Thyroid Therapeutics.

In this thesis I propose to describe the mode of administration, action and results of treatment by thyroid extract; based on cases which have come under my own observation in private practice; concluding with an argument on the apparent function of the thyroid gland, and some remarks on our present knowledge of thyroid therapeutics. The subject, as above sketched, may be conveniently considered under the following heads:

I Certain clinical cases treated with thyroid extract.

(a) Two of Ichthyosis.

(b) One of Myxoedema.

(c) Two of Exophthalmic Goitre.

(d) One of General Obesity.

The form in which the remedy was administer-ed in each case was, Messrs Burroughs and Wellcome's 5 grain tabloids; commencing with one, and after three or four days increasing to three daily, according to the effect on the patient.

At the same time I prescribed, at the com-mencement of the treatment, the following mixture:

℞

Tinct. Nucis Vomicae
Tinct. digital. āā ʒij
Syrup. ℥ii
Aquae ad ℥viii ft. mist.

Sig. A tablespoonful to be taken thrice daily.

I have found that patients can stand a considerably greater dose of the extract, after its administration for some time; and in this tolerance apparently lies the best chances of successful treatment; because, with only a continued limited dose, a certain point is reached beyond which no visible improvement seems to result; but, on further pushing it, (provided the patient can bear it) improvement, if it is going to take place at all, is very shortly seen.

In both of the Ichthyotic patients the results of thyroid treatment were temporarily excellent; but the diseased condition of the skin was liable to return on leaving off the remedy.

In the myxoedema case the diseased conditions were very chronic, having existed for twenty years; and fatty changes, difficult to remove, had doubtless occurred in the subcutaneous tissues - especially of the forearms + hands;

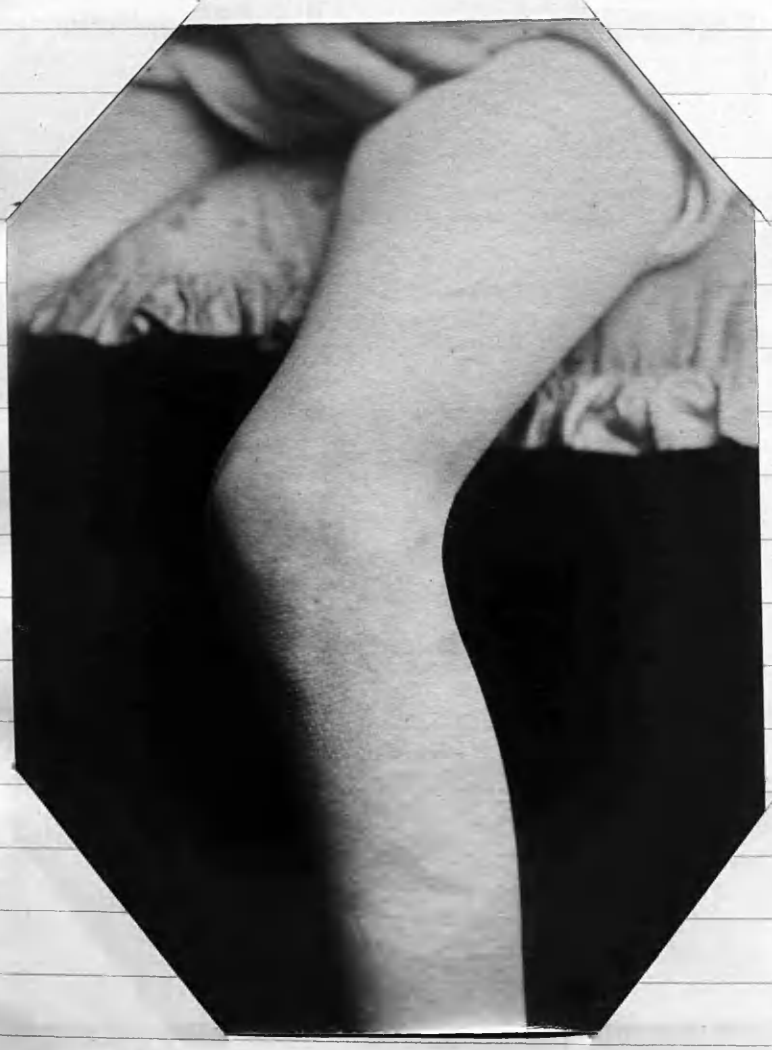
(1) Murray. (Brit. Med. Journ. Feb 8th 1896)

but, where the pathological changes were more recent, as in the face and body, the action of the thyroid extract was very marked.
In the treatment of the other cases (c.d.) the beneficial results were nil; but are nevertheless interesting even on that account.
Whether the continued use of thyroid extract in skin Diseases, would ultimately prove materially injurious to the general health remains to be demonstrated; but, I think, the rapid pulse, which it always induces, must in the end prove hurtful; and, therefore, the too prolonged use of the remedy is probably to be deprecated.
In myxoedema[11], cretinism, and insanity, however, arising from complete or partial absence of the thyroidal function in the economy, its lengthened artificial administration would not likely be so prejudicial.
Its remedial effect in skin diseases appears to arise from increasing the cutaneous vascularity, thereby stimulating the dermal nutrition, and,

The first case of Ichthyosis

G.T. aged 12. Condition of left leg before com-
-ment of treatment. (Photograph taken Sept

The first case of Ichthyosis.



G.T. aged. 12. Result of two months treatment with thyroid extract. (Photograph taken Nov. 14th 1896)

through diaphoresis, getting rid of effete material; certainly, its action on the skin is greatly assisted by concurrently using baths and gentle friction.

