SUPRARENAL INSUFFICIENCY IN TUBERCULOUS PATIENTS, WITH SPECIAL REFERENCE TO THE SODIUM LEVEL IN THE BLOOD SERUM.

by

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The subject of Addison's disease as dealt with in modern text-books of medicine refers to well established disease and the symptoms are those produced by advanced changes in the suprarenals.

The symptoms show great variation, but the diagnosis is still based on the classical description given by Addison in 1855.

The chief features may be briefly stated as follows:-

1. Pigmentation of the skin.
2. Myasthenia.
3. Gastro-intestinal symptoms such as anorexia, vomiting and epigastric discomfort or pain.
4. Loss of weight.
5. Hypotension, the systolic pressure frequently being below - 90 mm of mercury.
6. Subnormal temperature.

PIGMENTATION, the most outstanding feature, is most obvious on exposed parts such as face and hands, on parts of the body normally more pigmented such as axilla, nipple, genital, and anal regions and is also seen in the mucous membranes, especially that of the mouth.

Autopsies done on patients with this classical picture almost always show that practically the whole of the suprarenal tissue has been destroyed.

There has been no description of the clinical features of early suprarenal changes.

While suprarenal disease is not always due to tuberculosis, many cases of Addison's disease show extensive tuberculous infiltration of the suprarenal glands and it seemed that, an opportunity to study the early clinical state of suprarenal insufficiency might be afforded by a careful and routine investigation of every patient admitted to a sanitorium. Patients with pulmonary tuberculosis show gradual loss of strength, muscular weakness, low blood pressure and often some pigmentation. Whether these features are related to lesions in the suprarenals has not been

determined. Fishberg[1]. says 'low blood pressure as well as the weakness and lack of enduring powers, pigmentation of skin, etc., have been attributed to hypofunction of the adrenals. The great frequency with which these glands are affected in cases of phthisis, favours the view that they are due to insufficiency of the adrenals.'

BLOOD CHANGES IN SUPRARENAL INSUFFICIENCY.

Recent research has shown marked changes in the composition of the blood during suprarenal insuff-:iciency and it was felt that some of these features might be of help in detecting the presence of a lesion of the glands in tuberculous patients.

In 1926 Bowman and Kurland[2]. studied the effect of bilateral adrenalectomy on the electrolyte pattern of the blood in cats and found a fall in the plasma sodium. Later Marine & Bowman[3] prolonged the life of adrenalectomised animals by means of sodium chloride, as also did Stewart and Rogoff[4] using Ringer's solution. In 1930 Swingle and Pfiffner[5] prepared a potent cortical extract and using this extract Britton and Silvette[6]. came to the conclusion that the primary action of the hormone of the adrenal cortex is concerned with the maintenance of normal carbohydrate metabolism.

Loeb[7.8]. ,however, has shown that in adrenal insufficiency,whether experimental or due to Addison's disease, the most important and probably the primary change is a decrease in the total base of the body which occurs entirely at the expense of the sodium.

This finding of Loeb's has been borne out by further investigations [10,18,19,20,21], and many further changes in the elctrolytes have been shown.

The main blood changes as now understood may be stated briefly as, anaemia with an associated haemoconcentration, relative lymphocytosis, fall in serum sodium, chloride and sugar, a rise in the serum potassium, magnesium and protein and increased blood area.

The loss of sodium seems to be the primary change, this contention being supported by the great value of sodium in the treatment of Addison's disease.

It was decided to use the serum sodium value for this investigation and to determine whether or not it could be used as an index of suprarenal activity.

MATERIAL

This investigation has been carried out on a series of consecutive admissions to Glenlomond Sanatorium of the "Fife and Kinross Joint Sanatorium Board."

The majority suffered from pulmonary tuberculosis while a few showed other lesions such as bone and joint, kidney, spine, etc.

That such material is well suited for an investigation of suprarenal insufficiency, can be realised by considering the aetiology of Addison's disease and the frequency of suprarenal involvement in tuberculosis.

