Addison's Disease.

Thesis by A. J. Biesenmann

with notes on three cases under observation.

Addison's Disease - with notes on three cases under observation.

Definition. A morbid state dependent upon loss of function of the suprarenal glands due to various lesions, associated with increase of the normal pigmentation of the skin, & sometimes mucous membranes, with great Asthenia, tendency to Syncope & often severe gastric & intestinal symptoms ending fatally.

It was in 1849 that Addison discovered the connection between disease of the suprarenal capsules & the above train of symptoms whilst enquiring into the causes of pernicious anaemia.

He described 11 cases attributing the condition to lesion of the suprarenals.

Greenhow & Wilks held that the various symptoms known as Addison's Disease resulted from involvement of the Semilunar ganglia & sympathetic Plexus by disease affecting the neighbouring Suprarenal bodies.

This view has been abandoned.

The theory of internal glandular secretion established on an experimental basis by Abelous & Langlois in France & Schäfer & Oliver in England, led to a return to Addison's original view that the symptoms were due to interruption of suprarenal function.

Abelous & Langlois found that after destruction of the

suprarenals in animals injections of suprarenal extract kept them in good health otherwise they died in from 4 to 6 months from symptoms analogous to Addison's. Oliver & Schäfer obtained a substance from the suprarenal glands possessed of very powerful physiological properties. This extract which they obtained from the ~~cortex~~ medulla of the adrenals was found to be a very active stimulant raising the blood pressure.
This extract is absent in diseased glands. (Allbutt)
Abel described it as an alkaloid.
Since muscular tissue is kept in tone by this extract & stimulated by it - the extreme muscular & cardiac weakness met with in Addison's Disease is probably due to its absence.

Etiology.

The disease is rare. More common in the male sex.
Average age is 31. Rare examples have been recorded in infants (ref. Maladie d'Addison chez un enfant de 18 mois Bull. Soc de Paris 1905 in original)
a few cases have been recorded late in life (Allbutt).
A history of tubercle does not predispose to the disease nor is it hereditary.
It is of interest to note that the adrenals glands in the early years of life are remarkably immune to secondary infection of tuberculosis.

Traumatism & local injuries to the back have seemed to be the cause of the disease probably by rendering the organs vulnerable to the tubercle bacilli.
Or traumatism may have given rise to haemorrhage into the suprarenal substance either at birth or later
(H. Spencer Trans of Obstetrical Society of London 1892 p. 276)

Morbid Anatomy.

2. The commonest lesion is a fibrocaseous degeneration of the glands – tuberculous in character.
The tubercles form in the medulla with caseation & softening. In the process a large formation of fibrous tissue occurs due to the irritation of the tubercle & this may contain soft caseous matter.

2. Simple Atrophy. The organs cannot be found after death.
3. Chronic interstitial inflammation leading to Atrophy
4. Malignant disease invading the capsules.
5. Blood extravasates into the suprarenals.
6. No lesion of the suprarenals but a lesion of the Semilunar Ganglia.

The lesion is usually present on both sides & often in different stages.

The tuberculous change in the Suprarenals may ~~be~~ occur without any signs of Addison's Disease, or cases may occur where the tuberculous deposit in the Suprarenals may be the only seat of tubercle in the body.
Examples of simple Atrophy in association with Addison's Disease strongly support the view that the symptoms of the disease are due to loss of function of the suprarenals. (Rolleston. Brit. Med. Jour 1895 Vol 1.)

The absence of symptoms of Addison's Disease when post mortem the suprarenals are apparently destroyed by Carcinoma is probably due to death occurring before the symptoms had time to develop.

Lesions of the Suprarenal glands are present in 88% of cases of Addison's Disease.

In cases where there is no lesion of the Suprarenals but a lesion of the Semilunar Ganglia.
The Semilunar Ganglia & the Sympathetic have been attacked by the inflammatory process.
1st a stage of irritation is shown by redness & swelling.
2nd a stage of Atrophy & fatty degeneration.
But in many cases of Addison's Disease the nervous

structures have been healthy, thus the inconstancy of changes in the ganglia & sympathetic excludes any causal factor in the production of the disease

Other Anatomical Changes.

