

Clinical notes on Graves' disease / by Grainger Stewart and G.A. Gibson.

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CLINICAL NOTES ON GRAVES' DISEASE.

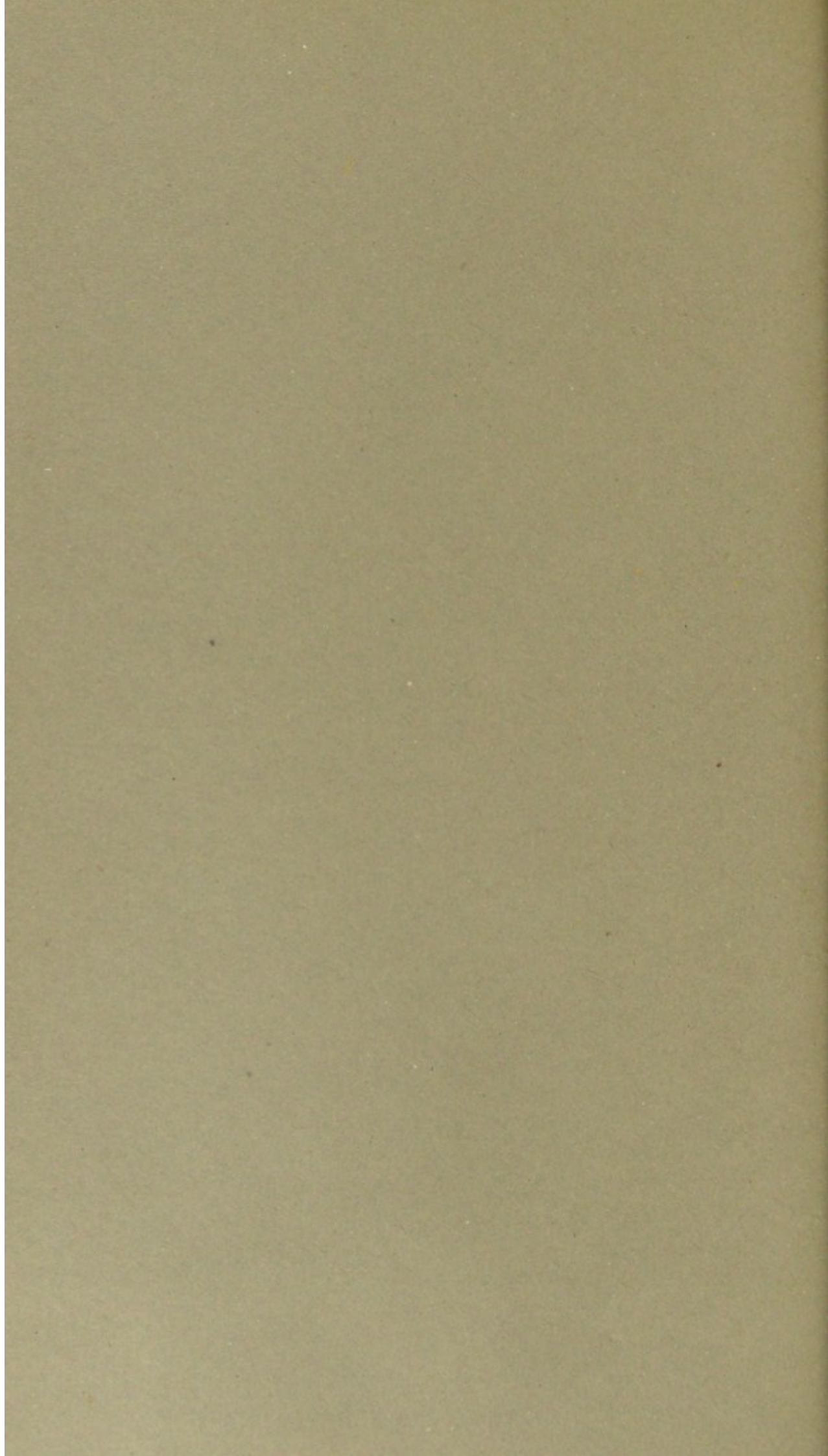
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Clinical Notes on Graves' Disease. By Professor
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Our purpose in the following paper is to comment briefly upon the symptoms generally recognised as proper to Graves' disease, to indicate some of its rarer complications, and particularly one or two which we believe to have been hitherto undescribed; and also to give a succinct account of some cases which we have had under observation in the Infirmary during the past year, with reports of two autopsies, including the microscopic examination of the most important structures involved. We shall endeavour, in so far as may be possible in detailing the more unusual or less generally recognised symptoms, to trace their relations to the primary phenomena and their probable causation. In the following pages we shall follow the method of investigation which is employed in the Royal Infirmary.

Affections of the *alimentary system* occur in almost every instance of Graves' disease, and we find amongst our cases a large proportion exhibiting disturbances both of stomach and bowels. Not only have we met with various forms of gastrointestinal crises, such as severe vomiting and profuse diarrhoea, together with symptoms like boulimia and pica, and complications such as hæmatemesis and melæna, but in one or two well-marked cases the tendency towards recovery was manifestly influenced by treatment of the attendant dyspepsia. In some instances, on the other hand, which have come under our notice, it has been obvious that a rapid development and fatal tendency of the disease have been attended by severe and intractable gastric disturbance. Germain Sée, in dealing with this subject, makes mention not only of paroxysmal vomiting, or gastric crises, but also of paroxysmal diarrhoea, or enteric

crises, and our experience justifies his descriptions. One of the most rapidly fatal cases of the malady, that described by Osler, showed remarkable symptoms of this kind. The patient, who had previously manifested no sign of Graves' disease, except a slight degree of prominence of the eyes, was suddenly attacked by severe vomiting and diarrhoea with tachycardia, throbbing of vessels, exophthalmos, and swelling of the thyroid gland. Death occurred on the third day of the illness. One of the patients under our observation has suffered from diarrhoea from time to time during a period of three years. On several occasions it has been so severe as to threaten death from exhaustion, while the onset of the attacks has often been alike sudden and unexplained.

When we seek to explain these gastro-enteric symptoms we naturally think first of abnormal innervation; and the acuter crises, with their frequently sudden onset, and occasionally abrupt termination, must undoubtedly be referred to this cause. The nervous system may operate through the vaso-motor functions, by modifying the processes of secretion and absorption, or by exciting the muscular fibre to increased peristaltic action; but we have certainly found evidence of extensive catarrh of the alimentary canal in two fatal cases, one of which is recorded in the sequel.

The *hæmopoietic system* is almost constantly implicated, but to a very varied extent. The blood presents no constant condition. In many cases the amount of hæmoglobin, and the relative number of red and white corpuscles, are within the limits of health; but in a considerable proportion of patients exhibiting symptoms of Graves' disease there are blood changes significant of varying degrees of anæmia.