AETIOLOGY OF ADDISON'S DISEASE.

Tuberculosis of both suprarenal glands has been the cause of Addison's disease in many cases but the figure quoted shows a wide variation from 45 to 95%. Rowntree[9] in 9 autopsies found 8 deaths due to tuberculosis of the suprarenals, Guttman 69.72% of 566 cases, Harrop et alia[10] 3 out of 7 deaths, Clark and Rowntree[12] 11 out of 17 autopsies and Colton[13] 6 out of 8. Levy Simpson[14] says 75% of Addison's disease is caused by tuberculosis, while Spence[15] believes atrophy of the suprarenals to be as common a cause.

ASSOCIATED LESIONS.

Knowing that tuberculosis is a general and not a local disease, it is natural to wonder what the frequency and type of other tuberculous lesions is in patients with Addison's disease. Colton[13] quotes Bell as saying 'adrenal tuberculosis is usually secondary to tuberculosis in the body elsewhere and

is usually haematogenous in origin.' Colton in 6 cases of his own found 3 had arrested or healed pulmonary tuberculosis, 1 a moderately advanced slightly active pulmonary lesion and 2 genito-urinary. Advanced tuberculosis elsewhere was present in 2 out of 7 cases of Addison's disease autopsied by Harrop[10].

Guttman from 243 autopsy cases in which the suprarenal glands were involved gives a detailed list of tuberculous lesions elsewhere, as many as 124 having pulmonary deposits.

FREQUENCY OF SUPRARENAL INVOLVEMENT IN TUBERCULOSIS

In 604 autopsies on patients dying from tuberculosis Fishberg[16] found tuberculosis of the suprarenals in 39 which is 6.4%.

Nolan[17] in 602 tubercle deaths found that tuberculosis of the suprarenals was the cause of death in 3 or .49%, while in 3.2% gland lesions were present.

In the light of these investigations it is evident that the present material should reveal some cases with tuberculous deposits in the suprarenals and maybe afforded an opportunity of studying the disease in all its stages. At the same time it may be possible to assess what role the suprarenal glands play in the production of the symptoms already mentioned.

METHODS OF INVESTIGATION.

1. Detailed study of symptoms and signs.
2. Blood Pressure.
3. Examination of blood.
   a. Complete blood count.
   b. Sedimentation rate
   c. Serum sodium.
4. Examination of suprarenal glands obtained at autopsy.
   a. By injection of crushed gland into a guinea pig.
   b. By serial sections of the suprarenals.

SYMPTOMS AND SIGNS.

Special notice was taken of any symptoms which could be referred to those occurring in Addison's disease namely: pigmentation, lassitude, loss of weight, anorexia and vomiting.

EXAMINATION OF BLOOD.

a. Complete Blood count.

At first this was done on all patients but it was found that by watching the level of the corpuscles in the sedimentation tubes after 24 hours, the presence of anaemia could be detected. In the later cases a red blood count was done only in those who appeared to have an abnormal count. A white count was done in most of the cases and the differential white count has been expressed as a ratio:-

$$\frac{\text{Polymorphs}}{\text{Lymphocytes}} \quad : \quad : \quad \frac{\text{Lymphocytes}}{\text{Monocytes}}$$

400 cells are counted in each case, all types of polymorphonuclear cells being included as polymorphs, lymphocytes being both large and small types.

Haemoglobin estimations were made on a Sahli type of haemoglobinometer.

b. Sedimentation Rate.

This estimation was made between 11.30 a.m. and 12 noon, 3 hours after the previous meal, and patients rested for half an hour before blood was with drawn.

·75c.cm. of blood was withdrawn from a vein and mixed with ·25 c.cm. of a 3.8% solution of sodium citrate in normal saline. A column of the mixture 10 cms long in a tube of .24 cms. diameter was set up vertically at a temperature of 20° C and readings made at the end of 1 hour. At first readings were taken at ½hr, 1hr, 2 hrs.and 24 hrs.. but it was found that 1 hr. reading was sufficiently accurate for routine examination.

