactory cases, to observe her rapid and complete recovery of health. The first noticeable change was the loss of peevish irritability which had characterized her before. She was relatively calm and tranquil after the operation, and two days later had ceased entirely to complain of any operative sore throat and pain in her neck. Coincidentally, one observed a steadying of the pulse and a gradual decline in its rate; the tremor also abated rapidly; dyspnea was never again observed; the sweating disappeared, and at the end of ten days her digestive disorders were greatly improved. The wound healed promptly and never disturbed us. The most noticeable fact, however, about this case, as about all successful cases, was the calm, tranquil and happy attitude of the patient herself. One may not in words clearly define this change, but it is so rapid and so striking in all successful cases that it suggests the relief brought by the timely and appropriate use of morphia to a person in pain and terror. It is the reverse of euthanasia; it is the confident return to a cheerful and comfortable life.

The operation I have described was done some eight months ago, and I have seen the patient four times since she left the hospital. It is too early as yet to pronounce her permanently cured; indeed, one symptom still remains, a slight exophthalmos, but in all other respects she appears and feels absolutely well and goes about her work in life with a vigor and a cheerfulness which she had not known for five years.

This case, in its later developments, was a

typical acute Graves', and in its ready yielding to treatment illustrates admirably the value of operation in proper cases. In no way was it especially remarkable except in the long and gradual onset of the symptoms and in the sudden accession of serious symptoms on the experience of a depressing grief.

Case 2 was atypical: Mrs. T. B. was a vigorous young woman, of active habits, some thirty-two years of age, and the mother of four children. With the exception of her obstetrical history, there was nothing in her past life of any special significance. She had always been regarded as peculiarly sane and well-balanced. Some two years before I saw her she suddenly became extremely nervous; within a week she took on symptoms that suggested to her physician a rapid neurotic breakdown; she was sleepless, fretful, irritable and almost impossible to live with, as her friends asserted. Within a week after the surprising development of these symptoms her physician discovered a marked tumor of the thyroid gland. There was no other evidence of hyperthyroidism, with the exception of the nervousness; there was no exophthalmos, no tachycardia or palpitation, no tremor, no digestive disturbance, no sweating; in fact, the diagnosis was founded almost solely on the nervousness and the rapidly enlarging thyroid.

This patient's physician had the courage of his convictions, and his convictions were sound and accurate. Without stopping to employ drugs, and without waiting to see the development of the case, he proceeded at once to a surgical operation, and his surgical activity seems to have been justified by the results. He removed the whole of the left lobe of the thyroid, leaving, however, the isthmus, with a considerable pyramidal lobe, and the whole of the right lobe. The lobe removed was much the most affected; those parts which were left seemed to be but slightly hypertrophied.

Mrs. B. promptly recovered from the operation and promptly recovered her normal health. Her nervousness disappeared, and her usual cheerful and equable temperament was restored to her. Her husband's later account to me of the year which followed was encouraging, if it had not been pathetic. At any rate, the operation showed brilliantly the immediate benefit of cutting out a greatly active gland which obviously was pouring toxins into the patient's organism. Mrs. B.'s after-history, however, was stormy and instructive. Her symptoms of hyperthyroidism gradually returned after a year and became more settled and more pronounced than before. Not only was she the victim of an intense nervousness on this second occasion, but she developed many of the classical symptoms of Graves' disease; her eyes became prominent, with the usual associated lid symptoms; the remaining lobes of the gland became enlarged to about four times their normal size; tachycardia developed, though not in an extreme degree, but her pulse came to range between 100 and 110; she became the victim of dyspnea and palpitation, while her digestive disturbances were poignant, — pain after food,

eructations and constant diarrhea, — associated also with rapid emaciation. Such was her condition when she consulted me, some fourteen months after the first operation.

I endeavored for some two months to relieve her symptoms and to build her up by the use of hydrobromate of quinin, but at the end of eight weeks she was but little improved, and the outlook began to appear very serious. Meantime, her husband and her physician, who had performed the first operation, both urged me strongly to proceed with a second operation. It was evident to all concerned that the failure of the first operation to effect a cure was due to the incompleteness of the work. It was said, with apparent justice, that much more of the affected gland should have been removed. At this time, that is to say, immediately before my own operation, which I undertook with some hesitation, the patient, while extremely ill in the thyroid sense, seemed to be an excellent surgical risk. She had herself well in hand and exhibited little of the terror and perturbation which these people usually show when an operation is anticipated; indeed, it did not appear to me that my usual course of psychic treatment was indicated; the patient was so perfectly familiar with her coming ordeal, and so keenly intelligent about preparing for it, that I thought it best to consult her about the day and the circumstances of the operation.