The Thymus gland is sometimes persistent & enlarged It is interesting to note this, as enlargement occurs in exophthalmic goitre & sometimes in cretinism and acromegaly - diseases of other ductless glands.

Pigmentation of the peritoneum has been met with & of the small intestine. (Allchin "Pigmented small intestine". Tr. Path Soc Lond. 1890-91 xlii p. 302).

Pathology.

Some anaemia generally accompanies Addison's Disease.

In four cases (Tschirkoff) the red cells before treatment numbered from 2,733,000 to 3,280,000.

Neumann reported a still more severe case 1,120,000.

Morphological changes are not marked but microcytes are abundant.

Leucocytes are commonly diminished but sometimes increased & subject to secondary variations of Anaemia.

Eosinophile cells are sometimes present.

Another class of cases shows an excess of red cells exceeding 5,000,000 / Case of Addison's Disease with great increase of red cells. Deutsche. Med. Wchnschr. Leip. 1894

H. Neumann. This case ended in recovery).
Ischirkoff found that the haemoglobin might in the early stages exceed the normal.
The pigmentary deposit has been thought to be due to minute thrombi & haemorhages in the superficial vessels - Riehl & Afanassiew - the latter observed the disintegration of red cells in pigmented areas.
(Clinical Pathology of the Blood. Ewing).
Ischirkoff thought that Addison's Disease was associated with a qualitative rather than a quantitative change in the haemoglobin of the blood, thereby resulting in an insufficient supply of Oxygen to the tissues.
He examined two cases of Addison's Disease with special reference to the pigments by Gland' Spectrophotometric method thereby estimating the relative amounts of Oxyhaemoglobin & reduced haemoglobin.
He found in advanced cases a greater amount of reduced haemoglobin than is present in normal blood & at times more reduced haemoglobin than Oxy-haemoglobin. When improvement occurred there was an increase in the proportion of the Oxyhaemoglobin at the expense of the reduced haemoglobin. The total haemoglobin of the blood remained constant (Clinical Path. of the Blood by Ewing).

There are three theories as to the method by which the symptoms of Addison's Disease are produced.
1. The Nervous Theory.
2. The Theory of Adrenal Inadequacy
3. Dual Theory (Byrom Bramwell).
In the Nervous Theory the important element is the lesion of the sympathetic. The changes are first irritative giving rise to vomiting & pigmentation, later degenerative changes occur associated with great debility & collapse.

2nd. The absence of the internal secretion.
In health the Adrenals contain in their medulla an active principle which raises blood pressure.
This has been shown by Oliver & Schäfer to be absent in the Adrenals from a case of Addison's disease. The fact that in Addison we have low blood pressure & muscular weakness & that the Suprarenal extract when administered relieves these symptoms favours this theory.

3rdly The Dual Theory is a compromise and it explains all cases as far as is known at present.
Byrom Bramwell holds that Addison's Disease is due to a combination of Suprarenal inadequacy & direct irritation of the

sympathetic & semilunar ganglia.

Physiology

The suprarenal bodies are essential to life (Brown Séquard)
Death followed removal of the adrenals in animals,
preceded by muscular prostration & other symptoms
somewhat analogous to those seen in Addison's Disease

Two views have been put forward as to the
function of the Adrenal glands.

1st That they are excretory

2nd That they provide a secretion which is necessary
to health.

It has not been proved that they are excretory.
Schäfer & Oliver have shown that the theory of
providing an internal secretion is probably correct.
They found that the medulla of the adrenal glands
yielded an extract which caused a marked rise
of blood pressure when injected into the circulation
due to constriction of the arterioles.

