

ORGANOTHERAPY.

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The treatment of disease by the administration of animal organs or of extracts prepared from them has existed in some form or other from the most ancient times.

Among the rudest savages the diseases from which they suffered were believed to be punishments inflicted by angry Gods and naturally an endeavour was made to propitiate them by sacrifice. Medicines were originally nothing but charms, in the application of which less attention was paid to the pharmaceutical properties than to those of an occult or sympathetic nature, which ignorance attributed to them. Animals, Plants and Stones being objects of worship were naturally enough employed to furnish remedies for all ailments and palliatives for every misfortune, and Man was not omitted from the *Materia Medica*. All excretions, solid or fluid, were invested with mystic properties and called into requisition on occasions of special import. Both the disease to be treated and the remedy by which the cure was to be effected were regarded as entirely beyond the domain of human knowledge.

In this way the use of parts of the body of Man or of Animals or of the excretions or secretions came into vogue in Medicine.

Among the ancient Greeks and Romans Organotherapy was in common use and that this method had not only a popular but a scientific character is evidenced by the fact that the Greeks /

Greeks, according to Pliny, believed that every healthy organ must have hid in it a special virtue, which could give soundness to the same organ when diseased, what we call today an "Internal Secretion." That their practice was based to some extent on the recognition of this theory is evident from the manner in which they used a particular organ from a healthy animal to cure derangements of the corresponding organ in man.

Dioscorides gives animal extracts a large place in his *Materia Medica*. He recommended as an aphrodisiac the testicles of dogs, which have been carefully fed and fattened, to be eaten raw or crushed or dried and powdered and taken in wine. A distinct anticipation of the discovery of Brown-Sequard. In nervous diseases he recommended the brain of Hares. In Hepatitis and Hepatic Cachexia wolves liver was administered. For disorders of the stomach, fowls gizzard, dried powdered and taken in wine. For Gravel Hares kidneys. For Dropsy drinking ones one urine or that of a Goat. For shortness of breath he recommended foxes lungs. Pliny in his *Natural History* also supplies a rich and varied animal pharmacy. Every animal and every secretion had its uses and the same principle of using the analogous organ of a healthy animal for the treatment of disease of the same organ in Man pervades his work. e.g. Wolves Liver dried and taken in wine for obstruction of the liver. /

liver. For pain ⁱⁿ the Kidneys, take the Kidneys of a Hare raw. For disease of the bladder, the kidneys of the Ass dried and powdered and given in wine. For Epilepsy, the brains of an Ass dried in smoke.

The use of the excrementitial parts became so prevalent in the treatment of disease that Aristophanes, a contemporary of Hippocrates, called the physicians of his time "excrement eaters". Flemming says in his "De Remediis ex corpore humano de sumptis" "Homo est Medicus et ex homine medicina paratur". Man being a Doctor from man medicine is prepared. They did not however limit themselves to the excrementitial products of the human organism but volumes were written on the preparation and uses of such products from the lower animals birds, reptiles, etc. The subject of Scatology in Medicine is a large and interesting study. The writings of Dioscorides, Pliny, Sextus Placitus and Avicenna teem with references and with prescriptions. No tissue or product of the body human or animal escaped their ingenuity as prescribers. Ordure and urine took the first place with many of them. Hippocrates employed milk, cantharides, honey, leeches and blood but does not seem to have employed ordure or urine to any great extent nor did Celsus or Galen.

Schurig devotes a chapter of his work "Chylologia" to a treatise "De Stercoribus Brutorum". The following will enable us to form some idea of the line of medical thought of the ancient practitioners :-

" Beginning with Goose Dung, we find it commended as warm ⁸ drying in /

in its effect, an aperient and endowed with power over the menses, also over the after-birth and urine, and hence of value in jaundice, scurvy and dropsy. It was also employed in many other diseases, principally in fevers, in whooping cough, in cachexy, liver troubles and when applied externally, as a plaster, was of such value in the treatment of sore eyes that the Emperor Maximilian resorted to its use with the greatest advantage. It was also used as a plaster in angina and mammary cancer. The dung of young geese was regarded as the best and it should be gathered, when possible, in the early spring, preferably in the month of March while still green on the Meadows. The dose of the dried powder was from half a dram to a full dram and it was administered in wine or mixed with cinnamon and sugar. It was frequently combined with hen dung or diluted with the urine of she-goats or he-calves. Some practitioners doubted whether it was superior to dove dung for the same diseases".