The thyroid gland may be said to be almost invariably affected. Trousseau refers, however, to a case in which it was never involved, and various subsequent authors have confirmed his observations. Amongst his 58 cases von Dusch found 3 in which there was no thyroid enlargement. The case of a lady who came under our notice with all the other cardinal symptoms of Graves' disease (including tachycardia, exophthalmos, and tremor), afforded us lately an instance of the affection without any change in the thyroid gland. The

enlargement of the gland, although usually bilateral, is very rarely symmetrical. In one or two cases we have found only one lobe to be affected. From our own observations we should be inclined to conclude that the left is more commonly the earliest and chief seat of enlargement, but from the time of Parry and Graves the majority of authors have found the right to take precedence. There can be no doubt that, as Graves and Stokes noticed, and other observers have corroborated, the size of the gland varies from time to time with the state of the circulation, and from other circumstances.

As to the nature of the morbid process it has been held to be due, in the early stages, to a simple hyperæmia, and in the later to a hypertrophy of the connective tissue. It will be seen, however, in the sequel that, from the result of post-mortem investigation in two of our cases, Dr. Robert Muir has found a glandular hyperplasia with catarrhal changes in some of the acini, a disappearance of the colloid material of the spaces, and some cellular proliferation of the interstitial tissue.

We can only recall one case of Graves' disease attended by enlargement of the spleen. This organ is described as the seat of an enlargement by other authors, and, in view of the frequency of anæmia in this disease, it might be expected to undergo an increase in size; but, even in cases which have been attended by pyrexia for some time, we have found, as a rule, no evidence of such a change, either in the living or the dead subject. The only exception to this statement occurred in a patient who had for a considerable time been in India, where he had suffered from malaria. His case will be found in the sequel (Case 6).

The *circulatory system* not infrequently shows subjective symptoms.

Even in the early stages of the affection, attacks of faintness are extremely common without structural changes in the circulatory apparatus. The subjective sensations of palpitation form one of the most frequent symptoms of the disease, and are linked with the objective phenomena of tachycardia. Severe cardiac dyspnœa, while most typically arising in cases of failure of the heart, has been present also in conditions

which would preclude any such diagnosis, and in these cases it appears to be produced solely by some functional disturbance of the nervous system. Such nervous dyspnœa is described by Germain Sée. Pain in the præcordial region, referred to also by the same author, will be seen to have been a prominent symptom in one of the cases (Case 7) described in the sequel.

Symptoms of dropsy are found only, for the most part, as the result of enfeebled cardiac activity. In this condition there may not only be a considerable amount of œdema of the lower extremities, but also so large a quantity of serous fluid in the pleural sacs and peritoneal cavity as to necessitate aspiration. It will be seen that such a train of symptoms was present in Case 7.

Tachycardia has been absent in no case under our notice and in at least one well-marked instance, already referred to, this symptom, although attended by exophthalmos and tremor, was not associated with thyroid enlargement. Tachycardia is usually accompanied by palpitation, but the subjective phenomena often fail to attract the patient's notice.

In some rare cases referred to by Eulenburg there has been neither tachycardia nor palpitation. Germain Sée will not allow that increased frequency of the pulse may be absent, and our observations are in accord with his opinion.

At times the frequency of the pulse is easily controlled by rest and drugs, but in many cases the tachycardia resists treatment.

Extreme irregularity of the pulse occurred in one of the cases described in the sequel. Although exceptional, the condition is well recognised, having been described in connection with this disease by Rendu and others.

Hypertrophy of the heart in Graves' disease was originally described by Stokes, and most of the subsequent authorities have coincided with him in this respect. Cardiac hypertrophy has been a frequent accompaniment of our cases; showing itself not only by outward displacement of the apex and increased force of its beat during life, but also by considerable increase of weight on post-mortem examination, as in Case 7.

Dilatation, however, has been much more frequent, especially

among severe cases, and we may hazard the opinion that the progress of cases of Graves' disease very largely depends on the nutritive possibilities of the individual heart. When the disease attacks those who have a considerable reserve of cardiac energy, hypertrophy is the rule; but if there be any cardiac inadequacy there is much downward tendency. In most of our fatal cases, whatever may have been the determining circumstances, death has directly resulted from cardiac failure.

As illustrating this mode of death, which will also be seen in Case 7, we may refer to a case which was under our notice some years ago. The patient was an able and hard-working professional man, who had for long been an excessive cigarette smoker, and had also been regularly in the habit of "inhaling." This gentleman, after a long courtship, married while already exhibiting some of the symptoms of Graves' disease. Before marriage he had a morbid dread of possible impotence, and eventually found his worst fears realised. After travelling for some years he improved somewhat in general health, and resumed work, but soon found rest again necessary. While travelling abroad he developed œdema of the lower limbs and ascites, with physical signs of cardiac dilatation. Rest in bed and digitalis, with careful dieting, produced a gradual subsidence of the dropsy, and rescued him from a condition of extreme peril. After his return home he continued free from dropsy, and was able to take riding exercise. One day after rather a long ride he flung himself from his horse at the stable door, and was walking up a slight incline to his home when he fell dead, evidently from sudden asystole.

This case resembles in certain respects one described by Trousseau, in which, together with an enormous thyroid enlargement, there was cardiac dilatation with great cyanosis. His case, however, terminated much more satisfactorily, for by means of bleeding, ice, and digitalis, a complete cure was effected. In a different aspect the case is somewhat like another mentioned by the same author, in which there was marked impairment of the male generative functions.

Although some writers, such as Greenmayer, have described many different forms of valvular lesion, more especially of the

aortic and mitral valves, as occurring in the course of this disease, we are inclined to think from our own observations that organic changes in the valves are relatively uncommon. In consequence of ventricular dilatation incompetence of both mitral and tricuspid valves has been so frequent in our cases as to be almost the rule, and yet the valves themselves have in every case been free from important organic lesion.

Great pulsation of the large arteries, especially those of the neck, has been invariably observed by all workers at this subject, from the time of Graves and Basedow.

The vascular walls have in our experience been for the most part free from degenerative changes, with the exception of a slight chronic patchy inflammation of the tunica intima, which is not uncommon in the aorta. We have never seen a patient suffering from formidable aortitis, or extensive calcareous changes in the arteries. Such changes are not common at the age when exophthalmic goitre prevails, and when from syphilis, or some other cause, they do appear earlier in life, such a deterioration of health is apt to exist as would prevent there being time for the development (under ordinary circumstances) of the full symptoms of exophthalmic goitre, even if it were threatening to appear.

The arterial tension seems to be almost uniformly moderate, and we find our own conclusions in this respect to coincide with those of Marie. The arteries are frequently, as Germain Sée points out, poorly filled.

Murmurs, approximately systolic in rhythm as compared with the cardiac cycle, are extremely common in the arteries, or may be produced by the slightest pressure.

Withusen observed that the retinal vessels were large, and Becker described exaggerated pulsation of the arteries of the retina. We are unable to confirm this.

The arterioles are, in many instances, easily affected by nervous influences, flushing and paling of the surface being frequent attendants upon the disease, while, as Trousseau showed, a tache is easily produced and the red line often shows distinct capillary pulsation.

The veins of the neck are usually the seat of a venous hum, and whenever cardiac dilatation is sufficiently marked, as it is

in the majority of cases, they show marked venous pulsation, while the veins throughout the body generally exhibit considerable evidence of stasis. Pulsation of the liver has been recorded in more than one case by Lebert, but this symptom has not been present in any of our cases.