Symptoms

An insidious onset of varying duration without
characteristic features.
Usually the patient has been losing strength
for some time before seeking advice.
Gastric trouble is generally the first thing noticed

by the patient. General debility & gastro intestinal debility as a rule precede the pigmentation but not always. The subcutaneous fat is not lost.
Probably in all cases of apparent acute onset the insidious character of the disease has escaped notice.
Pigmentation is the most prominent symptome, it is very variable both in degree & in time of appearance. It may appear early or late in the course of the disease.
It may be absent (Case of Addisons Disease without pigmentation. Counsell. Lancet Lond. 1890. 1. 960) or it may be slight, or of considerable intensity.

Occasionally it has preceded all other symptoms by years (Bronzing of the skin for 8 years T. Path. Soc Lond 1879 xxx. 346 Goodhart). Also Dr Munros case quoted by Greenhow, pigment lasting seven years before symptoms appeared.

The Bronzing is an exaggeration of the normal deposit of pigment.
Large areas are usually discoloured, there being a gradual shading off of tint into the natural colour of the skin.
The exposed parts are first attacked, such as the face, neck & backs of hands. Then the parts naturally pigmented such as the axillae

areolæ, dorsal surface of the forearm, genitals & groins. Thirdly seats of pressure or slight injury e.g. Garters Braces. Scars it shld be noted however in which the whole thickness of the skin has been destroyed remain white.

On the patches of pigmented area small darker spots may be seen like small moles. Greenhow considers these important in diagnosis.

The Linea Alba is sometimes pigmented.

Mucous Membranes may occasionally show pigmentation, eg the lips where they come in contact, also the tongue (Case of marked pigmentation of Tongue in Addisons Disease. Lancet 1883 Wilkin).

Pigmentation in these sites is usually due to irritation e.g. from carious teeth.

Pigmentation of the Labia Minora has been recorded (Tr. Path Soc Lond 1884-5 xxxvi 449 Taylor).

Asthenia is ushered in by a feeling of tiredness becoming more & more marked until the slightest exertion is impossible. Emaciation does not as a rule accompany the muscular feebleness. There is no peripheral neuritis. In Phthisis & other cases

of great debility there is not this striking loss of muscular power.

Circulatory System. The heart's action is feeble. This is shown by the small, soft, compressible pulse often scarcely to be felt at the wrist & also in the fatal syncopal attacks.

The extremities are cold. Palpitation & shortness of breath are frequent on movement.

The temperature is usually subnormal, but cases with fever shortly before death have been recorded. (Maclennan Brit. Med. Jour 1886)

Gastro Intestinal Symptoms.

The tongue is usually clean. Appetite variable often capricious. An early symptom is loss of desire for food which later passes into disgust.

Nausea & Vomiting are generally met with being always present in the later stages & often being so continuous as to cause death from exhaustion.

Constipation the result of loss of muscular tone is common, but severe attacks of diarrhoea may occur at intervals sometimes uncontrollable leading to death

Nervous System.

There is general depression with loss of tone, impairment of special senses, sight & hearing.

Mental powers generally remain clear till final coma or delirium.

During the unconscious stage muscular twitchings or rigidity, or even general convulsions point to the irritation of the nervous system.

Headaches & giddiness often associated with faintness are frequent.

Pain in the limbs, back, & abdomen are sometimes complained of. The lumbar pain is probably due to an extension of inflammation from the adrenals.

The urinary system presents no abnormal features.

Progress of the disease — is marked by exacerbations during which all the symptoms are intensified The patient makes an incomplete rally, the pigmentation proceeds pari passu with these attacks & though diminished in the remittent periods remains more marked than in the last attack.

Very acute cases may be fatal without pigmentation but one of the constitutional symptoms is constant — Vomiting & Diarrhoea in one class, Fainting

& breathlessness in the Cardiac type.
Throughout you have extreme Asthenia.
Duration of the disease is very variable, from a few weeks to ten years.
(Rapid course of Addison Disease. Lancet 1895 I. 283 Donkin also a case by Ewald "Mittheilung Einen fallen von acut tödlich verlaufender Tuberculose der Nebennieren." Berlin. Klin. Wochenschr 1893).
The average duration is 18 months.
Termination may be gradual from asthenia or typhoid semicomatose state, or sudden by syncope often before the patient is bedridden. (Case of Addison sudden death. Stone Lancet 1895 p. 284).
Vomiting & Diarrhoea may be the immediate cause of death.

