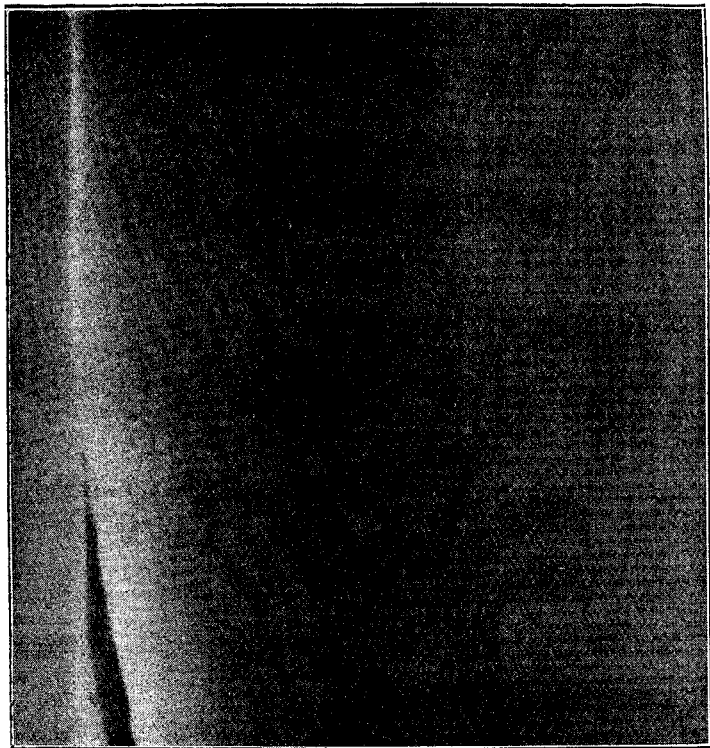


and included nearly the whole of the thickness of the shaft.¹ After extension of the incision and a further enlargement of the opening in the involucrum the sequestrum was removed. There was a considerable amount of granulation tissue surrounding the dead bone, but no pus was seen. During the operation there was a flow of whitish fluid almost

FIG. 4.



Quiet necrosis of femur.

like milk from the area of fluctuation noted on Feb. 26th. The granulation tissue was examined microscopically but showed no sign of any tumour formation or of tubercle.

The sinuses had healed before the patient left the hospital on April 24th, 1901, and the albuminuria was less. When seen some weeks afterwards he was much improved in every respect and had but a slight amount of albumin in the urine.

On admission this swelling resembled very closely that produced by an osteo-sarcoma of the femur. The absence of pain, the large extent of femur involved, a normal temperature, the presence of enlarged glands, the history of loss of flesh, and the anæmic appearance of the boy all pointed to the diagnosis of osteo-sarcoma.

In favour of quiet necrosis was the feel of the upper limit of the growth which was not clearly defined but faded gradually on the femur, and the presence of œdema of the lower part (not noticed by all), and later an area of fluctuation. Œdema of the subcutaneous tissue is in favour of some change of inflammatory character, but a point of fluctuation such as that found might simply indicate a cystic change or local hæmorrhage in the case of a growth. The albuminuria must, I think, be included amongst the evidence in favour of quiet necrosis, for it diminished greatly when the wound had healed and the process of disease had been arrested. I do not think that it has been noticed in quiet necrosis hitherto, but as it may result from dry caries of the spine there appears no reason why it should not follow a dry necrosis of one of the long bones and be, as here, an indication of amyloid change in the kidneys. A normal temperature is given as in favour of sarcoma, but the course of some of the rapidly growing sarcomata is accompanied by fever—100°, 102°, 103·6°—without local signs of inflammation. This must be remembered, for a grave condition is likely immediately to ensue should an incision be made into a sarcoma under the impression that it is an abscess. I recollect one case in which this was done by a medical man before sending his patient to the hospital. The hæmorrhage was so profuse that he thought he must have opened the femoral artery. In that case redness was

also present and the only guides were the long history of the case and amount of surrounding growth infiltration.

The examination by the x rays in our patient showed the exact condition; without it we might have been compelled to explore in order to make a diagnosis. Yet, as a small piece of necrosed bone might escape detection by this method, careful exploration should be made before amputation in all cases.

NOTE ON THE SERUM TREATMENT OF EXOPHTHALMIC GOITRE.