Finally, among circulatory accidents, must be mentioned hæmorrhage. Trousseau has recorded cerebral hæmorrhage as the cause of death in one case, and since his time other observers have narrated instances of hæmorrhage involving other regions.

In seeking an explanation of the subjective phenomena, it is natural to refer the faintness to deficient force of the ventricular systole, from impairment of innervation or incompleteness of contraction; but it may, perhaps, be associated with altered conditions of intracranial circulation, or with a combination of such changes, and those more especially cardiac.

The palpitation is, of course, in many instances the expression of the exaggerated action, while doubtless it may sometimes be felt with undue acuteness from over-sensitiveness of the afferent fibres.

Pain is clearly referable to undue irritability of the sensory nerves, while dyspnœa may be due to deficient action of the right, just as syncope results from impaired contraction of the left ventricle, or to changes in the pulmonary circulation, corresponding to such intracranial changes as we have mentioned.

Tachycardia must be referred either to an increased irritability of the muscular fibres, an exaggerated excitability of the accelerator nerves of the heart, a diminished activity of the inhibitory influence to which it is subjected in health, or a change in intraventricular pressure from alterations of the circulation within the vessels.

We are not acquainted with any facts which would justify the acceptance of the hypothesis of heightened muscular irritability, although we admit the possibility that such a condition may one day be demonstrated.

While it cannot be said that we possess evidence directly supporting the hypothesis of undue irritability of the sym-

pathetic ganglia, which are believed to be concerned in the supply of the motor impulses to the cardiac muscle, it appears to us reasonable to accept such a condition as affording a possible explanation of the phenomena. If this were so, it would lend a measure of support to the supposition that there is in Graves' disease an increased irritability of the sympathetic system generally. The results of morbid anatomy are too conflicting to be of any real service in the elucidation of this part of the subject, for while in eight published cases—those of Trousseau and Peter, Reith, Cruise and M'Donnell, Traube, Biermer, Virchow, Geigel, and Knight—there have been changes in the ganglia of the cervical sympathetic, there have been in four recorded instances—those of Paul, Fournier and Ollivier, Rabejac, and Wilks—no morbid appearances in any part of the sympathetic system. In three autopsies of cases under our care, two of which are described in the following pages, no changes in the sympathetic were perceptible.

The loss of inhibitory influence affords another possible explanation, and it must be at once admitted that gastric and respiratory symptoms also find a ready explanation by reference to the functions of the vagus nerve. Section of the vagus in the lower animals undoubtedly produces an action closely resembling, in the increased frequency with perfect regularity, the symptoms in Graves' disease.

That an explanation might be found in the altered intraventricular pressure, due to changes in the arterial system, appears to us to be rendered possible by the results of the use of drugs like nitrite of amyl.

The irregularity which is sometimes, if rarely, present is in almost every instance the result of cardiac failure.

Hypertrophy of the heart was originally explained by Cohnheim as being the result of long-continued over-action; and probably this is true, but as the tension in some cases is high, there may be an additional factor in this condition.

Cardiac dilatation, sometimes following or accompanying hypertrophy, is in every instance the result of muscular failure.

The increased arterial pulsation is always associated with

low arterial tension, which is probably its cause, while the turgescence of the veins and the dropsy are without doubt brought about by cardiac failure.

With regard to the *respiratory system* we have at times observed the development of striking subjective symptoms.

Severe nervous dyspnœa, with noisy respiration, was a prominent feature in the case of a lady whose symptoms gradually disappeared after the removal of a nervous strain, to which she had been subjected for some years.

Periodic breathing, at times amounting to Cheyne-Stokes respiration, has made its appearance in cases where there was pronounced tendency to cardiac failure.

Severe paroxysmal coughing in the course of the disease is regarded by Germain Sée in the light of a laryngeal crisis. We have observed it occurring as a symptom of different respiratory complications; it has, however, made its appearance apart, not only from such conditions, but also from such possible causes as pressure on the pneumogastric nerves, and under these circumstances it must be regarded as of nervous origin.

Bronchitis, pneumonia, and pleurisy have not infrequently occurred as complications in our cases, and have been in some the determining causes of death.

In one most interesting case, a hypertrophic condition of the mucous membrane of the naso-pharynx was present, and local treatment of this affection was followed by a marked diminution of the principal symptoms of the disease. This case is given in abstract (see Case 1).

The dyspnœa is no doubt in many cases due to the condition of the heart and vessels, pulmonary and systemic, as well as to the direct interference produced by the increased size of the thyroid gland; but it is extremely probable that the subjective respiratory symptoms are in great part dependent on the general increase of nervous irritability.

The very interesting case described in the sequel, in which treatment of the naso-pharynx produced so much improvement of the disease, may be compared with those cases of asthma in which the paroxysmal dyspnœa is the result of abnormal conditions in the upper respiratory tract.

With reference to the *integumentary system*, flushing, pallor, and œdema have already been mentioned in connection with the circulatory system. In addition to such changes we have often had occasion to note free perspirations and such appearances as chloasma, erythema, and urticaria. Vitiligo has been observed in connection with this disease by Arnozan and Leloir. Germain Sée refers, in addition, to scleroderma, and Oppenheim to Addison's disease as having occurred in some cases.

But of much greater interest are certain changes which we have observed in the condition of the cutaneous appendages. In several cases, some of which will be noted in the sequel, there has been an atrophy of the hair shown by its disappearance more or less entirely from such situations as the scalp, axillæ, and pubes, and by profound change in the character of that which remained. In one instance this altered nutrition of hair was much more marked on one side of the body than the other. We have known it to precede the occurrence of the more ordinary symptoms, but more commonly it follows their appearance. But this is not all, for in several very striking instances of the disease the nails have been seen to have undergone atrophic changes, becoming thin, weak, and brittle, sometimes indeed being represented only by a soft paper-like film. Our friend Dr. Tawse Nisbet, of Liverpool, who has independently recognised the nail-lesion, compares it very happily, in a hitherto unpublished communication, to a micaceous transformation. Sometimes both hands are equally affected, sometimes one is distinctly more altered than the other, sometimes individual nails are worse than the rest, and occasionally the corresponding nails of opposite sides are correspondingly affected. Besides the thinning of the nail structure we have sometimes seen a corrugated appearance, with a yellowish opacity like what is seen when pus lies below the nail. The only analogous change that appears to have been observed previously is an atrophy of the eyelashes, which has attracted the attention of Germain Sée.

In seeking to explain these integumentary changes we necessarily refer them to a trophic nerve influence, but our present knowledge does not warrant any definite statement as to the seat of the morbid process.

The *urinary system* presents at times some characteristic symptoms. Polyuria, which Germain Sée mentions as being first observed by Christison, is one of the more frequent accompaniments of the disease, and is probably connected with the profound vasomotor disturbances connected with the condition.

Albuminuria, first observed by Warburton Begbie as occurring in Graves' disease, has come under our notice in several instances, but these have been cases complicated with cardiac dilatation. From personal observation of one of Dr. Begbie's original cases, as well as from the admirable clinical description given by that author, it is clear that in not a few instances the symptoms would now be referred to the category of functional albuminuria, albuminuria of adolescence, or cyclical albuminuria.