Michael Etmuller in his "Opera Omnia" published in 1690 supplies the following List:-

Sumentur ex corpore vivente "Hair, Nails, Saliva, Ear Wax, Sweat, Milk, Menses, After-Birth, Urine, Ordure, Semen, Blood, Calculi, Worms, Lice, Caul" and Ex partibus corporis demortui "The whole corpse, flesh, skin, fat, bones, skull, moss growing on a skull, brain, gall and heart". He also gives the following parts of domestic kind as used in medical practice :-

"Horns /

"Horns, bile, liver, spleen, blood, marrow, tallow, fat, hoofs, urine, ordure, testicles, milk, butter, cheese, phallus and bones!"

With this comprehensive list we will leave this part of the subject reflecting, however, on the strange fact that these nauseous preparations should have so long maintained their position, even in civilised countries, as a part of the armamentarium against disease, reaching down to the middle of the eighteenth century. In the "Complete English Physician" London 1730, there are recipes which include dung of geese, dogs, doves, horses, peacocks, hogs and cows. In the "Complete English Dispensatory" London 1730 it is alleged that the salts obtained from the urine of a sound young man newly made were beneficial in rheumatism and arthritis. Cow ^{urine} ~~urine~~ is recommended as a purge. Excrementitious remedies are still to be met with in the folk-medicine of most countries. The writer has known human and cow excrement used as a poultice and knows a lady in affluent circumstances use "cow-wash" for the treatment of Eczema, a circumstance which makes one reflect on the limited resources of medicine.

It is however only when we come to the work of "Pasteur" that the use of organised bodies or of their products in medicine assumes a rational basis. The fundamental discovery of Pasteur was the presence of ferments, which are organised bodies, derived from like parents and transforming by /

by their nutrition and reproduction the medium in which they are formed. Pasteur was struck by the fact that an attack of certain maladies was followed by immunity and he found that this immunity could be induced by the inoculation of the same virus become attenuated by cultivation or taming as it has been called. It was this idea which guided Brown-Sequard, the pioneer of Organotherapy, in the injection of the testicular fluid. In 1869, in his course of lectures in the School of Medicine in Paris he expressed the opinion, that all Glands, with or without excretory ducts, give to the blood, by an Internal Secretion, principles, which are of great importance, if not necessary, to health and the absence of which are felt when these Glands are extirpated or destroyed by disease. He remarked on the effects of castration in childhood or adolescence among men, how it caused profound modifications of the individual both physical and moral. Especially how eunuchs are remarkable by their feebleness and by their deficient physical and intellectual activity. He also noted analagous defects in those who abused coitus or masturbation. He inferred that these facts, among others, clearly showed that the testicles gave to the blood by the reabsorption of certain parts of the sperm principles which give energy to the nervous system and probably also to the muscles. He was struck with the idea that if the sperm could be without danger injected into the veins of man that manifestations of rejuvenescence would /

would result. Guided by this idea he made a great number of experiments on Guinea Pigs and he ultimately at the age of 72 subjected himself to injections from the testicles of young dogs and was able to demonstrate the innocuity of the injections under the skin, the modes of administration and the methods of preparation of the liquid organic extracts. He stated that he experienced a return of vital energy which he had believed to be altogether lost and a rejuvenance of his physical and intellectual forces. He further asserted that he felt ten years younger, that efficient peristalsis, which had been absent for years, ^{ed} return^{ed} and that he regained power over his bladder and sphincter. Brown-Sequard considered that the result obtained was due to an altered metabolism and he formulated the theory that the testes normally secreted into the blood certain substances which produced a marked effect on metabolism especially of the central nervous system. He recommended its employment in the treatment of the mental and physical ~~deteri~~ deterioration incidental to old age. On June first 1889 he presented to the Societe de Biologie of Paris the results obtained by the subcutaneous injection of testicular fluid and in July 20th of the same year he published his results in the Lancet in this Country. In two articles in the British Medical Journal for June 3rd and 10th 1893 he summarises these experiments and facts and gives numerous examples, in his own practice and in that of others,

of /

of the beneficial results of the treatment. He then published, with A.D'Arsonval, researches on the liquid extracts obtained from other Glands and from other parts of the organism and their employment by subcutaneous injection as a therapeutic method. We thus owe to Brown-Sequard a method of treatment which in France bears his name as the "Method Brown-Sequard" and of which Dr.Byrom Bramwell has well said - "It is no exaggeration to say that this treatment constitutes one of the great therapeutic victories of the century." The principle of this treatment may be formulated as follows:-

That the use of definite Glandular Tissues or of their extracts for therapeutic purposes and the incorporation of them in the diseased organism, in which the analogous Glands or their products are wanting or deficient in activity, is based upon a rational physiological and experimental pathological foundation and depends on the theory that the missing products can be restored by the analogously acting products of another healthy organism.