Prognosis
The disease when diagnosis is evident is fatal, but it is possible that arrest of mischief may occur after symptoms of slight intensity.
Cases of recovery have been recorded (Brit. Med. Jour Lond 1895 II. 483 Jones) (also by Neumann in the Deutsche Med. Wochenschr. Leipzig (1894))

Diagnosis

In well marked examples this is easy but as a rule it can only be arrived at by a process of exclusion from

Tubercular Peritonitis,

Malignant disease of the Peritoneum accompanied by facial pigmentation.

In Abdominal diseases where by compression of the lymphatics of the suprarenals occur the condition is one of Addison's Disease e.g. Lymphadenoma.

Liver disease especially in Hepatic Cirrhosis (Hanot) marked pigmentation of skin may occur.

Jaundice has been confounded with pigmentation Pancreatic disease. Pregnancy & Uterine irritation all giving rise to pigmentation.

Granular kidney, Chronic Phthisis, Malarial Melanaemia, Melanosis. Exophthalmic goitre – here the pigmentation may be great.

Rheumatoid Arthritis, & Argyria also produce a discolouration of the skin. Arsenic given over long periods. Diabetes sometimes called bronzed diabetes because of discolouration. Uraemic diseases.

Exposure to Sun – coal etc. Also occupation must be borne in mind.

Addisons Disease without pigmentation is mainly diagnosed by exclusion from Pernicious Anaemia Splenic Anaemia & Bright's disease.

Treatment.

This falls into two classes.

First the replacement of the natural internal secretion by preparations of the gland

Second The symptomatic treatment on general principles

The Suprarenal extract was first given by subcutaneous injection but since Oliver & Schäfer have shown that the pepsin & hydrochloric acid do not impair its action it is simply given by the mouth in dry extract in the form of a pill.

The sheep's gland is usually employed.

One pill equal to gr xv of gland substance is given thrice daily. Probably this dose cld be greatly increased.

The active principle is present in the medulla & not in the cortex of the gland but since the suprarenal extract is prepared from the whole gland, the amount of active principle is uncertain.

In one case where simple atrophy of the glands was probably the condition great abatement of symptoms & lessening of pigmentation followed

treatment by raw renal capsules of sheep. The patient relapsed when this treatment was discontinued & improved when resumed. (Stockman)

Those cases in which Fibro Corneal Degeneration is present seem to derive no benefit from this extract treatment.

No cases have been reported in which bad results followed treatment.

The results vary. Temporary improvement in strength & some diminution of pigmentation is almost invariably followed by relapse.

Treatment shld be continued when improvement has taken place.

Byrom Bramwell who regards Addison's Disease as Glandular Inadequacy & an irritation of the Sympathetic, believes that in cases of failure there are adhesions & irritations of the sympathetic.

In cases where the adrenal extract gives satisfactory results there is probably only glandular inadequacy.

General Treatment.

Rest in bed is important during any exacerbation of symptoms & especially when there is any tendency to syncope.

Avoidance of all strain mental & physical

Easily digestible not irritating food shld be given.
Any constipation must be treated by the mildest aperients. Restrain Diarrhoea by Opium & Bismuth.
Vomiting shld be treated in the ordinary way.
Tonics such as Strychnine Arsenic & Iron may be given but with doubtful benefit.
The active principle of the Suprarenals may be given 1°. as fresh renal capsules - raw.

2nds. as an extract either dry or liquid.

It exercises a general tonic effect on all involuntary muscles, strengthens the heart's action, slows & regulates the pulse.

Intravenous injection produces the maximum effect
The suprarenal extract is of such strength that gr i equals gr viii of fresh suprarenal sheep's substance.