(a) The first case of Ichthyosis.

G.T. boy, aged 12 years. Had suffered from scaliness of the skin since birth. There was a hereditary history — grandfather had suffered similarly all his life; while a maternal uncle was very rough skinned, and subject to cutaneous fissures. The areas most affected were the back of the armpits, flanks, hips, thighs and shins; but on the body, the skin was also scaly, bran-like, and easily brushed off; on the shins and outside calf of leg, the fissures in the skin formed diamond-shaped patches, from an inch to an inch and a half in size.

Face muddy, covered with light fine scales — like the peeling in scarlet fever.

His condition was much aggravated in winter, when cold winds prevailed. At times large.

patches of epidermis were shed.
In spite of washing, the parts affected very quickly became dirty again, and could not be properly cleaned till the epidermis was detached. Curiously, he was said to perspire freely — mostly about the head and face.
There were very few nutmeg-grater areas, only those on the back, and posterior parts of the armpits.
On Sept. 12th treatment was commenced; and the following notes, taken from time to time, show in a rough way the progress of the case.

Sept. 12th. Pulse 96; Temperature 98.6°; commenced taking two tablets (=10 grs Ext.) a day.

Sept. 15th. Pulse 104; Temp. normal, but complained of a hot feeling of the skin — To take three tablets a day. (=15 grs Ext.)

Sept. 19th. Pulse 100; Vomited twice on the 17th; Temp. 99.8°. Tight feeling and aching over the eyes.

Sept. 26th Pulse 140; Temp. in axilla and mouth 98°. Felt very well, and no excessive sweating;

but skin very hot, and red looking in places.

Oct. 3rd Pulse 96. Temp. 99·4°. Vomited on Sept 29th; and, on Oct 1st and 2nd had considerable diarrhoea and nausea; (a fortnight after commencement of treatment).

Oct 10th Feeling well. Pulse 122; no sweating; condition of skin slightly improved. To take four tablets a day. (= 20 grs. Ext.)

Oct. 14th Pulse 120; no unpleasant symptoms; To take five tablets a day (= 25 grs. Ext.)

Oct. 17th Pulse 125; much sweating; appetite very good; and condition of the skin improving.

Oct. 24th Pulse 122; Sweating abated.

Oct. 30th Pulse 120, Sweating again great, but skin rapidly improving.

Nov. 7th Pulse 120; less sweating, skin smooth on face, arms and neck, from which the scales can be easily brushed off. Ordered sponging with glycerine and water (1 in 20) to remove scales.

Nov. 14th Pulse 130; Every portion of previously affected skin now smooth, soft and supple; but those

areas originally most affected present a trans-
-parent reddish blue appearance.

Nov. 21st Left off the treatment during the past week;
scurfy condition slightly returned.

Nov. 28th Pulse 126; Taking three tablets (=15 grs. Ex.) a
day for past week; the slight scurfiness
now gone.

Decr. 5th Pulse 120; skin quite clear and healthy;
no unusual sweating. Treatment discontinued.

Decr. 20th Pulse 90; skin normal, except on forearms,
where it is somewhat coarse-looking.

The second case of Ichthyosis.

F.L. girl, aged 4 years. The disease of the skin had
existed since she was nine months old; was worse
in cold, and better in warm weather; exposed areas
most affected; a well nourished and rosy-cheeked
child.

I first saw her on June 1st, when recovering from measles.
The face was covered with small fine scales; back and
upper arms very rough — like an aggravated "goose
skin"

The disease worst on shins and knees, the skin over these surfaces covered with patches of greenish gray detachable scales; between these areas deep cracks ran, nearly at right angles, giving a diamond-shaped appearance.
The measles had greatly aggravated the skin disease; although at times, previously, it had been as bad.
Had been treated with glycerine inunction with slight temporary improvement.
On July 1st the legs were better, with fewer flakes; but the outer surface of the upper arms, back, and thighs, felt nutmeg-grater-like, while the shins had an appearance as of chronic dry eczema. Unfortunately, no photograph was taken of the condition of the skin at this period. Pulse 100.
July 3rd Began treatment; to commence with 2½ grains thyroid extract, increasing to 5 grains on the 4th, 10 grs. on 5th and 15 grs. on 6th July.
July 20th Had continued with 15 grs. daily till July 13th and then ceased. To recommence remedy.
July 31st Pulse 130. Arms now greatly improved; the

July 31st

nutmeg-grater touch less, and the small papules thereof could be rubbed off with the finger; fissures on the legs less. The child irritable, and sweating greatly, but with good strength. Urine passed in excess.

Aug. 8th Taken 5 grs. thrice daily since July 20th; although weather colder, general condition much improved; shins show marked improvement; skin on the back and thighs now soft and supple; the face, however, retaining a dry eczematous condition, similar to that often seen in fair skinned young children; not sweating so much. Glycerine, half an ounce, to be added to a small bath, given twice weekly, and the scurf to be removed as much as possible.

Aug. 25th Very rapid improvement during the last fortnight; skin over shins, back, arms and thighs nearly normal; but on face still dry and eczematous looking.

Sept 1st Skin quite healthy; treatment discontinued;

Case of Myxoedema

Mrs S, aged 34. (Photograph taken before commencement treatment)

patient going to the country.

Jan. 3rd 1897. Patient again under observation; the ichthyotic condition has returned, though not so bad as before treatment.