Following on the publication by Brown-Sequard of his researches this method of treatment was extensively tried by Physicians in France and it was reported beneficial in diseases attended with debility, in senile changes, in pulmonary tuberculosis, leprosy, locomotor ataxy, general paralysis and anoemia.

The method of preparation of the various extracts for sub-cutaneous injection (adopted by Brown-Sequard as better than medication by the mouth or rectum) is that of A.D'Arsonval.

The /

The organ is removed with all possible antiseptic precautions and is cut into small pieces of about 1 c.c.. The segments are covered with pure glycerine and allowed to macerate for 24 hours. Before filtering two or three parts of distilled water are added. Sterilization is accomplished by means of Carbonic Acid gas under pressure.

Of all the extracts that of the thyroid gland was the first to give really permanently satisfactory results and is still the one most successfully employed. It was found, in the case of Myxoedema, that the method of administration of the Glands was practically immaterial, glycerine extracts hypodermically, dry extracts in powder, the raw, partially cooked or cooked gland and finally the tabloids of the extract or the official preparations by the mouth, giving equally satisfactory results.

The success attending thyroid -therapy has led to the employment of many other organic extracts in diseases of analogous organs and just as the early physicians allowed no organ to escape them, in their activity in the preparation of remedies, so now, in our own day, extracts have been prepared from almost every organ or tissue in the body. A practically complete list is as follows:-

1. SPERMIN also called Orchidin, Sequardin, Testin, Testiculin.
 This extract has the most historical interest.
 It entered largely into the Pharmacopoeias of
 the ancients and it was on the publication of
 the experiments which Brown-Sequard had performed
 upon /

upon himself that the subject of organotherapy was revived. This extract is also of interest on account of the investigations which have been carried out to discover its proper internal secretion. It contains a large per-centage of proteid which is ~~an~~ almost entirely nucleo-proteid. It also contains a number of extractives among which is spermin. Poehl claims spermin as the active principle. Another body which may be suggested is the nucleo-proteid probably however a considerable number of extractives are present. Extractives of the testis, including spermin, when injected into the circulation in animals, produce a fall of blood pressure, with slight cardiac slowing, followed by a rapid recovery. Another and very important effect of these substances is the vaso-dilatation to which they give rise. They all stimulate involuntary muscles and slightly increase peristalsis. Orchitic extract has been recommended in epilepsy, tabes, phthisis and for diseases of the nervous system. It has however been suggested, at some time or another, for every form of disease, in diabetes, locomotor ataxy and as an emmenagogue, in optic neuritis, Cholera /

cholera and malignant syphilis. There is no doubt that orchitic injections have a most powerful influence on metabolism, shewing itself especially by changes in the urine and leucocytes.

2.OVARIN

ovarian extract according to Brown-Sequard corresponds with orchitis extract but is not so powerful. It has been tried in amenorrhoea, chlorosis and dysmenorrhoea, at the menopause and for the nervous symptoms following the removal of the ovaries. It failed in the treatment of osteomalacia.

3.CEREBRIN

and MYELIN, Paul and Delpech prepared these remedies from the gray matter of the brains of sheep. Paul reported 11 cases of nervous disease neurasthenia, ataxia and tabes in all of which good results followed the subcutaneous injection of the fluid. No ill effects were observed. These might be tried for relief of chorea, epilepsy and melancholia.

4.CARDIN

Hammond introduced an extract of heart muscle of the bullock. It is said to increase the force and fullness of the pulse, the flow of urine and the number of blood corpuscles. Recommended as

a /

a cardiac tonic in nervous debility and in anaemia and chlorosis.

5.MUSCULIN An extract from the Muscles. Said to be of value in diseases of the muscular system not due to lesions of the cord.

6.PANCREATIN in some forms of diabetes a liquid extract of pancreas has been used. In this Country pancreatic feeding is preferred. One case is reported improved gaining eight pounds in weight and the amount of sugar being much decreased (B.M.J.Epitome 1895.) So far the benefits anticipated from this treatment have not been realised.

7.RENIN an extract of the kidneys has been recommended in suppression of urine and in Brights Disease.

8.GASTRIN M.M. Gilbert and Chassevant have prepared a gastric extract from the mucous membrane of the pigs stomach. It is found to be more active than ordinary pepsin. It is possible that the glands of the stomach may have in addition to the gastric juice an internal secretion. This preparation is used in the various forms of Dyspepsia. Dr.Widal has prepared an Extract of inestine and it has been used in constipation and in the different varieties of enteritis..