On the appointed day she walked to the operating room herself to take her anesthetic, and appeared reasonably placid. Her pulse was 106, of fair quality, but slightly intermittent. There were no evidences of degenerative changes in the heart or nervous system, though a slight, hemic, mitral murmur was obvious; the heart, however, was not enlarged. I anesthetized this patient with gas and oxygen with the greatest immediate success. The combination of these agents is usually peculiarly effective in cases of Graves' disease. At the same time, in order to block, so far as possible, the effects of hyperthyroidism, I followed the suggestion of Crile and infiltrated the skin about the tumor thoroughly with a 1% cocaine solution. I found the operation of thyroidectomy in this case unusually difficult. The previous operation had had the common effect of filling the operative field with extensive and dense scar tissue, through which there was an abundant blood supply. The dissection was most painstaking and bloody, though the total amount of hemorrhage or of blood lost was inconsiderable, I am convinced. At one time I counted 47 hemostatic forceps in the field of operation, and I am sure there must have been twice that number before the operation was completed. All this, of course, shows the difficulty of the operation and its length. The thyroid lobes seemed everywhere closely adherent to the surrounding structures. I found the stump of the old left lobe which had been removed, and proceeding thence I took out the somewhat enlarged pyramidal lobe and about half of the enlarged right lobe. I assured myself by this method — that is, by slicing laterally the right lobe — that the parathyroid glandules were

not disturbed. To the same end, the blood vessels were seized and controlled within the substance of the gland itself. The operation occupied about thirty-five minutes and was extremely tedious; the patient bore it well, however; her pulse rose but little, and while the stitches were being put in, it was counted at 112. While she was recovering from the anesthetic, that is, fifteen minutes later, her pulse had sunk to 100, and all promised well.

Every reasonable operative precaution had been taken to avoid increasing the hyperthyroidism. In spite of the dense adhesions about the gland, that organ had been handled very little, while after the operation abundant drainage was provided. Even so, one recalls with interest Crile's assertion, based on numerous investigations and experiments, that the escape of thyroid secretion during the operation has little or nothing to do with post-operative hyperthyroidism.

Trouble began immediately after our patient was put to bed. She was the victim of an intense and prolonged nausea, vomiting frequently and painfully for twelve hours. She awoke to consciousness in a state of excessive irritability, throwing herself about the bed, demanding to be taken up, crying out for the nurse every two or three minutes, continually asking for ease from her discomfort, a discomfort which she failed to describe; her apprehension became painful and extreme, her agitation seemed almost maniacal, and her former tranquillity was so far abolished that she complained bitterly and continually of her attendants and of the nature of her treatment. She bewailed the fact that she had submitted to a second operation, and assured us continually that she was about to die. At the end of twelve hours the reasonably slow and steady pulse had risen irregularly to 130 and 140, the heart action became embarrassed, intermittent and irregular; a rapid cardiac dilatation supervened; the patient was bathed in sweat; her exophthalmos became exaggerated in appearance and her misery became almost indescribable. In other words, here was presented a picture of extreme and grave thyroid poisoning, such a picture as one sees in the most advanced cases of Graves' disease immediately before death; indeed, death was imminent in the case of this unfortunate patient. I attempted in every way to relieve her misery by the use of appropriate drugs, but the rapid deterioration of her heart seemed to render them ineffective; opium alone gave her some slight comfort.

The situation was such as we used commonly to encounter after operating for Graves' disease two or three years ago, before the present effective technic had been devised.

The patient sank rapidly under her accumulated sufferings and died some thirty-six hours after the operation. She died of acute hyperthyroidism.

The case in its development and in its early features was conspicuously atypical, and although during that interval between the first and second operations characteristic symptoms accumulated, so that the case became almost classical in its

appearance, still the condition at no time was regarded as serious. One cannot but ask oneself what would have happened had no operation been done. In spite of the futility of this question, one cannot but feel that had no second operation been done, the patient must have continued on the edge of a volcano, and that at any time, almost, some slightest excitement or stimulus might have thrown her into a state of advanced hyperthyroidism from which she could not have been rescued. Looking back at my own relation to her illness, that is, during the last two months of her life, and at the course followed, I believe now that I should not have dallied with drugs, but should have followed the example of her first surgeon and operated immediately after she consulted me.

The two cases which I have related, eventually and pathologically, were cases of frank, acute Graves' disease. There was no evidence in the thyroid lobes removed that any retrograde changes had as yet begun in those organs. It is to such retrograde changes, with their associated symptoms, leading in the last event to the antipodes of Graves' disease, to an actual myxedema, that the physician must often look for spontaneous cure of hyperthyroidism. Neither in the case of Mrs. S. or of Mrs. B. were such changes evident.

These two cases, little as they resemble each other, illustrate that great class which should be treated by early thyroidectomy.

HYSTERIA -- WITH AUTOPSY.*

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AND

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IN January, 1909, a young colored girl, seventeen years old, came to the Nerve Department of the Boston Dispensary. She came reluctantly with her mother; and this is the story they brought:

At two and one-half years of age came her first sickness: she had whooping cough. For six to eight weeks she was very ill. It was nearly a year before there was full recovery. Then followed immediately measles, which was not a particularly severe illness. When she was five and one-half years old she was vaccinated. The first vaccination did not take. The second vaccination took. Up to this time the skin of her entire body was perfectly clear. A rash appeared with the vaccination and the swelling of her arm. From head to feet the entire body was covered with "white boils." These in healing left permanent white marks on her colored skin. These white spots distressed the girl greatly when she began to attend school -- at six years of age. During the following two years she was taken to the Carney and Homoeopathic hospitals, but she was never cured. Her body and scalp had a scaly eruption which was white, dry and did not itch. At times the eruption appeared to be gone; then it would return.

At eight years of age she had tonsillitis. She was in bed ten days. Following the tonsillitis appeared for

* Read at a clinical meeting of the staff of the Boston Dispensary, May 6, 1910.