A younger brother aged 2½ years, brought to me; with a rough and scaly skin, which has just made its appearance for the first time.

(b) Case of Myxoedema.

Mrs S. aged 34 years. Had complained of swelling of the whole body, more or less for twenty years; but aggravated for the last fifteen years; and now rapidly growing worse especially in face and body. Face, neck, and infraclavicular regions swollen, right hand and forearm very tense, and no "wrinkles" across the knuckles; left hand and forearm less affected; abdomen and buttocks much swollen, tense, elastic, and non-pitting on pressure; — the abdomen so enlarged that she is under the impression of pregnancy.

The hands spade-like, and their condition made worse by hard work; stiff, and requiring massage in the morning before they can be used; face anaemic and expressionless; also worse in the morning; skin round the lower jaw baggy, and lately great stiffness and difficulty in moving the jaw on awakening in the morning.
Skin dry and coarse over the most affected areas; eyebrows almost gone; hair dry and prematurely grey, and, for the past six years, coming out freely.
Passes a great quantity of colourless urine, which stiffens her linen.
Had three miscarriages, then a living child, who is now aged eight years, and healthy.
Mental condition lately deteriorating — not so lively as formerly; the least work tires, and she is inclined to be melancolic. Has a sister in a lunatic asylum, and another suffers from melancolia and delusions.
Disease was diagnosed as myxoedema at the

Westminster Hospital 14 years ago, while she was an inmate of that institution, — vapour baths were then suggested for her.

Urine pale. S.G. normal, no sugar or albumen, (repeated tests); but slight opaque ring above contact line of urine and nitric acid; no result with acetic acid.

Great pain at menstrual periods — flow usually normal.

April 18th Pulse 70. Temp. 97·6°. Commenced treatment.

To take one 5 gr. thyroid tablord for two days, then increase to one three times a day.

On the fourth day of treatment she felt very warm, and complained of the heat, although in reality the weather was cool.

On the fifth day severe sweating set in; but temperature which had risen to normal remained so.

Prescribed tonic mixture as before mentioned.

Complained of rheumatic pains

April 27th Face much thinner, more mobile and

in fact not looking the same woman;
felt brighter; her boy slightly less in size
Remedy discontinued owing to an attack
of tonsillitis, probably from "catching cold"
when sweating; urine normal.

May 1st Resumed taking one tabloid thrice daily.

May 6th "Wrinkles" across the knuckles and fingers
of the right hand now much more distinct.
Has "taken in" her clothes two inches at
the waist, and looks quite youthful in figure;
feels much more lively, and can do more
walking and work. Temp. 99°

May 12th Legs much swollen and oedematous,
pitting on pressure; sweating profusely.
Pulse 100, and weak. To take four 5 gr.
tabloids daily for a few days. Roughness
now gone from the skin, which presents
a gelatinous appearance on the backs
of the hands; fingers no longer stiff in
the morning, and easily moved. [illegible]
still thin.

June 1st Took five tabloids daily for three days last week; after which felt very weary and depressed. Condition unaltered.

June 18th Great oedema of legs; has been taking three 5 gr. tabloids, daily; profuse sweating; right hand does not seem to progress, but buttocks much smaller, and waist five inches less. (there has never been any ascites)

Aug. 8th Improved in every way; had discontinued the tabloids for the past fortnight, as the taste sickened her; but states she felt much better when taking them. To take five tabloids (=25 grs) daily till Aug. 13th.

Aug. 19th While taking five tabloids daily was very somnolent, sleeping all night and half the day. Pulse 88 — has taken no tabloids for three days.

Sept. 2nd Having left off the remedy, swelling recommenced, and she felt worse in her general health.

Sept 17th Again feeling better; she left off taking the tabloids for a fortnight, and the

face and hands commenced to swell again, while the feeling of illness returned.

Nov. 23rd Has been taking four five grain tablets daily since the 19th. Passing a great quantity of urine. Face and body much less swollen, but right hand not improving much, in spite of massage &c.

Nov. 28th Pulse 120. Still taking 25 grs of extract daily as above.

Decr. 3rd Pulse 100 much better in every way. "Taken in" her clothing at neck and waist.

Up to the date of writing (Jan. 1897) the improved condition is maintained but not advanced; although she is still taking thyroid tablets. This patient is erratic and wilful, and was with difficulty persuaded to persevere with the remedy.

The first case of Exophthalmic Goitre.

Mrs E. aged 33. Duration of disease 14 years.

15 grs daily for three weeks seemed to retardle the di

(c) The first case of Exophthalmic Goitre.