Osler mentions that out of 97 cases of Addison's Disease treated by suprarenal extract

7 grew worse
43, no effect
31, temporary improvement
16, permanently relieved.

(Allaria & Varanini (Adria Med) gave 165 tablets .0005 grms of ext in a case of Addison's Disease with no result. Med. Annual 1905) But a case

treated by Docks with ungparenal extract gtt iii thrice daily improved greatly — Med Annual 1905 .

Case 1.

J. S. act 40 was first seen August 7. 1903.
At that date he had been ailing for two years + was thought to be anaemic.
He had lost 3 st. in weight + complained that his mental + bodily power was failing, he being thereby unfitted for his business of grocer's traveller.
His memory was faulty + he suffered from extreme depression. He was unduly fatigued by the slightest exertion. Shortness of breath, giddiness + faintness were also troublesome.
He had been losing weight in spite of a good appetite. There were occasional attacks of sickness.
The bowels tended to constipation. Although it was very warm weather he always felt chilly.
A specialist whom he had recently seen thought the condition Leucoderma + Anaemia.
He had never had jaundice.

Physical Examination. Temperature subnormal.
The patient was found to be fairly well nourished there was some wasting of muscle but not of fat.
No oedema. The face was extremely pallid
Hair dark. Expression was melancholy.
Hands were glossy. Finger tips blue + cold.

Skin & Mucous Membranes

The skin was smooth & delicate. The colour of the skin generally was markedly white in contrast with well defined patches of pigmentation which did not fade into the surrounding whiteness.

There was no pigmentation on the face but some patches of leucoderma near the lips.

The backs of the fingers were discoloured – the rest of the hand was free.

Scattered patches were found on the extensor surface of the limbs.

The Axillae & other places where pigmentation is normally found were all deeply pigmented.

On the inner aspect of the thighs the pigmentation was strikingly symmetrical.

The lower part of the abdomen exhibited most discolouration. The penis was almost black having a piebald appearance, & the scrotum was much discoloured.

There was no discolouration on the front of the chest but patches were present on the shoulders & the spines of the vertebrae in the dorsal region were discoloured. One area of discolouration corresponded to the breasts. The lips at the junction of skin & mucous membrane showed pigmentation, & also the gums.

Circulatory System
Slight cyanosis of the finger ends.
Pulse regular, small, extremely soft + compressible. Barely perceptible at the wrist.
Heart's impulse felt with difficulty but normal in position. No increase of dulness
Heart sounds were faint - the first approximating in character to the second.
A basic systolic murmur cld be heard at the base + a bruit in the neck.

Abdomen + Alimentary.
Tongue was clean. No apparent dyspepsia. The appetite good. Occasional vomiting. Bowels inclined to constipation. No free HCl.
There was a great tenderness over the epigastrium + right hypochondriac region, but nothing abnormal cld be felt.
There was no lumbar pain.
Liver + Spleen cld not be felt.

Nervous System
An incapacity for mental exertion was a prominent feature. Headache + giddiness were frequent.
Insomnia was a trying symptom.

Under treatment temporary improvement lasting for four weeks occurred.
The occasional vomiting ceased. The patient gained 13 lbs in weight. There was a decided increase of strength – the patient after the first fortnight being able to move about.
The memory improved & sleep returned.
In September the weather broke up confining the patient to the house.
There was a sudden return of the vomiting & in spite of all treatment persisted with slight remissions. The patient was entirely confined to bed. Death occurred on Sep 19th from syncope, precipitated by severe vomiting & continuous diarrhoea.
There was no apparent increase of pigmentation in the last six weeks & no wasting.

Treatment by complete rest & open air was instituted. Drug treatment consisted in gtt V Liquor arsenicalis Fowleri thrice daily. Arsenic was also given in increasing doses on account of the anaemia.
The resulting improvement was marked, but did not last. The syncope was relieved by the

recumbent posture. Vomiting was the most troublesome symptom & no drugs afforded relief.