Glycosuria has been recorded as an accompaniment of Graves' disease by many observers, such as Eulenburg, in Germany; Germain Sée, in France; and Lauder Brunton, in our own country. In our own series of cases this symptom has also from time to time occurred, and one of the instances will be found in the following pages.

It is clear that these abnormal conditions of the urine might be referred to altered vasomotor states, but, considering that all of them are so frequent, we incline to refer them to changes, organic or functional, in the neighbourhood of the floor of the fourth ventricle, rather than to vasomotor alterations in the kidney or the liver.

With regard to the *reproductive system*, it has long been known that the catamenia in women, as a rule, are suppressed, and in almost all the cases we have seen this has been the state of affairs. But the contrary is sometimes observed, and an excellent example of such a condition will be found in Case 1.

So far as our present experience goes, we have only met with one case in which pregnancy has occurred after the onset of the disease, and we are inclined to conclude that usually the reproductive processes are seriously interfered with. But Trousseau and Charcot have observed cases in which pregnancy has not only occurred, but has been attended by improvement in the condition of the patient.

In the male sex, Trousseau, as we mentioned, has observed some interference with the generative functions, and a serious state of affairs of this kind has been disclosed in connection with a case previously referred to.

Anæmia and failure of nervous energy incident to the disease probably afford the explanation of these symptoms.

The *nervous system* manifests symptoms which are multifarious and characteristic.

A great liability to considerable fluctuations of temperature may be said to be eminently significant. In many cases a slight local hyperæmia is quite sufficient to induce high degrees of temperature, and not infrequently we have seen pronounced oscillations of the temperature curve without any ascertainable local cause.

Among sensory phenomena subjective symptoms are common; and these are not confined to the ordinary sensibility, for the special are involved as well as the ordinary sense-paths. Galezowski has described subjective luminous phenomena, and in several of our cases subjective auditory symptoms have been remarked. The ordinary as well as the special sensibility is, when tested, found to be increased, and hyperæsthesia is as universal in the sensory as tremor in the motor nervous mechanism.

The protrusion of the ocular globes is almost always bilateral; but it is extremely common to find one eye more prominent than the other. Occasionally the exophthalmos is confined to one side entirely. It is in rare cases altogether wanting, as in 4 out of 58 referred to by von Dusch.

Changes in the nutrition of the eyeball are rare; but inflammation and ulceration of the conjunctiva and cornea have been described by Basedow and subsequent authors.

The pupil is said, as a rule, to show no marked departure from the ordinary condition; but some observers, as Geigel and Friedreich, have noticed changes mostly in the direction of dilatation. By von Graefe this was not seen once in two hundred cases. We cannot understand how this can have been, for our own experience leads us to believe that dilatation is by no means uncommon.

The retina often shows dilated and tortuous veins, and Becker has observed excessive pulsation of retinal arteries.

Of motor phenomena, one is so constantly part of the congeries of symptoms as to be regarded in the light of a cardinal feature of the disease. This is the characteristic tremor first described by Charcot. In every case which we have seen this typical trembling has been present. Sometimes it is only observed in the hands and arms, but it is frequently found to involve the entire body.

Kahler has described choreiform movements, and Gueneau de Mussy has seen acute chorea in the course of the disease. Amongst other motor perturbations Ballet has seen epilepsy, and Möbius paralysis agitans.

Various paralyses have been recorded by different observers, such as monoplegia by Vigouroux, Dreyfus-Brisac, and Du-Cazal, or paraplegia by Charcot, Kahler, and Ballet. In many of these cases the basis of the symptoms was obviously hysterical, and in a large proportion of these there was well-marked contracture.

Paralysis of isolated ocular muscles has been described by Fereol, and Ophthalmoplegia Externa has received much attention from Warner and Bristowe. Paralysis of other bulbar nerves has also been observed by Ballet and Potain, and it is a matter of much interest to note that in some of these cases no lesion of the nervous tracts apparently involved could be discovered.

Diminution of the electrical resistance has been commonly recognised since the investigations of Vigouroux, and the subject has been very carefully studied by Kahler more recently. It seems probable that this diminished resistance is due to the greater amount of perspiration usually present.

The superficial reflexes present no constant condition, and the myotatic irritability differs much amongst patients suffering from Graves' disease. The knee jerk is sometimes increased, and ankle clonus even may be present, more especially in the cases manifesting a high degree of nervous excitability, but, on the other hand, the knee jerk may be entirely absent, as in one of the cases described in this paper (Case 6).

Some loss of co-ordination of muscular movement is com-

mon, at any rate in respect of the associated movements of the eyeballs and eyelids. The highly characteristic symptom, pointed out originally by von Graefe, and usually bearing his name, has never been absent in any case we have seen. Eulenburg says it may disappear, although the other symptoms persist, but no instance of such an event has come under our notice.

A loss of co-ordination and of the power of balancing will be seen in Case 6, and these symptoms, linked in that instance with loss of the knee jerk, and a fugitive Argyll Robertson sign, may be due to association with locomotor ataxy, such as has been noticed in this disease by Ballet.

Some vasomotor symptoms have already been mentioned; and we may add that the free perspirations we have seen have sometimes been unilateral. It is interesting to recall the fact that such unilateral perspirations have been recorded along with unilateral myosis, by Nitzelnadel.

We have also mentioned some trophic disturbances in connection with the integumentary system, and we would further refer to the fact, that unilateral cases of gangrene, obviously trophic in origin, have been seen by Fournier and Ollivier as well as by Rabejac.

A considerable degree of wasting is common, and this in some cases is excessive.

As to the higher functions of the nervous system, such features as unrest, insomnia, irritability, fickleness, and analogous symptoms, pointing to neurasthenia, hypochondriasis, and hysteria, are frequent even in the early stages of the affection, and in more advanced and more serious cases more pronounced aberrations of the brain may occur. The mental aspects of the disease have been more especially studied by Geigel, Solbrig, Ball, Andrews, and Carlyle Johnston. Although the affection seems to occur in families who have nervous or even insane members, it is but rarely that Graves' disease is found among the inmates of an asylum.

If we were able to explain satisfactorily the changes proper to the nervous system we should feel that we had solved the problem of the disease. The sensory changes are no doubt mainly referable to that irritability which is associated with

weakness. The motor phenomena may be explained in the same way; but the vasomotor and trophic effects have a distinctive character which marks them off from other maladies, and constitutes, in our judgment, an essential feature of the disease. Undue irritability of the sympathetic might well account for the tachycardia, the dilated pupils, the delayed descent of the eyelid, and perhaps also for the abnormal dilatation of certain sets of vessels, and if we were able to point to constant structural changes in the sympathetic ganglia or fibres we should feel that we had touched solid ground in regard to the matter. This, however, is not the case; for our own results, like those of some of the other authors mentioned, are purely negative. It is idle to deny that other nervous influences, such as paralysis of the vagus, advocated by Germain Sée, might bring about many of the clinical effects.