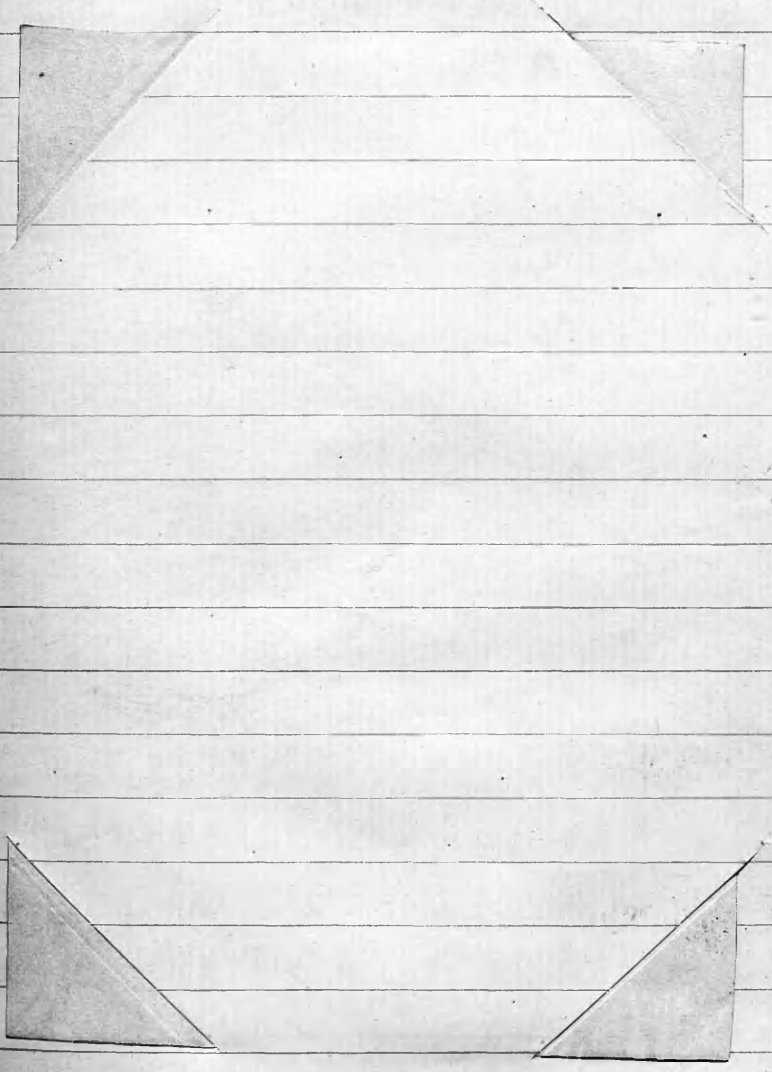
Mrs E. aged 33 years. Disease of 14 years duration; commenced during first pregnancy; the family history bad; her mother had a goitre, but it disappeared; her sister has a goitre, which also came during pregnancy.

The goitre not worse during subsequent pregnancies, or at menstrual periods; but increases at times. Suffers from hysterical fits; on any excitement is troubled with great palpitation; at times her eyes are said to be staring.

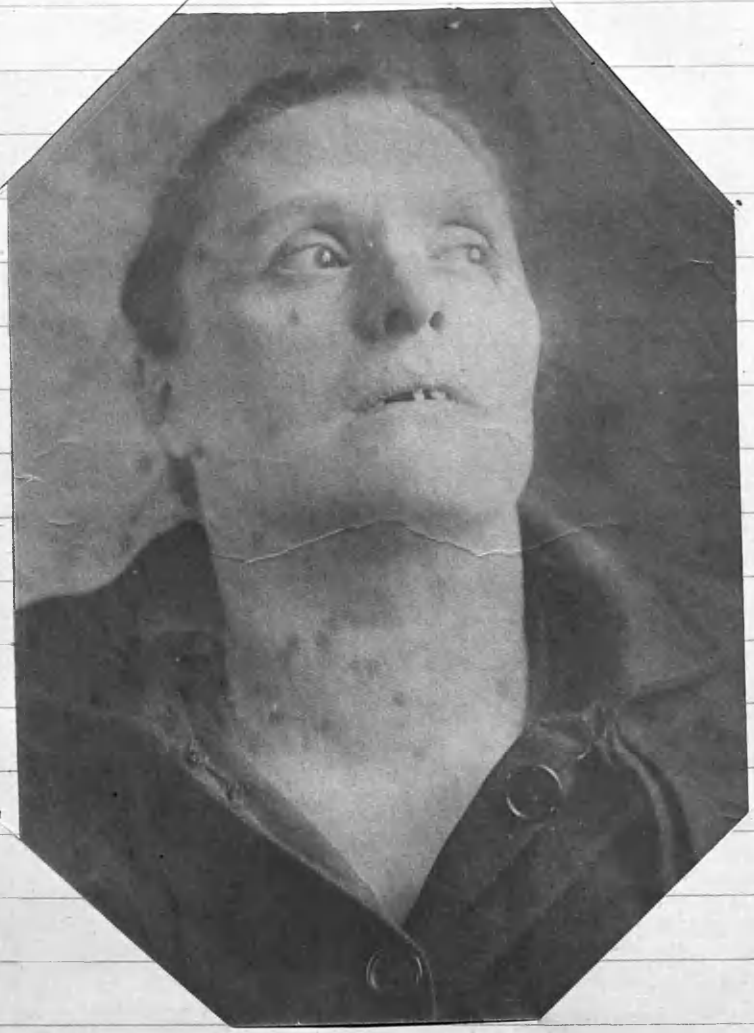
The goitre soft and more elastic on the right side; tense and hard on the left, where it appears to be cystic, but whether as a secondary change or not, the patient cannot say.

Urine very pale, contains no albumen, but a fair quantity of sugar. (repeated tests)

This patient took thyroid extract in doses of 15 grs. daily for three weeks, with no appreciable result to the goitre. The treatment was discontinued at her own request, on account of



The second case Exophthalmic Goitre.



Mrs A. aged 30. Duration of disease 3 (?) mon
15 grs. daily for a month seemed to have little or no

headaches, and the skin feeling hot and un-comfortable; the palpitation was increased; and a greater amount of sugar appeared in the urine; while owing to what she termed "peculiar feelings" (probably faintness) she refused to continue taking the extract.

The second case of Exophthalmic Goitre.