Peptonized milk foods were given during a period of two weeks & stimulants administered whenever required.

Post Mortem.

Body fairly well nourished. The amount of subcutaneous fat being rather striking.

The pigmentation was well marked as above described & had not altered.

Beyond the absence of the suprarenals nothing abnormal was found in the abdomen.

Heart was pale & flabby & smaller than normal.

No evidence of tubercle in the body.

Case 2.

J. W. aet 36. Gardener. Was first seen July 6.05
Complained of great prostration & weakness, feeling
faint on exertion. He had had fainting attacks
& thought he had "a touch of the sun" two weeks
before. He was quite unable to attend to his
duties & had been getting rapidly weaker.
There had been three attacks of severe vomiting &
diarrhoea in 3 weeks prior to seeking advice.
He suffered from pain in the back & headache.
He had always been thin & tanned readily
with the sun, & though it was summer time he
always felt cold.
On cross examination he stated that he had not
felt well for over a year, but only in the past
fortnight did he think it necessary to seek advice.

Physical Examination.
No oedema. There was marked emaciation - no
subcutaneous fat; the muscles were small & thin.
The face was deeply & evenly bronzed - the
colour being so marked as to suggest Indian ex-
traction. His sclerotics showed pearly white
against the surrounding dark colour.
Hair was dark - expression of face gloomy in the extreme.

Hands were thin & cold - ~~external~~ surface almost brown - the palms almost white.
Temperature subnormal.

Skin & Mucous Membranes
There was uniform discoloration slightly more marked in the exposed parts & in the normal places where pigment is found.
The skin felt soft but dry.
There was a line of pigmentation at the junction of the skin & mucous membrane of the lower lip

Circulatory System.
Shortness of breath & faintness were prominent symptoms. Pulse regular 120, small, soft compressible.
Heart's impulse hardly perceptible.
No increase of dulness. Heart sounds feeble no murmurs.

Abdominal.
Tongue was clean. There was nausea & vomiting Great inability to take food. Tendency to diarrhoea pain in back. Nothing abnormal could be felt in abdomen.

Urinary system. normal.

Nervous system

Extreme depression, extreme irritability, insomnia & restlessness. Sense of hearing impaired.
Mentally clear.

Diagnosis.

The pigmentation combined with the gastro intestinal symptoms & Asthenia made a typical picture of Addison's Disease.

Treatment.

Rest in bed with the greatest amount of fresh air obtainable. Careful feeding with milk & albumen water combined with administrations of suprarenal extract.

In the course of ten days - diarrhoea ceased & vomiting diminished but a tendency to syncope was marked even in the recumbent position.

The slight improvement quickly gave place to a relapse - the diarrhoea returning & vomiting being almost continuous.

Rectal feeding was impossible owing to diarrhoea

The liquid extr of suprarenal gland was now given hypodermically in XV m doses 8 hourly.

The patient rapidly became comatose & died Aug 10. 05.

This was probably an instance of an insidious onset with an acute termination.

The general pigmentation pointed to the condition having existed for some considerable time.

No post mortem was permitted.

Case 3.

L. W. aet 19. Housemaid. First seen Dec 1904 when the following history was obtained.

She had enjoyed good health till November 1903 when she had a severe chill which she did not throw off. In April 1904 a troublesome cough set in & she noticed the extreme loss of weight & therefore consulted a doctor.

She understood she was suffering from anaemia & that one of her lungs was affected.

From then till December she remained in a feeble state of health & subject to fainting attacks.

Her friends noticed how thin she had become. She slept badly & often walked in her sleep. She said her mind "felt weak"

At this time complained of pain in the left hip which rest did not relieve

Family History.
History of Phthisis on Fathers side.
Mother died of Tubercular meningitis.

Physical Examination.
Considerable emaciation was a prominent feature.
There were old scars in the neck of tubercular glands - on both sides - but no suppuration.
The muscles as well as the fat were greatly wasted
No oedema. Face pale & anaemic looking. Skin dark. Manner gloomy expression.
Hands were cold & blue & finger tips blunted.
Temperature normal.