We conclude this paper by giving in abstract some notes of all the cases which we have met with in hospital work, during the year from October 1891 to October 1892.

CASE 1.—ANN A., æt. 42, engaged in household duties, has presented herself at the Royal Infirmary from time to time during the year.

Father died at 66 of chronic bronchitis, mother at 54 of apoplexy. Patient is the eleventh of twelve children, of whom five—two brothers and three sisters—survive; one brother was drowned, another died of typhus fever, and the third of bronchitis; three sisters died in youth of measles, and another during adult life of uterine cancer.

The patient was married at the age of 20, and had a child eleven months after marriage, since which she has not had a birth or miscarriage.

Her health, prior to the onset of the disease, was always good.

About New Year, 1889, she had a swelling of the neck, which disappeared under treatment. Soon after this she received a severe fright, and the sight became somewhat indistinct, for which she consulted Dr. Argyll Robertson, who ordered spectacles. During a subsequent visit he observed that the eyes were unduly prominent, and sent her to Ward

25, which she entered on 6th June 1889. In the month of February of the following year, she was sent for nasal symptoms to Dr. M'Bride, who cauterised the mucous membrane of the throat and nose, and removed a polypus from the nose. After a short time, during which she remained *in statu quo*, she began to improve.

Her present condition is in many respects greatly better than it was when she was in the Royal Infirmary.

The alimentary system shows no evidence of any departure from health; the different viscera are within their ordinary limits, and perform their functions well.

The hæmapoietic viscera are not in any way, so far as can be ascertained, abnormal. The spleen reaches the mid-axillary line. The thyroid gland shows no enlargement, and no murmur can be heard on auscultation.

The patient suffers from no palpitation or dyspnœa. The pulse is 80, regular, of moderate fulness and tension. The apex is in the fifth interspace, $3\frac{1}{4}$ inches from mid-sternum. The left border of the heart is $3\frac{1}{2}$, and the right $2\frac{1}{4}$ inches from mid-sternum. There is a faint murmur at the apex, propagated to the axilla, and fading away before reaching the sternum. Another murmur is heard with its maximum intensity at the junction of the fifth and sixth left costal cartilages with the sternum. There is no murmur at the base. A faint continuous venous hum is heard over the jugular veins on both sides.

The respiratory and urinary systems are normal.

The catamenia have been regular in occurrence, and normal in amount throughout her life, even during the worst phases of the illness.

The integumentary system has no morbid appearances, except a thinness of the hair of the scalp, and scantiness of that of the axilla, where it is very soft and pale.

Since receiving the fright the patient has always been very nervous. She used after that occurrence to suffer from severe headaches, but these have not troubled her for a couple of years. There is a well-marked tremor. The eye-balls are still unduly prominent, and show the sclerotic all round the iris. The symptom of von Graefe is still present.

The pupil reacts normally in every way. The knee jerk is normal in extent, and the superficial reflexes have not undergone any alteration. There is some tendency to the production of a tache on drawing the nail along the skin. No other nervous symptoms can be elicited.

The case of Mrs. A. is interesting, not only in regard to the completeness of all the ordinary symptoms, but with reference also to the integumentary symptoms and the improvement which was noticed after the mucous membrane of the nose and throat had been treated by local measures.

CASE 2.—MARY L., æt. 20, unmarried, biscuit-maker; presented herself in the medical waiting-room on the 2nd November 1891, complaining of pain in stomach and thirst, and was admitted the same day to Ward 25.

Her father died of heart disease at the age of 46. Her mother is alive and well. The patient has only had one brother, who enjoys good health.

She has had hard work, and has been badly cared for.

Until recently her health has been good; five weeks ago she began to suffer from a sore tongue and pain in the stomach. Thirst and vomiting have troubled her greatly since then, and swallowing has been painful.

The patient's lips, on admission, were found to be dry and rough, the teeth much decayed, the tongue dry, red, and cracked, with prominent papillæ. The stomach was dilated, reaching almost to the umbilicus. The liver was of ordinary size.

The spleen reached the mid-axillary line. The right lobe of the thyroid gland was considerably enlarged and pulsating, and over it a systolic murmur could be heard. Palpitation and faintness were often complained of. The pulse was 96, regular, small, and of low tension. The apex beat was in the fifth interspace, $2\frac{1}{2}$ in. from mid-sternum, the left edge 3 in., and the right $1\frac{1}{2}$ in. from the mid-sternum line. There was a faint systolic murmur at the base of the heart, and a continuous hum over the right jugular vein.

The respiratory system was normal.

The urine amounted to 127 oz. It was pale, acid, and of

1045 sp. gr. It contained 4·5 gr. per oz. of urea and 55·7 gr. per oz. of glueose.

The catamenia had been absent for three months. The skin was dry and harsh. The hair of the scalp was coarse and dry. The axillary and pubic hair was very scanty.

The patient had a general muscular tremor. The reflexes were normal. Both eyes were prominent, especially the right. There was delayed descent of the upper eyelid, more marked on the right side. The patient was deaf on the left side.

In this case, in addition to the one-sided tendency of the disease, as regards the thyroid gland and eyes, there was a co-existence of Graves' disease and diabetes mellitus.

On the 6th November the patient was attacked by influenza, which was then raging in Edinburgh. On the 8th, dyspnœa made its appearance, and deepened into the characteristic breathing of diabetic coma. The pupils were widely dilated and failed to react to light; the pulse became feeble, and a considerable degree of cyanosis was present. Some attacks of cardiac failure were relieved by appropriate stimuli, and an attempt was made to improve the patient's condition by means of intravenous saline injection, kindly performed by Mr. Cotterill; but in spite of every effort the patient gradually sunk, and died quietly on the afternoon of the 9th.

A post-mortem examination was made by Dr. Barrett, of which the following is a brief account:—

"EXOPHTHALMIC GOITRE, DIABETES MELLITUS, INFLUENZA.—Ward 25. Mary L., æt. 20; died 9th November; post-mortem, 10th November 1891.

"*External appearances.*—Length, 65 in.; circumference, 36 in. Rigor marked, and general lividity moderate on dorsum. Body well nourished. Pupils dilated moderately, and equal. Slight degree of exophthalmos present in right eye. Ocular tension equal and present. Superficial veins of both legs slightly engorged. Slight bruise of right forearm. Two or three punctures as of hypodermic needles. Incision, inner bend of right elbow recent, as if for venesection.

"*Cavities.*—Abdominal cavity contained about 1 oz. of

slightly blood-stained fluid. Left and right pleuræ had recent adhesions by delicate lymph to costal pleura on both sides, chiefly in the middle and lower parts of the lung; easily detached. Thymus gland in the anterior mediastinum $\frac{1}{8}$ in. thick and $2\frac{1}{2}$ –3 in. long. Pericardium anterior, thin and dry; contained $\frac{1}{2}$ oz. serous fluid. No pericarditis.

“*Heart*.—Right heart engorged. Left ventricle contracted. Left auricle contained small post-mortem clot. Right ventricle and auricle dark post-mortem clots. Left ventricle small dark post-mortem clot. Right and left appendices dark post-mortem clots. Post-mortem clots extend along the pulmonary arteries.