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THE treatment of exophthalmic goitre still leaves much to be desired, for although good results are obtained in many cases by our present methods improvement is often slow and some cases do badly. More especially do we require some efficient means of treating those cases in which the symptoms rapidly become acute and the patient dies within a few days. It has been my misfortune to see several of these cases where the patients have died after a few days of acute illness and it has seemed possible that in this class of case, in which the symptoms are evidently due to a toxæmia, an antitoxic serum might be useful. The evidence we at present possess tends to show that the symptoms of this malady are due to the morbid condition of the thyroid gland and are the result of an excessive formation and absorption of thyroïdal secretion. Whether this secretion is simply increased in amount, while it retains the same physiological properties as in health, or is changed in constitution is still an open question which, however, may have an important bearing on the preparation of an antitoxic serum. Assuming, in the absence of proof to the contrary, that the excessive thyroïdal secretion has similar physiological properties to that which is formed by the normal gland, there are different ways in which serum treatment might be of service. Thus, a cytotoxic serum prepared in the manner described by Portis might have a specific action in inducing atrophic changes in the redundant secretory epithelium of the enlarged thyroid gland and so diminish its over-activity; or an antitoxic serum might be prepared by Moebius's method or by the method adopted by Lepine and by myself, which would directly neutralise the action of the excess of secretion in the blood. We may regard the symptoms as being due to a toxæmia the source of which is the diseased thyroid gland, just as much as the toxæmia of diphtheria or tetanus is due to the production of toxins in the locally infected area; and although we have no reason to regard Graves's disease as infective in origin I see no good reason why an antitoxic serum should not be obtainable by suitable methods similar to those employed in the case of the infective diseases.

Portis¹ endeavoured to produce symptoms similar to those which follow removal of the thyroid and parathyroid glands in animals by means of specific cytotoxins selective in action on the thyroid and parathyroid cells, causing their degeneration and loss of function. The possibility of this had previously been indicated by the preliminary reports of Mankovsky² and of Goutscharukov,³ both of whom had stated that they had produced thyrotoxic sera, injections of which produced symptoms like those of tetany, the thyroid cells showing evidences of degeneration. Mankovsky introduced the thyroid glands of dogs into the peritoneal cavity of cats at intervals of a fortnight and after the third injection bled the cats and separated the serum which proved toxic to dogs. Goutscharukov also used the thyroids of dogs, injecting them into rams and so produced a serum which he considered to be thyrotoxic. Portis employed increasing doses of an emulsion of dog's thyroid. Beginning with one gland he increased the dose up to ten glands, injecting the emulsion into the peritoneal cavity of a goat, not more than one month being allowed to elapse between

¹ Journal of Infectious Diseases, No. 1, Jan. 2nd, 1904.

² Russ. Archiv für Pathologie, 1902, pp. 571-91.

³ Centralblatt für Allgemeine Pathologie und Pathologische Anatomie, 1902, Band 13, S. 121-24.

¹ See St. Thomas's Hospital Museum Catalogue.

the injections. After the third injection he began to bleed the animal for the study of the serum. As a result of his experiments with serum prepared in this manner he came to the conclusion that the serum of goats when injected with suspensions of the thyroid gland or the thyroid colloid of dogs acquired certain new properties. Injected into dogs it caused depression, convulsions, vomiting, rapid breathing, hæmoglobinuria, and early death; in cases which survived longer there were some fever, lacrymation, emaciation, and progressive loss of weight. Microscopical examination of the thyroid gland showed removal of colloid from the acini, desquamation, and disintegration of the epithelial cells, followed later by the development of papillary proliferations. The liver, the spleen, and the kidneys also showed marked degenerative changes. The action of this serum is not solely thyrotoxic as it induces changes in other organs as well, and is therefore not suitable in its present form for use in the treatment of exophthalmic goitre as degenerative changes would probably be set up in other organs as well as in the thyroid gland.

Moebius approached the preparation of an antitoxic serum from another standpoint. He assumed that the blood of an animal after thyroidectomy would contain certain bodies which normally would have been destroyed or neutralised by the thyroid secretion and that they might conversely be employed to neutralise the ill-effects of the excess of thyroid secretion in exophthalmic goitre. Lanz working on similar lines had employed the milk of goats from which the thyroid gland had previously been removed in the treatment of six cases of this disease with good results. Moebius's serum has been prepared by Merck by removing the thyroid gland from a sheep and after several weeks bleeding the animal and separating the serum. Good results have been obtained by Moebius and by Schultes. I have also employed this serum but was unable to attribute any special result to its use.

A more rational method of preparing an antitoxic serum appeared to me to be by treating an animal with gradually increasing doses of thyroid extract so as, if possible, to induce the formation of antibodies in the blood and then to make use of the serum in the treatment of Graves's disease, and this is the method I adopted. Lepine⁴ has also prepared a serum in a similar manner. He fed a goat on gradually increasing amounts of the thyroid gland of a sheep or of another goat. Four lobes of sheep's thyroid were given every two or three days. Large doses at first caused diarrhoea, tachycardia, exophthalmos, and dyspnoea. After several months from 20 to 25 lobes of the gland could be tolerated. The serum of this animal when injected into the dog caused loss of weight and slowing of the heart. In the abstract of Lepine's paper which I have seen no mention is made of the results obtained by treating Graves's disease with the serum.