9.SUPRARENAL GLAND SUBSTANCE

This extract /

This extract has been tried in Addison's Disease, in neurasthenia, in simple goitre, exophthalmic goitre and anaemia. It is used locally as an astringent and haemostatic. A solution in water painted on the inside of the nostrils is said to relieve hay fever. It is used with cocaine in solution hypodermically to obtain bloodless and painless operation. . Two substances adrenalin and epinephrin are claimed to be the active ingredient of the suprarenal capsules.

10. LUNG EXTRACT M. Demons tried this extract in pulmonary hypertrophic osteo-arthropathy.

11. BONE MARROW the marrow of ox bones and sheep's ribs has been used as a remedy for pernicious anaemia, chlorosis, scurvy, purpura, haemophilia, lymphadenoma, rickets and leukaemia.

12. LIVER EXTRACT this has been studied by M. M. Gilbert and Carnot in glycosuria and diabetes mellitus, in cirrhosis and in jaundice. Cases with ascites are said to require paracentesis less frequently under this treatment. It has also been tried in gout and in eczema. The extract is specially indicative^{ed.} for slight insufficiency of the liver. Brown-Sequard suggested that cod liver oil might have some of its beneficial effects owing to the liver /

liver extract. Ox bile and pig bile have been used in catarrhal jaundice and in dyspepsia with constipation.

13. PITUITARY GLAND SUBSTANCE.

An extract has been used in the treatment of acromegaly. It seemed to relieve pain and to cause diuresis. B.M.J. Epitome 1895. It has been used in epilepsy with no good effects.

14. PROSTATE GLAND SUBSTANCE.

A dry extract has been given to patients suffering from enlargement of the prostate gland with doubtful results.

15. SPLEEN EXTRACT .

It has been tried in cases of lymphadenoma. One case reported ~~ameeri~~ ameliorated B.M.J. 1893 page 889. It has been suggested in anaemia, chlorosis, rickets and phthisis. Improvement has followed the use of spleen and its extract in cases of Graves Disease. It is said to hasten recovery in typhoid fever.

16. THYMUS GLAND SUBSTANCE.

The dried extract has been given in states of defective nutrition in childhood, also in exophthalmic goitre, leucocythemia, chlorosis, anaemia, haematemesis and haemophilia.

17. RESIDUUM RUBRUM.

The dried residue of venous and arterial blood.
This /

This has been used in anoemia, osteo-arthritis and scurvy.

18. EXTRACT OF UTERUS.

This was tried without result in puerperal mania.

19. GLANDULEN. An extract prepared from the bronchial glands of sheep has been tried without effect in Phthisis.

20. THYROID GLAND.

This Gland and preparations made from it have been employed in cases of arrested growth, to backward children, in cretinism, in myxoedema, in skin diseases (psoriasis lupus eczema and keloid) in simple goitre and as a galactagogue. Also in acromagaly, obesity, syphilis, tetany and torticollis. It has been used to arrest haemorrhage in uterine disorders and in cases of ununited fracture. Success has been most notable in cases of myxoedema cretinism and goitre. In-sane persons have also improved under its use. In 1896 Dr. Beatson of Glasgow suggested the treatment of inoperable cases of carcinoma of the mamma by removal of the tubes and ovaries combined with the administration of thyroid extract. It seems probable that a percentage of these cases are benefited by the combined treatment /

treatment. Two preparations of the thyroid gland are now official the liquor thyroidei and the thyroideum siccum. In 1895 Baumann under the title of thyroïdin described a substance, now known as iodothyryn, which may be definitely regarded as the only active substance produced by the Gland.

21. SERUM-THERAPY.

This is a special subject by itself about which much that is good could be written.

Dr. M. Bra in his Book "La Therapeutique des Tissues" gives a most exhaustive exposition of the work done on the subject of organotherapy. Going most carefully into the physiology of each gland, the preparation of the liquid extract, the strength of the solutions, the preservation of the liquid, the choice of syringe, the points of election for the punctures, the sterilization of the skin, the dose, the frequency of the injection, and gives numerous illustrative cases and a very complete bibliography. It must be admitted nevertheless that recent medical experience has not confirmed the assertions of the value of these remedies, except in the case of the thyroid gland. A leading article in the "Brit. Med. Journal June 17th 1893 while admitting the good results in some cases utters a warning note on many of the so called cures and quotes Massa-longo /

-longo to the effect that it is "a new ^{phase} face of suggestive therapeutics". One must not however forget that converts are always enthusiasts and that while it may be wise to view these results in a spirit of scientific doubt, it is unwise to class them with what was then the recent developments of Matteism.