The results are expressed in mms. of clear fluid and are similar to those obtained using Westergren tubes.

c. Serum Sodium.

This was estimated by the uranyl zinc sodium acetate gravimetric method as described by Butler & Tuthill[22]. Duplicate analyses were made in most cases, the difference rarely being greater than 1%.

Blood was withdrawn at 8.30 a.m. before breakfast and may be considered as the fasting level of sodium in serum.

Syringes and needles were washed and sterilised in doubly distilled water, thus excluding Sodium contained in ordinary tap water.

Results are expressed as mgms. of sodium per 100 c.cm. of Serum.

4. AUTOPSY EXAMINATION.

In many who died the suprarenal glands were obtained.

A portion of one was cut into small pieces, ground in a mortar with 5 c.cm. of 6% sulphuric acid, centrifuged for 20 minutes, the acid decanted and replaced by sterile distilled water. The sediment was mixed in this, centrifuged for 10 minutes, the subnatant fluid removed and replaced by 1.5 c.cm. of sterile distilled water. The suspension obtained on mixing was injected subcutaneously into a guinea pig which if not dead within eight weeks was killed and examined.

The remaining portion of suprarenal and the other suprarenal were fixed and examined by serial sections. Every 8th section was taken, mounted and then stained by haematoxylin and eosin.

In suspected cases of amyloid degeneration the stain was methyl violet.

CLASSIFICATION OF CASES

174 Patients have been investigated and sub-division into groups is difficult.

It seems best to use two main groups namely:-

1. Patients with serum sodium above 315 mgms. per 100 c.cm of serum.

2. Patients with serum sodium below 315 mgms. per 100 c.cm. of serum.

Each group is sub-divided into:-

A. Dead
B. Ill
C. Moderate
D. Well.

It is admitted that, save in the eyes of a biochemist, a classification of patients on a single serum sodium estimation is a doubtful procedure. Justification will be attempted later.

In those patients with pulmonary lesions the Philip system of classification is used, which includes both extent of lung involved and degree of systemic upset. Disease in other organs is indicated by suitable letter.

The letter K indicates a pathological lesion of the kidney while T means that a tuberculous bacilluria was present.

Results.

The clinical findings in the present investi-:gation are shown in the comprehensive tables of Appendix I.

Appendix II contains detailed description of the cases in those patients who died.

STANDARDS OF NORMALITY.

Prior to discussing the results of this investigation it is essential to state clearly what values for blood pressure, blood count, sedimentation rate and serum sodium are considered as normal.

BLOOD PRESSURE.

Blood pressure is considered as low when the systolic is under 100 mm. of mercury, which is much lower than the normal value for adults. (Rolleston[23]). It is necessary to place a low limit of normal in these tuberculous patients, as many of them were on complete rest in bed, while they were all in their usual surroundings and were examined by a physician to whom they were well accustomed.

SEDIMENTATION RATE.

Westergren[24] states that using his method a result of over 12 mms of clear fluid is definitely pathological. Trail[25] has shown that in a tuberculous patient a sedimentation reading over 10 mms indicates a more serious prognosis than a read-ing under this level. In a series of normal people done here the average was from 1 to 6 mm., these results being obtained without any question of a rest prior to venupuncture. Undoubtedly over 10 mm is a pathological finding and the prognosis is increasingly serious as the rate increases.

WHITE COUNT RATIO

It is not claimed that this is an accurate way of assessing the differential white count, but it does give some indication of the state of the patho-logical lesion. The ratio is on the line suggested

by Flinn[26] and takes into consideration the work of Sabin, Doan and Cunningham[27] and Medlar[28].

A rise of the polymorph/lymphocytes ratio with a low lymphocyte/Monocyte is found in advanced cases with breaking down or secondary infection. A marked rise in the lymphocyte/monocyte indicates that healing is taking place.

Approximately a normal white count may give a result of, polymorphs 70%., lymphocytes 25%, Hyalines 5%.