“*Orifices*.—Pulmonary competent, C.D. .92 in.; aortic C.D. .8 in.; competent, thin, and penetrated; otherwise healthy. Tricuspid, 1.15 in.; segments healthy. Mitral, 1.06 in.; segments very slightly gelatinous at free margins. Inter-auricular septum perfect. Papillary muscles of right heart very small. Two or three minute patches of fatty degeneration at base of left ventricle. The heart generally looks small and undeveloped. Aorta healthy. Weight, $7\frac{1}{2}$ oz.

“*Lungs*.—Left, 1 lb. Recent small amount of fibrin along outer aspect anteriorly, posteriorly, and over lower lobe. Lower lobe dark, partially collapsed areas of 2 or 3 lobules, and between there are patches of compensatory emphysema. Upper lobe emphysematous. Lower lobe on section generally congested. Some of the interlobular septa œdematous. Marked patches of broncho-pneumonia at the extreme base. Large bronchial tubes congested, and contain thick viscid muco-pus. Right, 1 lb. 3 oz. Upper lobe and anterior margin emphysematous. Delicate recent *fibrous* adhesions between lobes. Delicate recent *fibrinous* lymph posteriorly on lower lobe. Lower lobe, on section and external appearance, in same state as lower lobe on left lung.

“*Liver*.—3 lbs. 3 oz. Gall-bladder semi-distended, dark fluid bile. Lobules indistinct. Pale areas irregular and indistinct, including several lobules, probably fatty degeneration.

“*Spleen*, 6 oz. Pulp congested. Malpighian bodies pale and large. General consistence fairly firm.

"*Kidneys*.—Left, $4\frac{1}{2}$ oz. Capsule strips easily, foetal lobulation marked. Tissue flabby. Vascular lines at cortex distinct; bases of pyramids congested. Parenchyma of cortex distinctly pale, diminished in size and slightly fatty. Right, $4\frac{1}{2}$ oz. Lobulated. Irregular shape, hilus being long, otherwise same as left kidney.

"*Thyroid*.—External. About normal in size. Left lobe and isthmus extend higher than normal. Right lateral lobe also extends higher than normal. Lobulation of right lateral more marked than normal. No accessory thyroids visible.

"*Veins*.—Inferior thyroideal veins engorged. Axillary and pubic hair scanty and softer than normal.

"*Brain*.—Skull-cap very thin. Brain tension above normal. Dura thinner than normal. On reflecting dura the pia over both hemispheres and vertex has lost its glaze. Convolutions flattened and broader than normal, but superficial capillaries not engorged. No adhesions across subdural space.

"Pituitary congested and prominent, and dura thin over it. Basilar artery contains blood semi-fluid. Brain weight, 3 lbs. 1 oz."

Dr. Muir has kindly examined the thyroid gland, and we are indebted to him for the following description of the microscopic characters which it showed:—"Some parts of the gland show a change similar to that fully described in the case of E. A. (see page 215), in others this change has been followed by a marked fibrous overgrowth, so that there are seen numerous small spaces in a dense stroma containing small collections of epithelial cells. In others still, the normal structure has been retained, but there is a tendency to cystic dilatation of some of the acini, with colloid material, and also more fibrous overgrowth. The change in this thyroid appears to be of the same nature, but has occurred irregularly, and some parts have reached a more advanced stage."

Dr. Bruce has kindly given us his valuable assistance in examining the central nervous structures, and the cervical sympathetic ganglia and nerves, with results which are entirely negative.

This case was very interesting on account of the larger size of the right lobe of the thyroid gland, the well-marked change in the hair, and the presence of diabetes mellitus.

CASE 3.—PETER C., æt. 31, accountant, unmarried; was admitted to Ward 22 on 19th July 1892, complaining of swelling of the legs.

His father is alive and in good health. His mother died at the age of 75, of cardiac failure. He has had a brother and a sister, both older than himself. His brother is in excellent health, but his sister died of enteric fever at the age of 27.

The patient states that his health has always been good, except that he had last autumn a rash on the legs, which, from the scars left behind, has clearly been rupia.

About three years ago he fell from a height of about 30 ft. into a harbour. He suffered for nine months afterwards from chronic diarrhœa, and soon afterwards noticed that the eyes were more prominent than they used to be, and that he had a certain amount of palpitation. Breathlessness and swelling of the legs showed themselves shortly afterwards.

The alimentary system shows no abnormal symptoms.

The thyroid gland is enlarged almost uniformly on both sides.

The pulse is 88 per minute, vessel empty, tension high, blood-waves small.

Apex beat in fifth intercostal space. Right border of heart $2\frac{1}{2}$ in., left border 4 in., from mid-sternum. There is a continuous venous hum over the jugular veins, and a systolic murmur over the thyroid gland. There is a soft systolic murmur at the apex, propagated for some distance towards the sternum, and for a longer distance towards the axilla. In the tricuspid area there is a soft blowing murmur continued up the sternum as far as the pulmonary area. There is no change in the second sound.

There is a trace of albumen in the urine, but no tube-casts can be found.

Marks of old rupia are seen on the legs. The skin shows no increased perspiration, but the hair of the scalp, axilla, and pubes is rather more scanty than formerly.

The patient's eyes are equally staring, and show the sclerotic above as well as below the iris. There is no change in the pupil reflex, but there is distinct delay in the descent of the upper eyelid.

He has a distinct hyperæmic *tache*, some exaggeration of the knee jerks and characteristic muscular tremor.

The patient is hypochondriacal in a high degree.

Under the influence of bromide of potassium, digitalis, and iron, the patient's symptoms greatly improved, and he left the hospital in much better health than when he entered it.

This case is a typical instance of Graves' disease, without marked disturbance of the general health. The presence of albuminuria, the scantiness of the hair, and the probable causation by a shock are points of interest.

CASE 4.—JAMES K., æt. 36, weaver, was admitted to Ward 22 on 14th September 1892, complaining of protrusion of the eyeballs, swelling of the neck, and palpitation.

The patient's father is alive and in good health. His mother died, at the age of 48, of aneurism of the transverse portion of the arch of the aorta. He is an only son, but had eight sisters: two are alive and well; two are alive but have been blind since early adult life; two died of smallpox; and two of diseases whose nature is not known to the patient. His wife has only had one child, a son, aged 9 years.

His social conditions have always been good.

Three months before admission he began to feel weak, and to suffer from palpitation. One night he had a severe attack of vomiting, and fell into a state of unconsciousness, during which the doctor who attended him found that his pulse was 160, and his temperature 105°. The weak state of health increased, and the palpitation became more severe after this attack. He states that the swelling of the thyroid gland showed itself first on the right side (in July), and about a month afterwards the left side began to enlarge.

The alimentary system presents no symptoms of disease.

The thyroid gland is greatly enlarged. Both lobes as well as the isthmus are much increased in size, the enlargement

being almost symmetrical. Very marked pulsation, a distinct systolic thrill, and a loud systolic murmur are present.

The spleen reaches the mid-axillary line.

The pulse is 112, full, bounding, and of moderate tension.

Pulsation very visible in the arteries of the neck.