The history of myxoedema and the evolution of the method of treating it by thyroid preparations is quite as interesting as the evolution of the treatment by testicular fluid. In 1871 Hilton Fagge, in a paper read to the Medico Chirurgical Society of London - transactions Vol.33 - on Sporadic Cretinism, ventured to predict some of the leading features which the disease would be likely to present in the adult. He says "we must conclude that the most marked features in such a case would be coarseness and thickness of the soft parts of the face, especially the lips and perhaps of the subcutaneous tissue of the hands and feet, besides the presence of supra-clavicular fatty tumours and possibly a wasting of the thyroid body". Myxoedema or Mucin Oedema was the name given by Dr.W.M.Ord to a peculiar group of symptoms first described in 1873 by Sir William Gull as a "cretinoid state" supervening in adult life in women. Dr.Ord also called attention to the atrophic condition of the thyroid gland. The next step in the history was the discovery, in 1883, by Dr.Reverdin of Geneva and Professor Kocher /

Kocher of Berne that excision of the thyroid gland was followed by "cachexia strumipriva", a train of symptoms similar to those of myxoedema. Professor Kocher found that those patients in whom the extirpation had been incomplete remained well while all in whom the Gland had been wholly removed presented after a time these remarkable symptoms. In the following year Schiff, Wagner and Sanquirico successfully removed the thyroid in dogs and found that the operation was followed by cerebral disturbance, tremors and convulsions, ending in death by coma. Victor Horsley, in 1885, confirmed this by removing the thyroids in monkeys. He suggested the transplantation of the thyroid into the peritoneal cavity. This was successfully done by Lannelongue who transplanted a sheep's thyroid into the subcutaneous tissues of the left breast of a myxoedematous cretin. So long as the transplanted thyroid maintained its vitality the myxoedematous state was arrested. The obvious difficulties and dangers of this operation were fortunately rendered unnecessary by the employment of hypodermic injections of a glycerine extract of the gland. The idea of the hypodermic injection had occurred, in 1890, to Dr. Hurry Fenwick (B.M.J. Oct. 10. 1891) and Brown-Sequard and D'Arsonval, having observed its usefulness in animals after thyroidectomy, suggested this method in July, 1891 (Archives de Physiologie). Dr. Murray first carried out the treatment in April 13th 1891 and it is undoubtedly owing to his paper read at the annual meeting of the British Medical Association at Bournemouth in July /

July, 1891 and published in the British Medical Journal in October 10th, 1891 that this method of treatment became known to the profession. The administration of the Gland by the mouth was suggested by Dr. Hector Mackenzie (B.M.J. Oct. 29th 1892) and this is the method now almost universally adopted, in one form or another.

Following upon this happy discovery numerous cases with the most excellent results were reported. The knowledge of the disease and of its successful treatment became general and a great hope was born that remedies for other diseases, kindred in their etiology, in the deficient or in the excessive functioning of other glands, might be found. On the one hand there are a number of diseases in which the outstanding feature consists in the atrophy or non production of an individual tissue element. On the other hand there is another class of cases in which precisely the opposite condition obtains and in which there is an over production of some one tissue element. In these cases we are justified in believing that by discovering the principle in the blood which controls the growth and development and the maintenance of these tissues in a healthy condition we may be able to replace it from another healthy animal.

Reports on three cases of myxoedema and a case of Addison's Disease occurring in Dr. Roxburgh's practice and treated by Organic Extracts

CASE 1. Mrs L. aet. 38, married, housewife. Came under observation on 21st Oct. 1894, complaining of great weakness and depression of spirits, with swelling of the body, headache and drowsiness.

FAMILY HISTORY. Mrs L. is strongly of opinion that her mother suffered from the same condition. She remembers that her mother got very stout and was always complaining of being tired. Apart from this nothing relative is known.

PREVIOUS HISTORY. Though never robust patient enjoyed fair health until the last pregnancy, two years ago, from about which time she dates the onset of this illness. During the pregnancy she had considerable general oedema, pitting on pressure, and albumen was present in the urine. She lost more blood at this labour than on any previous occasion. The oedema and albuminuria soon disappeared after her recovery which was fairly rapid. She has had four children all living and healthy. She has had no miscarriages. She had been greatly troubled with toothache for years before this illness had definitely set in and had over a dozen decayed teeth extracted. She had never weighed more than 9 stone.