Mrs A. aged 30. Duration of disease stated to be three months, but probably longer; according to patient's account the goitre appeared in one night. It increases on getting up in the morning and at menstrual periods. Pulse 90; suffers greatly from palpitation; getting thinner and paler; face very anaemic; subject to neuralgic headaches in the morning; heart slightly hypertrophied. Father and five brothers and sisters died of phthisis; one son has phthisis and hip-joint disease.

Urine, colour normal; S.G. ditto; no albumen or sugar; slight deposit of mucus.

This patient also took 15 grs. thyroid extract daily

for a month, with practically no result at all; in fact she felt no difference, and complained of nothing particular except the nauseating taste of the tabloids. Her pulse rate increased slightly; but otherwise the extract seemed to have no effect either good or bad

She afterwards improved slightly when put on Bella-Donna and digitalis, — but disappeared from further observation.

(In both of these patients there were few, if any, exophthalmic symptoms.)

(d) Case of General Obesity

Mrs M. aged 62, excessively stout for the last ten years; has been confined to the house, from inability to get about, for two years.

Walks with great difficulty; waist girth 70 inches thigh 34 inches.

July 10th Commenced with one 5 gr. tabloid daily, increasing in three days to one thrice daily.

Aug. 6th As a result, sweated slightly at first;

but not latterly; feels uncomfortably hot, depressed and irritable; face easily flushed, and complains of her eyes feeling hot and smarting. Pulse 88, of low tension; refuses to continue the treatment owing to feeling very hot and depressed.

There was no reduction in her size at the end of the month's treatment; but nervous depression was much greater than in any of the other cases.

Some references

(1) (Brit. Med. Journ. Jan 4th 1896) Smith.
(Brit. Med. Journ. June 24th 1894) Mason.

(2) Hugh Beevor. (Brit. Med. Journ. July 13 1895)

(3) H. Swift. (Australas. Med. Gazette June 20th 1896)

(4) Thibierge. (Sem. Méd. Aug. 17th 1895)
Zum. Busch. (Dermatol. Zeitschrift Sept. 1895)
Wolcom. (British Med. Journ. Feb. 16th 1895)
Auld. (Brit. Med. Journ. July 7 1894)

(5) Swift. (Australas. Med. Gazette June 20th 1896)
Parker. (Brit. Med. Journ. April 18th 1896)
Zum. Busch. (Dermatol. Zeitschrift Sept. 1895)

(6) Smith. (Brit. Med. Journ. June 2nd 1894)
Bramwell. (" " " March 24th 1894)
Mason. (" " " Jan. 26th 1894)

without any necessary sweating.

(II) Increased action of the cutaneous glands; thereby accelerating the excretion of waste products, and keeping the surface in a supple condition.

(III) Regrowth of hair; as shown in myxoedema[1], and some cases of general alopecia[2].

(IV) Increased activity of the epidermal layers; causing desquamation of unhealthy epidermis, and the reproduction of a new covering; as observed in Ichthyosis[3], psoriasis[4], certain cases of chronic eczema[5], and also in some cases of myxoedema and cretinism[5].

(6) The stimulant action on the heart: In doses of 15 grs. daily, it causes a pulse of 120 to 140 beats a minute, which may be, either of high or low tension, varying, in different patients. But it also rapidly exhausts the latent cardiac force; for, if the dose be unduly increased, or if the patient has not got fully accustomed to it, then the heart soon tires, and the pulse, although quickened, is weakened; inducing irritability, depression and faintness.

(C) Excretory action. It is difficult to say whether this is due to direct irritation of the secreting glands; or whether, in regard to the skin & kidney, not rather the result of increased blood pressure from cardiac acceleration.
In toxic doses, the action on the kidney and bowel, is not unlike that of alcohol taken in excess; first, stimulation of the heart and kidney. Secondly, cardiac depression and irritation of the gastro-intestinal tract, with nausea and diarrhoea.

(d) Action in increasing the temperature. This is usually seen at the commencement of the thyroid treatment in skin affections, and seldom afterwards; a result, I consider, due to greatly increased metabolism of the tissues, without at the same time sufficient surface cooling, through diaphoresis; — from the skin not acting in a natural manner; for, when the skin becomes healthier, although the remedy may be pushed, I have not then found appreciable rise in temperature.

(E) Action on the nervous system generally;

In myxoedematous conditions it appears at first to be stimulant, giving rise to a sense of cerebral exaltation; which some observers account for, by the removal of mucinoid substances accum--ulated in the neuroglia of the brain.

But in the non-myxoedematous cases in which I have given it, its action was mainly depressant; the patients complaining of feeling debilitated and low.

In the myxoedema case described, it seemed at one time to act as a soporific; so much so that the patient slept half the day after the previous night's rest; and, in a child, to whom I am at present administering thyroid extract, there is at times great sleepiness.

(1) Baumann and Roos (Zeitschrift für Physiol. Chemie. April 1896)

III Argument on the apparent function of the Thyroid Gland.

That a chemical compound called thyro-iodin is formed in the thyroid gland has been demonstrated by the experiments of Prof. Baumann and Dr. Roos.[1]

These observers succeeded in extracting that active principle, and, by its administration obtained results, exactly similar to those found in giving the thyroid gland itself internally.

Thyro-iodin is remarkable as a compound of great chemical stability, in spite of its being a combination of organic and inorganic radicals. It is not destroyed by exposure to a temperature of 100° Cent. or by the action of strong mineral acids; and is sparingly soluble in pure alcohol, but readily in caustic alkaline solutions.