The apex beat is in the fifth intercostal space outside the mammilla. A systolic thrill can be felt over the greater part of the præcordia. Cardiac dulness extends from $2\frac{1}{2}$ in. to the right as far as $5\frac{1}{2}$ in. to the left of the mid-sternum. There is a loud blowing systolic murmur heard over the whole præcordia, but with three points of maximum intensity, *i.e.* in the mitral, tricuspid, and pulmonary areas, of which that in the tricuspid is the loudest.

The respiratory and urinary systems have no symptoms of disease.

The patient perspires profusely, and there is a marked loss of hair over every part of the body where it usually grows.

The genito-urinary functions are perfect.

His eyes are extremely prominent, more particularly the left. The pupils are equal, and react normally to light and accommodation. There is delayed movement of the upper eyelid, but the eyes can be entirely closed. The various reflexes are normal, and no abnormal nervous symptoms are present except insomnia and excitability.

The patient, by means of digitalis and potassium bromide, greatly improved in health generally, and the cardiac symptoms abated to a great extent; but when he was discharged, the ocular and thyroid appearances were much as when he was admitted.

This patient presented a very complete picture of the disease in almost every respect.

CASE 5.—CHRISTINA R., æt 31, married and engaged in household duties, was admitted to Ward 25, on 30th September 1892, complaining of palpitation.

The patient's father died at the age of 48, of pneumonia. Her mother is in good health. She has three brothers and five sisters in excellent health. One brother died in boyhood of whooping-cough, and two sisters died in infancy of diseases

whose nature is unknown to the patient. She has two children, both of whom are very well.

Her social condition has been good, and her previous health left nothing to be desired.

Three years ago she had a great fright, when in the puerperal state, and had afterwards marked palpitation, which has persisted since. In March of the present year the eyes became prominent.

There are no abnormal phenomena connected with the alimentary system.

The thyroid gland is very slightly enlarged, the increase in size being uniform on both sides. There is neither pulsation nor murmur over it.

The pulse is 100, full, of moderate tension and perfect regularity. The apex beat is in the fifth intercostal space, rather outside of the mammillary line. The right cardiac border is 2 in., and the left 4 in. from the mid-sternal line. A soft venous hum is heard in the neck. There is a faint systolic murmur in the mitral area propagated for a short distance in all directions, and a louder systolic murmur in the tricuspid area, conducted upwards to the pulmonary area when it is much less distinct.

The respiratory, urinary, and integumentary systems have no symptoms of any departure from health.

The eyes are prominent, but show no sclerotic above the iris, and closure of the lids occurs perfectly. There is no delayed movement of the upper lid. The pupil reacts perfectly. The nervous system in all respects appears intact, except for slight tremor of the muscles, some excitability and insomnia.

In this instance we have a very good example of the kind of case that may be regarded as on the borderland of Graves' disease. The absence of the exophthalmos is the most striking feature.

CASE 6.—ALEXANDER N., æt. 46, married, and employed as a labourer, was admitted to Ward 22 on 24th October 1892, complaining of palpitation, dyspnœa, and pain in the left side of the chest.

The patient's father was drowned at the age of 40. His

mother died in childbed when 21 years old. He is an only child. He has been twice married. There were two children by his first marriage, a son and a daughter, the former of whom died of some inflammation of the mouth, and the latter of smallpox. He has also two children by the second marriage, a boy and a girl, both of whom are well.

His previous health has been good, except that during a service of fourteen years in the army he had ague when in India, and that he was invalided in consequence of a splinter of a ball injuring the left eye.

The present symptoms began three years ago, and have persisted since that time.

The tongue is raw. The liver is rather larger than the normal, measuring 6 in. in the mammillary line.

The isthmus of the thyroid is enlarged, and the lobes also, but not to such a great extent. There is faint pulsation, and a soft systolic murmur.

The pulse, about 95 per minute, is very irregular, small, and of low but variable tension.

The apex beat is in the fifth space, 4 in. from mid-sternum. The right border of the heart is $2\frac{1}{4}$ in., and the left, $3\frac{3}{4}$ in. from the middle line. There is a soft systolic murmur at the apex, and another soft systolic murmur in the tricuspid area. A harsh murmur, systolic in rhythm, is heard over the manubrium.

There was some pleuritic friction over the lower lobe of the left lung when he was admitted.

The urine varies from 70 to 80 oz., and has a trace of albumen.

The patient perspires profusely, and has scanty hair on the scalp, in the axillæ, and in the pubic region.

The eyes are slightly prominent. There is delayed movement of the eyelids. The right pupil sometimes shows the Argyll Robertson phenomenon, at other times it does not. The left is immobile from the result of the accident. There is a distinct muscular tremor over the whole body. The knee jerks are almost abolished. The patient cannot stand with his feet together and the eyes closed.

The patient is still in hospital, but has greatly improved in health under the use of digitalis and iron.

The most interesting points in this case are the coexistence of Graves' disease with some ataxic symptoms, and the extreme irregularity and variable tension of the pulse.

CASE 7.—ELIZABETH A., æt. 36, married, engaged in household duties, was admitted to Ward 25, on 25th October 1892, complaining of breathlessness and swelling of the feet and abdomen.

Her father, æt. 60, suffers much from chronic rheumatism. Her mother, also 60 years old, is healthy. She had two brothers, one of whom died at the age of 25 of phthisis; the other, æt. 34, is also phthisical. She had also two sisters, one of whom died at 23 of phthisis; the other is married, but is very delicate, and her children are all strumous.

Her previous health was good until the beginning of 1892, except for some degree of anæmia. She has had five pregnancies, three of which were in every way satisfactory, the other two resulted in miscarriage at the seventh month.

Ten months before admission the patient began to feel weak and tired; she observed palpitation and breathlessness on exertion; shortly afterwards she noticed swelling in front of the neck, and undue prominence of the eyeballs. In June the condition became much worse; the abdomen and legs began to swell, the palpitation and dyspnœa increased, and a persistent cough commenced which has remained since. The abdomen was tapped eight times before admission.

There is no suggestion of any occurrence in the past which could account for the onset of the disease.

On examination the patient is found to have a fair appetite but great thirst. The tongue is very raw and red. The liver extends up as far as the third intercostal space. The lower border cannot be made out distinctly, on account of the abdominal condition. Considerable ascites is present.

The thyroid gland is uniformly enlarged in every direction, but the increase is not very great. The size of the spleen cannot be ascertained from the ascites.

The pulse varies between 140 and 160; it is slightly irregular, small, and of low tension. The apex beat is in the fifth interspace, $1\frac{1}{2}$ in. outside the mammillary line. The right

border is $2\frac{1}{2}$ in., and the left border $4\frac{1}{4}$ in. from the mid-sternum. There is very great pulsation in the arteries of the neck. Over the thyroid gland a systolic murmur is heard, and over the jugular veins a continuous hum. In the mitral, tricuspid, and pulmonary areas loud systolic murmurs are heard.

There is great frequency of inspiration, the breathing being 60 per minute; severe dyspnoea, and much cough. Over the entire lungs sibilant and sonorous rhonchi are heard, and over the lower lobes behind there are abundant fine and medium crepitations.