Working out the ratio

$$\frac{P}{L} = \frac{70}{25} = \frac{2{\cdot}8}{1}$$

$$\frac{L}{M} = \frac{25}{5} = \frac{5}{1}$$

So that the combined ratio of

$\frac{P}{L} : \frac{L}{M}$ may be expressed simply as 2·8:5 and this gives an approximate normal value.

The sedimentation rate and white count ratio have been included in the tables as a graphic proof that the various patients have been correctly grouped as ill, moderate or well and together give a rough indication of the prognosis. Apart from this they have no bearing on this investigation and will not be discussed further. The red blood count has been of no assistance.

SERUM SODIUM.

One great difficulty has been in deciding upon a normal range of variation for the serum sodium and it was necessary to consider the group of patients clinically well as a control group, taken as normal,

From a consideration of the literature it can be seen that various authors have found a very different range of normality. That given by Dailey[28] is from 294 to 342 mgms per 100c.cm. with an average of 316 mgms. Guttman's[28] range is 319 to 327, Keys[30] 317 to 354 mgms., Rourke[31] 330 to 347 mgms. McCance[32] gives 330 mgms. as the normal value, Allott[19] 320,

and Gamble, Ross and Tisdall[34] 330 mgms. per 100c.cm.

Dailey's result obtained by a Rourke modification of the Kramer Guttleman method may be excluded as this method tends to give lower results.

In order to verify the average normal reading of serum sodium, the sodium content was estimated in pooled sera from blood sent for the Wasserman reaction. These specimens came from the serum of 100 to 200 individuals, presumed non-tuberculous, and the sodium estimation made in three different groups, the results being 326, 332 and 336.

These investigations suggest that a normal range of serum sodium is from 315 to 350 mgms per 100 c.cm., which content will be borne out by the results in the control group.

RESULTS OF SERUM SODIUM INVESTIGATION.

The serum sodium has been estimated in 174 patients the range being from 282 to 343 mgms per 100 c.cm. A variation of 17.7%. In 114 patients the result was above 315 mgms per 100c.cm. and under this level in 60.

The control series, that is tuberculous patients who are clinically well, contains 59 patients, 40 being males and 19 females. Of the 40 males the serum sodium was above 315 mgms. per 100 c.cm. in 35, with an average of 330, and below this level in only 5, in 3 of whom a subsequent estimation was about 340.

In the 19 female patients, the serum sodium was above 315 in 16 with an average of 323.4, the other 3 being just under this level.

These findings bear out the previous suggestion that 315 may be taken as the low limit of normal and that the ~~average~~ range of 315 to 350 is an ample limit of normal.

CAUSES OF A LOW SERUM SODIUM.

Having fixed a normal range of serum sodium it is natural to ask why it should be low in 60 tuberculous patients. As is well known there are many causes of a low serum sodium such as, excessive

sweating, persistent vomiting, severe diarrhoea; in cholera, in some cases of chronic interstitial nephritis; while rarely such curios as repeated tapping of ascitic fluid and a secreting papilloma of the gall-bladder.[35] Van Slyke says fasting has no effect on the base content of serum. McCance[32] during experimental sodium deficiency noted a fall of serum sodium from 355 to 320. After a four day fast Gamble, Ross and Tisdall[34] found that the serum sodium had fallen from 330 to 327, but on the 6th day was down to 303, rising to 318 on the 9th and 324 on the 12th day.

The following table is given by McCance showing the sodium level in the serum under various conditions:-

Normal -	330 mgms per 100c.cm.
Pyloric Stenosis-	315 " " "
Diarrhoea(severe)-	300 " " "
Intestinal Obstruction -	290 " " "
Sweating without drinking -	380 " " "
Sweating with drinking -	290 " " "

In some established cases[15] of Addison's disease a normal serum sodium has been obtained, but in the majority is is low[10,21,32], more especially during a crisis. Allott[19] in 8 cases of Addison's disease found all had a low serum sodium, the range being from 251 to 295, falling to 219 during a crises. Investigations on patients with Addison's disease and in adrenalectomised animals have led to the conclusion as stated by Loeb[8] "that the adrenals exert a regulatory effect upon the sodium metabolism analagous to that of the parathyroids on the calcium and phosphorous metabolism. One function of the adrenal glands may be to control the concentration of sodium in the blood and tissue fluids".