In my own experiments, commenced last year, I endeavoured if possible to obtain an antitoxic serum in as simple a manner as possible for the purposes of practical treatment and so made use of rabbits and fed them with thyroid extract by the mouth. This is easily done by using a hypodermic syringe without a needle and injecting the dose into the rabbit's mouth, when owing to the sweet taste it is readily swallowed. On Oct. 18th five rabbits, varying in weight from 4 pounds 1 ounce to 6 pounds 12 ounces, and one Belgian hare, weighing 7 pounds 13 ounces, were given each ten minims of liquor thyroidei each weekday. On Oct. 25th the Belgian hare aborted and so the treatment was discontinued for a time. On Oct. 31st the daily dose was reduced to five minims as the animals were losing weight on the larger dose. This was continued up to Nov. 20th when the first rabbit was killed by bleeding and the blood was collected with aseptic precautions into two sterilised flasks. These were allowed to stand for 48 hours, after which the serum was decanted into small sterilised glass bottles, 0.2 per cent. of carbolic acid was added, and the glass stoppers were sealed with paraffin. Several batches of serum were prepared in a similar manner, the dose of thyroid extract given and the length of time of administration being varied. It was found that for prolonged administration a dose of five minims three times a week was as much as could be given to a rabbit without causing progressive emaciation. When larger or more frequent doses were given continuously the animals progressively lost weight and even died in two instances. Before employing this serum in the

treatment of exophthalmic goitre ten minims of it were injected subcutaneously into a rabbit. No ill-effects followed until three weeks afterwards when the rabbit became ill, the forelimbs were rigidly flexed, the eyes widely opened, and there were general tremors. These symptoms soon disappeared completely and it is doubtful if they were due to the serum injected three weeks previously. The following two cases of exophthalmic goitre were treated with the serum prepared in the manner described above.

CASE 1.—A single woman, aged 20 years, was admitted to the Newcastle Royal Infirmary on Dec. 22nd, 1903. Prominence of the eyeballs had first been noticed 18 months previously; six months later the goitre developed. She complained of nervousness, palpitation, and loss of weight. This patient was a typical case of exophthalmic goitre, with well-marked enlargement of the thyroid gland and exophthalmos, Stellwag's and von Graefe's symptoms both being present. The pulse was 120, the skin was moist, and fine tremors were present. After she had been in the hospital for a fortnight the pulse was found to vary between 96 and 124. Serum treatment was commenced on Jan. 9th, 1904, five minims being given by the mouth each night. On Jan. 12th this dose was given three times a day. On the 15th the dose was increased to seven minims and on the 22nd to ten minims. After this seven minims were given (with the exception of four days) thrice daily up to Feb. 8th, when it was stopped. After this electrical treatment was given for a fortnight. From Feb. 23rd to March 9th Moebius's antithyroid serum prepared by Merck was given in five-minim doses thrice daily. While taking my serum the patient gained in weight, the tremor diminished, the breathlessness disappeared, and the exophthalmos became less marked. She also continued to improve under the influence of the electrical and Moebius's serum treatment. In this case, however, the improvement was nothing more than what frequently takes place in a patient at rest in a hospital ward on the ordinary medicinal treatment and I was unable to trace any special effect to either of the two sera employed.

CASE 2.—In this case of exophthalmic goitre of five and a half years' duration in a single woman, aged 19 years, the serum was given for three weeks in similar doses. The pulse diminished in frequency somewhat but no special effect could be attributed to the serum in this case either.

Although no very definite results have been obtained in these cases I think it is quite possible that if larger animals were employed and larger doses of thyroid extract were given a serum might be obtained which could be used for hypodermic injection in acute cases or for administration by the mouth in chronic cases where prolonged treatment would be required, and for this reason I have thought it advisable to record the above observations.

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THE RADICAL CURE OF PATENT URACHUS (URACHAL URINARY FISTULA).

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SUCH an operation as the one described below does not appear to be included in the present works on operative surgery. Most of the operations on the urachus deal with the umbilical end alone and neglect the vesical end. Cures are attempted by obliterating the umbilical opening by caustics or cautery; these measures may close the fistula at the umbilical end but leave a patent tract lower down or a urachal retention cyst. Such a condition does not free the patient from the pain which is so constant on attempting micturition, especially when the bladder is full, for this increases the pressure in the urachus which bears to the bladder the same relation as a pressure-gauge to a boiler. After seeing a tall, strong youth who had borne this distressing condition for 17 years it struck me that something radical might be done to relieve him. The umbilicus was bulged forwards and, in fact, was a small hernia of sub-peritoneal fat, the skin was in an eczematous condition from the continual acid moisture, and the whole area was very tender. The patient always experienced considerable pain when he voided urine from the back pressure effects mentioned above.

⁴ Epitome, Brit. Med. Jour., Feb. 22nd, 1904, p. 35.