It contains a considerable amount of nitrogen, together with phosphorus, equal to 3%, and

Iodine to 1%. Its discoverers think that its action "is not due to the minute quantity of iodine present in thyro-iodin; but is produced by the specific action of the peculiar organic compound formed in the thyroid gland under normal conditions."

It appears, therefore, that thyro-iodin is formed, or exists, in the thyroid gland in combination with albuminoid substances—which "Bubnow" alleges are analgous to the globulins.

The question arises, whether the active principle may be secreted, as such, in combination with these substances; or, whether being first secreted by itself, it combines with them afterwards.

The researches of Baumann and Roos do not agree with Notkin's theory, namely, that toxic "thyro-proteid," which he isolated and which he thought was produced by the metabolism of the tissues, was rendered innocuous by.

the secretion of thyro-iodin.
Although this theory might explain the occasional occurrence of tetany after removal of the thyroid gland, and the rapid toxic death of carnivorous animals following its extirpation, the former researches seem to have the greater weight of evidence in their favour.
For, we know that the results of destruction, or enucleation, of the human thyroid gland are those of defective nutrition, and non-elimin-ation; as shown by the arrested development in cretinism, and the accumulation of mucinoid substances in myxoedematous persons; which go to prove that the thyroid secretion has a real nutritive power (possibly by making certain substances, into better chemical form, more easy of assimilation); as well as an eliminative action;—but the latter may indeed be but part of the former, accord-ing as we regard the sequences in function.
Mr Victor Horsley holds, that the function of

(1) E. Roos. (Zeitsch. für Phys. Chemie)

the thyroid gland is the control of the mucinoid substances in the body; which seems to be the case; but, the question arises; In what way would it so act?
I think it is a fair deduction from clinical observation, that thyro-iodin probable acts by splitting up, or transforming the mucinoid substances into less highly organised compounds; and thus favouring their assimilation, or better fitting them for elimination.
Its action in making them fit for nutrition, may be similar to that of the saliva or pancreatic juice; but, the one fact, that thyro-iodin resists boiling, removes it from among the ferments.
Dr Roos[1] finds that "in normal animals the output of nitrogen, sodium chloride, and phosphorus pentoxide is increased by doses of the gland. In abnormal animals, however, deprived of their thyroids, while the excretion of nitrogen and sodium chloride is greater,

... that of phosphorus pentoxide is less by half; and on giving doses of the gland to the latter (abnormal) animals, the excretion of phosphorus pentoxide becomes greatly increased."
This goes to show that thyroid extract increases protein metabolism, especially that in which phosphorus takes a prominent place; and this may explain the connection of thyroid diseases with cerebral affections; with imperfect nutrition of the bones in cretinism; and with the defective brain function found both in that condition and myxoedema — but, in the latter, as already mentioned, disturbed cerebral function may also arise from accumulation of mucinoid material in the central nervous ganglia.
Further, it may be that, the occasional occurrence of tetany after removal of the gland, is due to phosphorus pentoxide not being eliminated, and acting similarly to the toxic materials of uraemia.

"Kocher" found that sodium phosphate greatly relieved many of the symptoms of exophthalmic goitre; in which there is probable increased thyroid activity; and of which the explanation may be that, the natural phosphorus being too rapidly used up or excreted, the sodium phosphate artificially thus supplied the want.

Although no one has succeeded in rousing the gland to greater activity by nervous excitation, still, it is doubtless under direct nervous control; and it is probable, artificial stimulation cannot be sufficiently prolonged or sustained to induce excessive action; for, most of the diseased processes connected with the gland are of a chronic nature, and it's pathological changes usually very slow.

It may be also noted in this connection (nervous) that exophthalmic goitre, which seems accompanied by overaction of the gland, occurs usually in young females whose vaso-motor

systems are easily upset, and in a high state of tension.

From the thyroid gland being ductless, it is quite evident, that any material elaborated therein, must be taken up either by the blood or the lymphatics, in order to become of use in the body at large; and from the fact that mucinoid substance is found in the lymphatic channels between the acini; the presumption is strong, that it must reach the blood through this road.

The fact also, that, after removal or destruction of the thyroid, mucinoid substances are deposited, (or perhaps not destroyed) and collect in the connective tissues, shows that the gland produces an element which has an affinity for such substances, and acts on them.

This element cannot act solely in the acini, for, after destruction of the gland, if thyroid extract be given the mucinoid

(1) (British Med. Journ. Dec. 5th 1896)

substances which collect in the connective tissues are absorbed by the blood and eliminated. It is conceivable, that normally the mucinoid materials are elaborated in the gland and altered by thyro-iodin; but after destruction of the gland, no laboratory being left for them, the blood deposits them as practically effete in the tissues.

Another question is suggested. Would blocking of the thyroid lymphatics, by preventing removal of mucinoid substances cause a goitre, especially, in the form due to the great accumulation of such materials?

In this way certain sporadic cases of goitre, where no outside cause can be assigned, might be accounted for.