It may be that derangement of suprarenal

function is the cause of the low serum sodium in the present series, but it is necessary to exclude first many other, and more obvious causes.

INFLUENCE OF SYMPTOMS ON THE SERUM SODIUM.

Several of the causes of a low serum sodium mentioned above are frequently present in tuberculous patients although rarely of a severe degree. Most tuberculous patients sweat readily, while some have severe night sweats, vomiting and diarrhoea are common, while anorexia with a very deficient dietary is frequently present in the late stages.

Patients in whom these symptoms were present are shown in Tables 1 and 2 which also include the level of serum sodium and pyrexia. With pyrexia there is usually an increased fluid loss from the skin even without any complaint of sweating. The most striking feature of these tables is that in Group II, 12 out of the 15 patients are dead, while in Group I only 3 out of 10. This would suggest more serious symptoms in Group II but of those symptoms included in the tables were equally severe in both groups. The girl H.W. Table I.2. had diarrhoea, passing four or six fluid stools daily, frequently vomited after meals, had periodic severe night sweats and ran a hectic temperature, yet over the course of a year she maintained her serum sodium at the lower limit of normal. Similarly case 4 in this table group, in whom there was severe night sweats, and periodic vomiting, a normal level was maintained. Of the Group II patients symptoms were most severe in cases 5,6, and 12 and it was after the onset of symptoms that a low value was obtained.

Cases 10 and 15 despite the continuation of symptoms showed a higher value for serum sodium.

It is thus obvious that symptoms of equal severity are associated with a low serum sodium in some cases, or with a fall from normal, or with a high value in certain others. While this does not exclude the symptom, such as vomiting or diarrhoea,

from being the cause of the low sodium value, it suggests that some other factor must be operative.

This factor would ensure compensation for decreased sodium intake or increased excretion.

SYMPTOMS AFFECTING SERUM SODIUM.

TABLE I.

Serum Sodium above 315 mgms. per 100 c.cm. Serum Group I.

No.	NAME	SYSTEM	DATE	Serum Sodium	DIARRHOEA	VOMITING	SWEATING	PYREXIA	NUMBER IN GROUP $\bar{1}$
1.	Mrs J.	L_3S + Abd. + U		321	++	+	+	++	A.1.F.
2.	H. W.	L_3S + Abd + U	9-3-36	318			+	++	B.2.F.
			29-3-37	317	++	+	+	++	
3.	M.W.	L_3S + Abd		332	++			++	B.6.F.
4.	W.F.	L_3 S	10.2.36	321		+	++	++	B.5.M.
			23-5-37	320		+	++	++	
5.	P. S.	L_3 S		324			+	+	B.3.M.
6.	W. M.	L_3S + Abd.		317	+	+		+	B.1.M.
7.	C.McF.	L_3 S		317			+	++	B.14.M.
8.	J. A.	L_3S + Abd. + U		317	++			+	A.3.M.
9.	J.A.S.	Spine + Amyloid		317	++	++			A.1.M.
10.	J. B.	L_3		323	+				C.12.M.

7 patients with diarrhoea 5 having tuberculous lesions of the abdomen and 1 amyloid degeneration.

5 patients with vomiting, 5 with sweating and pyrexia was present in 8.

SYMPTOMS AFFECTING SERUM SODIUM.

TABLE 2.

Serum sodium below 315 mgms. per 100 c.cm. Serum.
Group II.