MODE OF ONSET. The swelling was first noticed in the abdomen /

abdomen and gradually extended over the whole body. With the increase in size she has got persistently weaker and now with the greatest effort performs the lightest household duties. She is always tired and drowsy and no matter how much she slept was never refreshed. She felt the cold acutely and had a repugnance to go into a room without a fire. The urine had been scanty and high coloured for a long period and at one time recently it had been suggested by another Physician that she suffered from Bright's Disease (the late Dr. Mahomed held that these cases were examples of Bright's Disease)

PRESENT CONDITION. The body is swollen all over, The swelling is most marked in the abdomen. The face also is swollen and broad, though not coarse looking. The hands and legs are not so much swollen. There are distinct fatty swellings above and below the clavicle. The swelling is firm and solid and does not pit on pressure nor does it vary from change of position. The complexion is ivory. There is a diffuse rosy blush over the cheeks. The eyelids are swollen and there is the characteristic raising of the eyebrows. There is no capillary injection in the cheeks. The lips are thick and red. The tongue is swollen and slightly coated and marked round the edge with the remaining teeth. The gums are red and tender where the teeth still persist. Where the teeth have been extracted the gum is sound. There is a brassy /

brassy mettalic taste in the mouth. The nose is not red or broadened. The skin is dry but not rough or cracked. It is not discoloured. There are no moles or warts. The hair of the head is dry brittle and falling out. The nails are not brittle nor cracking. The thyroid gland cannot be felt. Appetite is bad. She also feels chilly, is never warm unless in bed. She has constant frontal headache and is very drowsy. She sleeps all night and has to have two hours sleep in the afternoon. Her eyesight has become defective and she has taken to using spectacles. Perspiration is entirely absent. Saliva is constantly excessive, the pillow being wet in the morning where she lay. Hearing and smell are good. Taste is not good. The catamenia have been regular with the exception of the last period which lasted four weeks. Speech is not slow nor are the tones of the speaking voice altered but she cannot now sing. There is great muscular weakness. The slightest task is an effort. She cannot walk without fatigue and seldom goes out. Memory is very bad especially for immediate purposes. For instance, she will go to the cupboard for something, say a spoon, and will require to ask what she rose for. On another accoasion on taking goods from an errand boy she took to him a packet of flour instead of the empty basket. She is constantly doing such things and cannot depend on herself to go shopping. She has no delusions. Pulse 52. Very soft and compressible /

compressible but regular. Temperature 97°F. There is no evidence of organic disease of the heart or lungs. She now weighs 11 stone 7 lbs

Urine	quantity	15½ oz in 24 hours
	S.G.	1033
	albumen	absent
	sugar	absent
	urates	excessive.

TREATMENT AND COURSE OF THE CASE.

On October 21st, 1894 patient was put to bed and one 5 gr. tabloid of thyroid extract (B.W. & Co.) was administered at bedtime. There was great reaction from this doze. Profuse sweating, flushing of the face, breathlessness, palpitation and shooting pains throughout the body. She passed a sleepless night and felt very weak in the morning. Oct. 22 and 23. One tabloid administered each night. Reaction not so severe.

Oct. 24th. Ordered one tabloid night and morning.

Oct. 26th. Tabloids stopped owing to excessive menstrual flow.

Nov. 1st. 14 grains of the raw gland administered minced in hot beef tea. Still the same reaction. Evening temperature 99°F. Pulse 70.

Nov. 4th. 20 grains of the raw gland given.

Nov. 8th. 40 grains of the raw gland administered. Extreme distress during the night coming on soon after the dose was administered.

Nov. 12th. 40 grains of the raw gland given. Again experienced extreme distress during the night. Felt so ill that /

that Dr. Roxburgh was summoned.

Nov. 16th. Since last note this patient has shewn undoubted symptoms of improvement but still complains of weakness.

Urine	quantity	38 oz. in 24 hours
	S.G.	1020
	albumen	absent
	sugar	absent

This increase in the amount of the urine has been gradual and persistent and is a striking example of the diuretic action of the gland.

It was now evident that a small dose was the right procedure in this case. She continued to take one 5 gr. tabloid twice weekly till my next note on June 5th 1895 which is as follows:- This patient may now be said to be cured of the symptoms of myxoedema. She has lost 7 lbs in weight. The urine is increased in amount. The temperature and pulse are improved. Her memory is better and her eyesight is so much better that she has dispensed with the use of the spectacles. She is now able to do household work and to walk a considerable distance without undue fatigue. Menstruation is normal

Urine	quantity	28 oz. in 24 hours
	albumen	absent
	sugar	absent
	urea	320 32 grs.

This is the only occasion on which I estimated the urea. The quantity may be considered satisfactory.

CASE (2) Mrs L. aet.62 married,housewife. Came under observation on 16th October,1896. Her previous history is good. She has had eight children,two to her first husband,died in infancy,the others are alive and healthy. She has had no miscarriages.