Skin & Mucous Membranes

The skin was very harsh & dry & there was no discoloration anywhere.
The mucous membrane was pale & anaemic.

Circulatory System

The pulse was regular small & rapid - 116.

Easily compressible. Bruit heard in the neck.
Slight blueness of the extremities.
Apex beat normal in position but feeble.
No increase of dulness.
Heart sounds feeble, no murmurs.
Tendency to syncopal attacks.
Shortness of breath on exertion.

Lungs.
Impaired movement of right apex - weak
breath sounds no rales - otherwise normal.

Alimentary System
Appetite ravenous. Attacks of vomiting at infrequent
intervals.
Tongue red & raw - almost like a Diabetic.
Constipated.
Nothing abnormal was felt in the abdomen.

Urinary System
No sugar or albumen.
No Uterine or Ovarian visitation.
Menstruation ceased for 5 months.
Nervous System
Irritability, excitability & restlessness were marked

Sleeplessness & often headache.
Pain in the left hip was a prominent symptom

Muscles Bones & Joints.
Evidence of Rheumatoid Arthritis specially marked in left hip. Pain & fixation of limb almost resembling early hip disease.
There was grating in the shoulders & knees, less marked after movement.
There was considerable muscular wasting specially marked in the left thigh & about the shoulder.

Progress of the case.
The patient was put on Arsenic & Iron with great benefit to the Rheumatoid condition & improved greatly - gaining flesh & strength & being able to get about.
This lasted till Aug 1905 - a period of 8 months - when a sudden collapse occurred with rapid wasting associated with vomiting & syncopal attacks.
Notwithstanding the vomiting the appetite was voracious & the thirst great.
The urine was again tested for sugar & albumen

but as the sec result.

The patient was kept in bed & carefully watched
The motions were examined & much undigested
food found — especially milk.
On albumen water the patient improved & the
vomiting ceased. Raw meat juice was added
in increasing amounts & milk cut off.
At this date end of Aug 1905 slight discolora-
tion was noticed round the mouth for the
first time - but none elsewhere.

Improvement was maintained & she
gained weight. At the end of September she
was able to be up.
Her mother then called attention to the staining
of her combinations especially marked where her
stays pressed, there was a slight discoloration
of the corresponding areas of the skin namely
the wrist & the front of the chest (not Tinea
Versicolor)
This train of symptoms pointed to Addison's
Disease & treatment by Suprarenal extract
was commenced gr v thrice daily.

There was again a relapse with frequent
vomiting & the patient went down to 6st 10lbs.

in weight.
She had severe syncopal attacks - with shortness of breath.
During October & November she was kept in bed & there was a diminution of the fainting attacks & vomiting.
In December a sudden & surprisingly rapid improvement set in. The patient lost on weight thereby gaining over a stone.
The vomiting had entirely ceased & the patient was able to be dressed.
Her chief complaint was her sensitiveness to cold.
From this date improvement was maintained.
There were no gastro intestinal symptoms except very slight vomiting.
Menstruation has been absent since the beginning of the illness.

During the past four months the treatment with suprarenal extract has been continued the patient taking gr XV a day.
The pigmentation is now only just visible.
She has gained weight & her digestive disturbance & vomiting has ceased.

No vomiting attack has occurred.
There has been no return of the joint conditions.
The patient is able to take short walks without discomfort.
Throughout the disease there has been no diarrhoea. No dark freckles have been noted as in Rheumatoid Arthritis.
The continued improvement has rendered increased dose of suprarenal extract unnecessary.
This improvement continues to the present date.

Considering the rarity of this disease the presence of these cases, within the past three years in a small rural district, is of more interest.