The urine is scanty, varying from 20 to 30 oz. per day; it contains no albumen.

The lower extremities are very oedematous. There is constant moisture on the surface. The hair is scanty in the usual situations.

There has been amenorrhœa for nearly a year.

No sensory symptoms are present. There is a constant rhythmic tremor of the muscles, continuous day and night. The reflexes show no change. The patient has, as already noted, vasomotor and trophic changes connected with the skin. The mental condition is unstable, characterised by emotional tendencies and general excitability. The eyeballs are very prominent, and the sclerotic is shown all round the iris. There is marked delay of descent of the upper eyelid.

The day after admission the patient's temperature rose to $102^{\circ}\cdot8$ Fahr., and the following day it reached $104^{\circ}\cdot2$ Fahr.

The dyspnoea became very severe and the swelling increased in spite of frequent doses of strophanthus, and the constant administration of diffusible stimulants. It was somewhat relieved by the removal, on two occasions, of 45 and 35 oz. of fluid from the abdomen.

On the 30th she was seized with an agonising pain in the præcordia, closely resembling an attack of angina pectoris. It was accompanied by a marked increase of the lividity of the face. The symptoms yielded to diffusible stimulants and hot applications, but the patient was much weakened by the attack, and although the temperature had fallen to the normal, she gradually sank in spite of every remedy, and died on the night of the following day.

The post-mortem examination was performed on the day after death by Dr. Muir.

EXOPHTHALMIC GOITRE, CARDIAC DILATATION. Ward 25. ELIZABETH A., æt. 36; died 1st November 1892; post-mortem, 2nd November 1892.

External appearances.—Height, 68 in.; circumference, 32 in. Body, fairly well nourished. Marked dropsy of lower limbs. Lividity present posteriorly. Rigidity well marked. Thyroid can be felt distinctly enlarged. Almost no hair in axilla or on pubes.

Thorax.—The serous cavities contain no fluid, and there are no adhesions.

Heart.—Heart *in situ* is seen to be greatly enlarged. The right auricle is much distended, and projects 2 in. from right border of sternum. Left ventricle also much enlarged, and its apex somewhat rounded. There are patches of thickening of the epicardium, especially on the left ventricle. Length (greatest) of the heart, 7 in.

The right ventricle contains a small quantity of mixed clot. The left ventricle distended with dark clot. The aortic and pulmonary valves are competent.

Cone diameter—aortic, .9 in.; pulmonary, 1 in.; mitral, 1.3 in.; tricuspid, 1.5 in. Aortic and pulmonary segments are healthy. The mitral segments are a little thickened, and the chordæ tendineæ a little shortened. Tricuspid is normal.

Left ventricle—length, $4\frac{1}{4}$ in.; thickness, $\frac{3}{8}$ to $\frac{1}{4}$ in. It is proportionally wide. Right ventricle slightly dilated and hypertrophied in its thickness, in some places slightly exceeding $\frac{1}{8}$ in. Weight of heart, 15 oz.

Lungs.—Left, 1 lb. 2 oz. Marked congestion and œdema, some parts being almost airless. Also some chronic venous congestion present. Bronchi contain an abundant yellow frothy serum. Right also shows chronic venous congestion and marked œdema. Weight, 1 lb. 6 oz.

Liver.—3 lbs. 10 oz. It is slightly irregular on the surface, and the capsule is irregularly thickened. Hepatic veins are distended with dark-coloured blood. It shows on section a typical nutmeg appearance, well marked and irregularly distributed.

Spleen.—6 oz. Irregular thickening of capsule. Organ firm, but section shows a pinkish-red colour, and the Malpighian bodies are slightly swollen. Condition, chronic venous congestion with some more acute congestion.

Kidneys.—Right, $7\frac{1}{2}$ oz. There are very slight adhesions between the capsule and the surface. Cortex of normal size and regular. Colon is normal. Slight congestion of medulla. There is probably slight interstitial change. Left, 7 oz. In a similar condition, but rather more congested.

Thyroid.—It is considerably enlarged, measuring about 3 in. across, and enlarged upwards and downwards proportionately. The two sides are symmetrical. The surface is fairly smooth, and of a pinkish-red colour, the superficial veins being somewhat distended with blood. On section, the organ fairly firm and of a slight pinkish colour, mottled with yellow; the appearance being very like the section of a salivary gland or the pancreas. It is not very vascular tissue, and there are no cysts. Stroma not very abundant.

Brain.—On removing the dura the brain substance was seen to be of a pale waxy-like colour, and the sulci contained a colourless fluid in considerable quantity. Nothing abnormal was found, and the brain was kept to be injected, etc. Weight, 3 lbs. 3 oz. The posterior part of the orbit was removed, but the tissue presented no abnormal appearance, there being chiefly an increase in the amount of fat.

Dr. Muir has kindly furnished us with the following report on the microscopic character of the thyroid gland:—

“The thyroid showed a marked alteration in structure, which may be described as a glandular hyperplasia with catarrhal changes in some of the acini. The latter are much more numerous and smaller than usual, and they are separated by a delicate connective tissue stroma. The colloid material has almost entirely disappeared, most of the spaces containing none. There is interstitial change, attended with much cellular proliferation spreading inwards from the capsule at places, but this has not advanced to any great extent. The trabeculae contain a considerable number of blood-vessels, some of which are of large size, but the gland is not markedly vascular.”

These appearances are represented in the illustration which accompanies this paper.

Dr. Bruce has been so kind as to examine the various nervous structures, and has pronounced that there is no change in any of them, with the exception of the medulla oblongata. On the floor of the fourth ventricle there is a small hæmorrhage, which penetrates for a short distance into the medullary tissues. Sections of the bulb, carefully examined not only by Dr. Bruce, but also by Dr. Muir and Dr. Miles, show that the hæmorrhage is associated with the formation of the so-called colloid bodies.

This case is in every way a most instructive one, as showing a complete example of all the great features of the disease, with termination in cardiac failure. The occurrence of the severe anginous pain—or cardiac crisis of Germain Sée—is an additional point of interest.

With regard to the pathology of this disease as a whole, we can have no hesitation in referring it to a morbid state of the nervous system. That this nervous state implies marked disturbance of the sympathetic can scarcely be matter of doubt, but whether the change originates in sympathetic structures, apart from the central nervous system or not, is open to question. Our fatal cases must be added to the list of those in which careful investigation failed to discover structural alteration either in the sympathetic ganglia or nerves, or in the cerebro-spinal centres, with the exception of the change in the bulb above described, which is probably accidental. We doubt whether much advantage can accrue from a discussion of the arguments in favour of a paralysis of the vagus, as urged by Germain Sée; a paralysis of the sympathetic, as argued by Eulenburg; or a change in the medulla, as Benedikt holds. We are of opinion that in the meantime the matter must be regarded as *sub judice*, and hope that in some future volume of the *Hospital Reports* we may be able to contribute or chronicle some more definite views on the subject.

DESCRIPTION OF PLATE II.

This Plate shows the microscopic appearances ($\times 220$) of a section of the thyroid gland from Case 7, referred to on p. 215.

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