This case presented all the typical signs and symptoms of myxoedema in an advanced stage. The body is very much swollen especially the abdomen.Face,arms,hands.legs and feet. The arms and legs are ponderous. There are distinct fatty swellings above and below the clavicles. The thyroid cannot be felt. The swelling is firm and solid and does not pit on pressure. The eyelids are swollen. The water~~y~~ eyes being with difficulty seen peering through. The eyebrows are almost gone. The sparse^s brittle hair is present only on the sides of the head and the top of the head is covered with a brown scaly eruption. The nose cheeks and lips are purple and capillary injection is very marked. The skin is everywhere very dry coarse and brown. The skin of the legs is cracked like old leather. The nails are dry and cracked. The voice is very deep but not unmusical. Speech is very slow measured and deliberate. Movements are all slow and apparently methodical. She always feels chilly and sits constantly by the fire,if not in bed. . The diminished activity of the sensory side of the nervous system is very marked. One would be on the point of repeating a question /

question, supposing it to be unheard, when the answer would come, usually correct, and often with a spice of drollery in it. She suffered from a delusion which had become a fixed idea viz:- jealousy of her husband who was 75 years of age and suffering from paralysis agitans. This delusion never left her and she constantly suspected the presence of ~~sta~~ strange women in the house, on which occasions her language became more forcible than polite. Pulse. Almost imperceptible and cannot be counted with accuracy (perhaps to a certain extent due to the thickening of the subcutaneous tissues). Heart sounds with great difficulty heard. Temperature 96°F. Urine copious and free from albumen.

TREATMENT. and course of the case.

Altho' every effort was made to get this patient to take the thyroid gland, and assurance of improvement given, she never made a steady attempt to pursue the treatment.

It was evident that when comfortably esconced in bed or in her arm chair by the fire that she did not feel ill. She drifted on till her death which took place quietly from asthenia on the 10th March, 1901.

CASE (3) Mrs K.aet.55.Widow.Came under observation on 4th September 1898 complaining of swelling of the body and of the dry, dirty looking condition of the skin of the palms of her hands. She does not complain of weakness. With the exception of rheumatic fever, at the age of 28, patient has enjoyed very good health. She has had five children, all living and healthy. She has had no miscarriages.

PRESENT CONDITION. She feels fairly well and does not complain of weakness or cold. The whole body is swollen, especially the face, abdomen, and hands. The nose is broad and swollen and the lips thick. There are very well marked fatty tumours above and below the clavicles. The hands are big and coarse and can hardly be closed so stiff are they. They are becoming spade-like, the fingers marking one another at the sides. The swelling is firm and solid and does not pit on pressure. While she formerly had no colour the cheeks are now rosy. The skin of the body generally is very dry but not discoloured. The skin of both palms is very dry cracked and dirty looking though they have been well scrubbed. There is a well marked patch of psoriasis in front of each knee. This has lately become worse and bleeds if roughly washed. She suffers from rheumatic pains especially at the elbows. All her teeth with the exception of two which were drawn have fallen out. The gums are not tender. Her memory is bad. She forgets often what she is talking about.

She /

She has no delusions.

PULSE. 72 regular strong. There is a well marked V.S. murmur at the apex. The urine is copious and free from albumen.

TREATMENT. and course of the case.

She was advised to take one 5 gr. tabloid of thyroid extract each night at bedtime. The result was very striking. After the first tabloid the skin of the hands moistened and after six tabloids had been taken it was soft and supple and clean looking. She became reduced in bulk especially about the neck and bust.

This patient requires to take two tabloids weekly to keep herself well. There is much sweating after each doze and slight distress. She makes a point of taking one tabloid on Saturday night so that she may enjoy the Sunday's rest.

On comparing and contrasting these three cases many interesting points are elucidated and notwithstanding individual variations the symptoms present a degree of uniformity which is specific of the disease. In all the body is very much swollen and the features altered so that their friends fail, on many occasions to recognise them. In all the swelling is firm and does not pit on pressure. All have fatty swellings above and below the clavicles. In all the skin is dry, they never perspire. They all complain of loss of memory. They present nevertheless many points of contrast

	CASE (1)	CASE (2)	CASE (3)
FEATURES	Face not much swollen	Face very much swollen and coarse looking	Face very much swollen
HANDS	not enlarged	much enlarged	very much enlarged and spade-like
SKIN	dry but not rough	very dry, brown and cracked	dry and rough
CHILLINESS	feels cold acutely	not so acutely	not at all
VOICE	speaking voice not altered	very much altered	not altered
URINE	very notably diminished	not diminished	not diminished
DELUSIONS	None	present	None
WEAKNESS	great depression and profound weakness	dull and apathetic not so weak	no complaint of weakness
PULSE	very slow and feeble	practically imperceptible	not altered
ALIVATION	profuse	not present	not present