Victor Horsley[11] has shown that hypertrophic compensation in the thyroid gland presents very similar microscopic characters to those found in exophthalmic goitre. He also states that colloid material in the acini disappears in such

conditions, leaving merely a watery fluid; but, whether this is due to excessive secretion of the active principle, it is difficult to say. The question further arises; Does thyro-iodin act on mucinoid substances in the gland, or in the tissues themselves? I have already pointed out, that it causes their excretion by acting in the tissues themselves, in myxoedema, and allied pathological conditions; but, it does not follow that normally it acts in this manner. A chemical comparison of the mucinoid material of the thyroid itself with that found in the tissues in myxoedema might elucidate this. Certain observers—"Langendorff" in particular, have noticed two kinds of cells, lining the acini of the gland, having different staining reactions; one of which suggests the elaboration of mucinoid material. From which it is inferred, one set may secrete mucinoid material, and the other the active principle; but, in sections of the thyroid, I have never been

able to detect any difference whatever in these cells — possibly from want of skill.
But if this theory be accepted, then an explanation is forthcoming why goitre is sometimes found in cretinism, and sometimes not; for, if the cells, producing the active principle only, be affected, but not those forming mucinoid material, then a goitre would result. It would also follow from this theory, that in myxoedema the whole gland must be involved; without secretion either of active principle or of mucinoid material.
Following up the theory, it may be further reasoned; that, exophthalmic goitre results from excessive activity of the 'active principle' cells, and consequent upset of the balance between the two kinds of secreting cells; and this, even although, excess of administered active principle in the blood, does not artificially produce exophthalmic goitre. In sections I possess of the thyroid gland

of a four month's ~~old~~ foetus, I find no mucinoid material between the acini, and very little within them; hence, I imagine, that whatever part, if any, the thyroid plays during early foetal life, such material does not there prominently enter.

But the amount of mucinoid material in the gland cannot be taken by itself as a sign of its activity; for, in some pathological conditions where the thyroid is probably functionally inactive, there is positive accumulation of colloid material — though possibly this may be a degenerative condition.

I am inclined to think, the thyroid is not functionally active during foetal life; and, that mucous tissue being a physiological tissue of the foetus does not require to be changed in form; but, that mucous tissue, not being a physiological tissue of the adult, the thyroid is brought into play, to render it

(1) Rogowitch (Arch. de physiol. 1892)
(2) Cobb (Brit. Med. Journ. Nov. 29th 1895)

fit for use in the economy. —
As far as clinical observation goes at present, the thymus in some indefinite way seems related to the thyroid gland; might it therefore be suggested that in early life the thyroidal functions are to a certain extent discharged by the thymus?
It is probable that the thyroid shares in common with the other ductless glands, a certain amount of interchangeability of function; for its extirpation has been followed by hypertrophy of the hypophysis cerebri[1]; and in a recent case reported by Dr Coats[2] of a girl aged 21, who died of Graves' Disease, an hypertrophied thymus was found. In a case at present under my own observation, extirpation of the spleen has been followed by a general enlargement of the lymphatic glands.

Some References

(1) Smith (Brit. Med. Journ. Jan. 4th 1896)
Braunwell (" " " March 24th 1894)
Mason. (" " " June 24th 1894)
Ewald. (Berlin Klin. Woch. Jan. 14th 1895)

(2) Jelloff Smith. (Brit. Med. Journ. June 2 1894)
" " " " " Sept 12th 1896.
Parker. (Brit. Med. Journ Sept. 12th 1896)
George. (" " " Sept 12th 1896
Braunwell (" " " Jan 6th 1894)

(3) Angerer (Munch. Med. Woch. July 10 1894)
Maragliano. (Gaz. degli Ospedali Oct. 20th 1894)
Wharry. (Brit. Med. Journ. June 2nd 1894)

IV An estimate of the value of Thyroid treatment in Different Diseases.

The administration of thyroid extract in cases of myxoedema,[1] sporadic cretinism,[2] and cachexia arising from the destruction or enucleation of the gland,[3] produces results so marked in character, and of such decided value to patients suffering from these diseases, that the remedy must be classed among the foremost discoveries in therapeutics of late years.

Not only does its beneficial effect in such diseases appear from the published cases in which it has been used; but the fact has also been established beyond doubt; that disorder of the thyroidal function is the true origin of such pathological con-ditions.

In looking over the recorded cases of the above diseases, treated with thyroid extract by various persons; we cannot but be struck

(1) Mikulicz. (Berlin. Klin. Woch April 22nd 1895)

Bruns (Deut. Med. Woch. Oct 11th 1894)

Marie (Sem. Méd. Nov. 13th 1895)

Inoai, Vas, & Gara (Deut. Med. Woch July 9 1896)

with the beneficial changes, physical and mental, which it produces; idiotic cretins, dwarfed and deformed, grow in mental capacity, stature and symmetry; myxoedematous adults, unsightly, hairless, and practically disabled, cease to be burdens on society, and again enjoy life. — Such valuable results, entitle thyroid extract to be placed in the premost rank of modern remedial agents; and classes it supreme among the so-called animal extracts.

Thyroid Extract not only acts as a mere stimulant or depressant, (or whatever special class it may be put into in therapeutics) but, also appears to supply an essential element in the economy; similarly as iron salts do in anaemia

The results of its administration in ordinary endemic goitres[1], seem to show that, at all events, in young people, with recent thyroid enlargement, it may be used with good hope of benefit.