Comparing the above cases
Pigmentation was present in all three & especially marked in the two fatal cases.
J. S (case 1) showed very marked pigmentation the pigmented areas being sharply defined owing to the presence of patches of leucoderma

In G. W (Case 2) Pigmentation was just the opposite being almost uniform - resembling the dark races.
In both pigmentation of lips was present.
In the female patient the pigmentation was comparatively slight - & only noticed on parts of pressure

None of her mucous membranes were discoloured & vomiting & purging attacks preceded the pigmentation by one months.

Vomiting & diarrhoea were the severe features of J. S & G. W's cases eventually leading to death.
In the female case the vomiting was severe but there was no diarrhoea.
In all three cases syncopal attacks of varying intensity occurred, being the immediate cause of death in case 2.
J. S. was fairly well nourished with plenty of subcutaneous fat - smooth & supple skin, contrasting with the emaciation & hard dry skin of cases 2 & 3.
Asthenia was very marked in the first two cases less marked in the third.
All three patients suffered from irritability depression & sleeplessness.
J. S had epigastric tenderness & also in right

hypochondrium.

It is interesting to note that post mortem the disappearance of the suprarenals was the only change noticed. There was no matting together of surrounding nervous structures.

This case shld have benefited from the administration of suprarenal extract if Bramwell's conjoint theory is true.

One wld have expected a fibrocaseous change in the suprarenals.

In G.W. we had severe pain in the back. No post mortem was permitted.

In the Female case the presence of Rheumatoid Arthritis probably accounted for her emaciation.

This case had all the appearance of a Diabetic.

The pigmentation which appeared months after the Rheumatoid condition was not due to this.

Treatment.

Considering that the disease is due to loss of function of the Suprarenals the administration of the Suprarenal extract is the only rational procedure.

Silsprarenal extract — was given in all 3 cases

with temporary improvement in case 1.
no improvement in case 2
& in case 3 no improvement resulted in the two months of administration & then a sudden improvement set in which has since been maintained.
It is difficult to say whether this improvement is due to the extract or to a natural arrest or remission of the disease.

In cases where vomiting & diarrhoea are severe it is doubtful whether the suprarenal extract given by the mouth is absorbed. Hence in case 2 liquid preparation was administered hypodermically.

Although the open air treatment was tried in all 3 cases, special interest attaches to this method of treatment after reading Byrom Bramwell's article in The Brit. Med. Jour Oct 1905. in which great improvement took place in a case of Addison's Disease under open air treatment & the administration of suprarenal extract.

Discussion.

A series of pulse tracings taken before & during the administration of suprarenal extract might be of value in prognosis.

A careful note shld be made of the character & rapidity of the pulse.

It is still open to question whether the active principle is excreted by the kidneys.

Do cases of Addison Disease ever have art. sclerosis

It might be interesting to know whether an increase of suprarenal secretion can occur similar in its effect to the condition seen in exophthalmic goitre - a high arterial tension & a slow pulse.

The active principle has been given in health but there was no increase of blood pressure (Grünbaum in Encyclop. Med)

In Addisons Disease there is no tendency to Purpura or Haemorrhage, which considering that Adrenalin constricts & blanches tissues is worthy of note. Is the fact of haemorrhage not taking place due to feeble circulation?

No case of Addison's Disease in connection with Interstitial Nephritis has ever been reported - it would be interesting to note whether the high arterial tension of renal disease would be lowered - provided the renal disease did not prove fatal first.

Large doses of suprarenal extract kill animals if made from the healthy gland but the active principle is lost where Addison's Disease exists.
The first case mentioned above bears out Addison's Theory.
Could you have Addison's Disease in albinos?

Much attention has been directed lately to the treatment of Addison's Disease by the administration of suprarenal extract.
In some cases it appears to have done good & reports of cases are to hand.
In the majority of cases no benefit has resulted, but it is early days to give a positive opinion.
The inconstant results of treatment by adrenal extract support Dr Bramwell's view that thromb some cases may be due to inadequacy the remainder are due to an additional lesion of the sympathetic.

References were made to the following.
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Encyclopaedia Medica.
Roberts. Osler. Taylor. Ewing.
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