The results of treatment in Cases (1) and (3) are eminently satisfactory. Case (1) was rapidly going downhill and would inevitably have soon become bedridden and a fatal issue have resulted. Case (3) was never so ill. The rapidity of action however of the treatment on the skin and on the tendency to heap /

heap up fat was remarkable. The dose is an important consideration. I have no doubt that within just limits the more gland the cases get the better. Unfortunately ~~however~~ however its administration has a most unsettling effect. There is no doubt that a small dose, at intervals of 24 hours, is the safest method to begin with, the patient lying down for a time after the dose or better still taking it in bed. Hector Mackenzie in introducing the Raw Gland (B.M.J. Octr, 29th, 1892) does not say how much by weight he administered. He gave 2 sheep's thyroids at one dose. After weighing many sheep's glands I have found that the lobes vary in weight from 16/ grs. up to 60 grs. It is thus plain that in using the raw gland it will not do to prescribe one lobe or half a lobe but a definite quantity by weight beginning with 10 grs. and certainly not more than 20 grs. The great desideratum now in this treatment is, if possible, to eliminate the principle in the gland secretion which tends so much to increase for a time the weakness complained of and which I am sure restrains the cases, when not under direct supervision, from taking the amount necessary to a complete disappearance of their unhappy symptoms. Cresswell Baber (B.M.J. Jan. 7th, 1893) suggests that the aching and depression ^{are} due to the circulation in the blood of the products of the solid Oedema. I have however frequently given Thyroid Gland Extract in cases of Obesity, Psoriasis and Simple Goitre and in all cases depression resulted. Crary (Amer. Journal of Med. Science vol. 107 page 523) states that the various /

various bad effects of thyroid seem to be caused by too large dosage and that during what Murray has called the "first stage" of treatment while the patient is getting rid of the myxoedematous symptoms, great care should be observed, unusual exertion or mental excitement avoided, and that rest in bed is advisable. On the introduction of the tabloids rash dosage also prevailed three, six and nine 5 gr. tabloids being commonly administered daily. It is now recognized that it is only safe to begin with $1\frac{1}{2}$ or $2\frac{1}{2}$ gr. once daily and to increase the amount with caution.

CASE (4) J.H. aet. 27 male. Farmer single. Came under observation on 16th February, 1898 complaining of loss of strength failure of appetite and sickness

FAMILY HISTORY. Father died at 60 of pneumonia. Mother alive aged 74 and in good health. Four ~~en~~ sisters living all healthy. Patient has no knowledge of phthisis among near relatives.

PREVIOUS HISTORY. Patient has never been robust but up till the onset of the present illness has not had any serious trouble. There are no enlarged glands nor cicatrices.

MODE OF ONSET. About a year ago he began to feel weak and occasionally had sick turns and vomited. He had frequently pain in the stomach. The discoloration of the skin became marked six months ago and was first noticed on the face and neck and backs of hands.

PRESENT CONDITION. The patient is fairly well nourished and does not look ill. The temperature is normal. The pulse is very much accelerated, 110 per minute, small, and weak, but regular. Cardiac impulse almost imperceptible and the sounds distant. There is no evidence of valvular disease and no enlargement of the cardiac area. The lungs are normal. He complains of faintness on exertion palpitation and shortness of breath. The appetite is very poor. He frequently feels sick and often vomits. The tongue is moist /

moist and slightly furred. The bowels are constipated. There is no enlargement of the spleen. The face neck and backs of the hands are a deep yellowish brown. The skin of the body generally is dark. The areolae of both nipples are almost black. The genital organs and the perineum are very dark. The skin is smooth and moist. The lips gums, tongue, and buccal mucous membrane are all pigmented. No nervous symptoms are complained of but patient is very quiet and sedate. The urine presents no abnormality.

TREATMENT and Course of the case.

Patient was advised to lead a very easy life and to avoid any sudden exertion. He was given Easton's Syrup and one 5 gr. Tabloid of Supra-renal Extract to be taken, at first once daily, at bedtime, ultimately taking 3 tabloids daily. His strength however gradually failed and the attack^s of sickness and vomiting became more frequent. After six days obstinate vomiting he died suddenly, though not unexpectedly, on the 29th Novr. 1898 having previously risen to stool.

So far no authentic of undoubted cure of Addison's Disease has yet been recorded. On the theory of an internal secretion defect improvement should be anticipated /

-pated. It would appear therefore that the active substance has not been properly administered or that the requisite material is not present in the supra-renal bodies as at present prepared for administration or that the lack of a certain internal secretion is not the sole or predominant factor in Addisons Disease

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