Some references

(1) Cunningham. (New York. Med. Record Jan 15th 1895)

(a) Med. (Brit. Med. Journ. July 7th 1894)

McKenzie. (" " " July 21st 1894)

Ferguson. (" " " Oct. 20th 1894)

Signin. (Repertoire Universel d'Obstet. June 25 1895)

(2) Bruce (Journ. Ment. Science No XLI p. 50 1895)

But of its use in exophthalmic goitre[1] the reports of different observers are very contradictory, although the great weight of evidence is clearly unfavourable.
In one of my own cases it certainly aggravated the disease; as also in a case reported by Dr Auld,[a] which is probably less to be wondered at, when thyroidism and the symptoms of exophthalmic goitre are compared.
The probability is, that in those cases where benefit was thought to be derived, there were secondary changes in the gland, which impeded the due performance of its function.
In mental diseases[2] I have no experience of its use, but my friend Dr Harr, of Woodilee Asylum, informs me that he has had good results in cases of stupor, nervous exhaustion, and slight dementia; one case of stupor of 5 years duration cured after

(1) Reinhold (Munch. Med. Woch. July 31st 1894)

four months' treatment); he also states, that in those cases in which there was improvement, the excretion of urea was below normal, and that a dose of extract which rendered it normal did the most good.

The insanity associated with myxoedema and cretinism, as is well known, disappears concurrently with the other pathological conditions.

There is strong presumptive evidence that disease of the thyroid and certain cases of insanity are closely allied; for, in my case of myxoedema, two sisters of the patient are mentally affected; and in a case of exophthalmic goitre, which I am at present treating with thymus extract, the family are extremely neurotic; one sister being in a lunatic asylum.

Hence, it may be that apart from any medicinal value, thyroid extract supplies a want in the system; in those cases where

(1) McKenzie. (Brit. Med. Journ. July 21st 1894)

improvement takes place; and for this reason, I consider very careful inquiries as to family history should always be made.

In general obesity (11) thyroid extract does not seem suitable; for, to produce any benefit, the remedy must be pushed, and to do that in obese patients, who generally have weak hearts, is dangerous. In my case the feeling of cardiac depression was very great, more so than in any of the other diseases treated with the extract.

In chronic skin diseases in which thyroid extract has been given with good effect, it is still open to question whether its use is to be approved, as a routine treatment.

It undoubtedly seems to exert a considerable influence on the vascular supply of the skin, and in this respect appears equal to arsenic; but

(1) Swift. (Australas. Med. Gazette June 20th 1896)
[Zum. Busch. (Dermatol. Zeitschrift Sept. 1895)

the objection may be made that its action on the system, as a whole, is such, as to preclude its use generally in skin affections. Are there, however, any drugs given internally for skin diseases which are entirely free from a similar objection? Arsenic certainly is not one of them.

Like all remedies given internally for skin diseases, it is rendered more efficacious by concurrent outward applications.

Its action in Ichthyosis[11] seems to me so beneficial, that, if any constitutional treatment is attempted, it should be the one. Thyroid extract does not seem, however, to have been much employed for that disease; which is the more remarkable when its peculiar action on the skin is considered. In my two cases the results were very good, and a patient at present under treatment is progressing favourably; so that a further trial of the remedy seems warranted; but,

(1) Robbs. (Brit. Med. Journ. March 30th 1895)

(2) Thibierge. (Sem. Méd. Aug. 17th 1896)
Zum. Busch. (Dermatol. Zeitschrift. Sept. 1895)
Wilson. (Brit. Med. Journ. Febr. 16th 1895)
Squire. (" " " Jan. 6th 1894)
Abrahams. (" " " Jan. 13th 1894)
Pearce. (" " " March 30th 1895)
Sarabini (Vratch hos. 25 & 26 1896)

(3) Menzies. (Brit. Med. Journ. March 24th 1894 & July 7th 1894)
Gordon. (" " " Jan. 29th 1894)

(4) Barclay. (Brit. Med. Journ. Oct. 24th 1896)
Brunwell. (" " " April 14th 1894)
Marson. (" " " March 21st 1896)

patients should be warned that it may not cure but only alleviate.

A case of ichthyosis[1] in a general paralytic patient, is reported, in which the skin condition, under 8 months thyroid treatment, improved; while the paralytic symptoms, were also retarded for the time being.

Some observers have obtained good results from the extract in psoriasis[2]; I have no experience of its use in that disease; but, judging from the reports, it might be tried when other remedies have failed; especially when the disease is very extensive, and there is difficulty in applying local treatment.

Syphilitic eruptions[3] have been benefited; and probably in obstinate cases it would relieve, in conjunction with other suitable remedies.

Its effects in eczema, and lupus[4] are, according to published cases, for the most part favour-able; and judging from its action in ichthyosis,

(1) White. (Univ. Med. Magazr. August 1895)

(2) Stieglitz. (New York Med. Journ. May 4th 1895)

(3) Beevor. (Brit. Med. Journ. July 13th 1895)

(4) McKenzie. (" " " July 20th 1895)

(5) Scatchard. (" " " March 30th 1895)

its administration in dry chronic forms of eczema, should assist in the return to a healthy condition; in lupus its action is difficult to understand; unless it is reactionary, like tuberculin.

Successful cases of its use are reported in Keloid[1], rough brown nails[2], and general alopecia[3]; but in other cases of alopecia[4] and one of Pityriasis rubra[5] its action has been doubtful.

Our present knowledge of the value of the remedy may be broadly summed up as follows: Favourable in myxoedema; sporadic cretinism, and where the thyroid has been extirpated, or destroyed; Doubtful in skin diseases, except ichthyosis.

In many cases of skin disease its use would be precluded; for it is not of much value, even in those deemed suitable, unless the patient can bear it being freely pushed.

I should not give it in exophthalmic goitre; but would certainly try it in the endemic

form.

<u>Finally</u>: the remedy will require much further careful testing, before it's true value, or demerits, can be definitely pro-nounced upon, in those diseases in which it has already been tried; whilst of course, it's use in other pathological conditions remains a therapeutic problem of the future.