No.	NAME.	SYSTEM	DATE	SERUM SODIUM	DIARRHOEA	VOMITING	SWEATING	PYREXIA	NUMBER IN GROUP 11
1.	H. M.	L_3S + Abd.+U		301	+++		+	+++	A.F.1.
2.	R. W.	L_3S + Abd.		301	+++			+++	do 2.
3.	C. C.	L_3S + Abd.+ U		301	+++		+	+++	do 3.
4.	Mrs McA.	L_3S + Abd.		286	+++		+	+++	do. 4.
5.	J. A.	L_3S + Abd.+U	24.2.36	330				+++	do.6.
6.			2.11.36	282	++	+		++	do.do.
6.	Mrs B.	L_3S + Abd.+U	2. 3.36	326	+		+	++	do. 7.
			13.7.36	300	++		+	++	do.do.
7.	A. G.	L_3S+ Abd.+U	13.7.36	315			+	+	do. 8.
			2.11.36	312	+	+	+	+	do.do.
8.	E.McF.	L_3S + U	2.3.36	297					A.F.9.
		L_3S	3.6.36	321					
		L_3S + Abd.	5.1.36	293	+	+		+	
9.	A.McK.	Jaw + Amyloid		305	+			+	A.F.10.
10.	M.McI	L_3S	21.3.36	303			+	+	A.M.10
			2.11.36	330			++	++	do.
11.	J.McB.	L_3S	9.3.36	313			+	+	A.M.15
			25.1.37	291		+	+	++	
12	F.McG.	Abd.+Glands+L_1	27.1.36	328	+		+	+	
			15.9.36	284	++		+	+	
13.	J.R.D.	L_3S		309		+	+	+	B.M.1
14.	T.R.	L_3S		306		+		+	B.M.2
15.	R.R.	L_3S	25.1.37	306	+	+		+	B.M.6
			24.5.37	317	+	+		+	

11 patients with diarrhoea, 9 having tuberculous lesions of the abdomen and 1 having amyloid degener-:ation. 7 cases with vomiting.

PYREXIA.

The degree of pyrexia was examined in all cases, was marked in over 50% of Group II cases but in only 6% of Group I cases.

The difference certainly suggests continued pyrexia as a factor in producing a low serum sodium, but of course does not show how it is done. There may be an increased loss of salt by sweating, but on the other hand pyrexia is an index of toxaemia and toxic action on the cells of the suprarenal may be the cause. No definite conclusion can be drawn from these figures.

TABLE 3.

Degree of Pyrexia.	No. in Group I.	No. in Group II
Marked	18	34
Slight	14	6
None	82	20

PLEURAL EFFUSIONS.

According to Sunderman, Austin and Camach[36], in pleurisy with effusion the serum base and chloride fall, their results being low in eight out of ten cases. Sunderman also says that the electrolyte content of a pleural effusion is the same as that in the serum.

Ten patients in this series had serious pleural effusions, the serum sodium being above 315 mgms per 100 c.cm. in 6 and below this level in 4.

The serum sodium, the quantity of fluid aspirated and in some the content of sodium in the effusion are shown in Tables 4.

The outstanding feature of this table is that in those with a serum sodium above 315 mgms. per 100 c.cm., the effusions were small, while 3 of the 4 with a low serum sodium had a large quantity of fluid aspirated.

SEROUS PLEURAL EFFUSIONS.

Table IV.

No.	Name	Date	Serum Sodium	Date	Ounces of Fluid ASPIRATED	Sodium in Effusion	REFERENCE
1.	W. B.	17.6.36	318	15.6.36	8	-	Group I.A.6. M.
2.	R. I.	29. 3.37	322	30.3.37	22	320	Group I.B.12. M.
3.	F. M.	4. 5.36	320	8.6. 36	18	-	Group I.D.13. M.
4.	J.McN.	4. 5.36	317	2.9.35	22	-	Group I.D. 8. F.
				12.5.36	6	-	
				16.1.37	8	-	
5.	Mrs A.	6. 4.36	318	17.12.35	8	-	Group I.D.4.F.
				9. 4.36	11	-	
6.	Mrs B.	5.4.37	318	18. 4.37	20	-	Group I. C.5.F.
7.	D. B.	12.4.37	300	4. 3.37	60	325	Group II.B.3.M.
				7. 3.37	40	-	
8.	J. P.	13.5.37	304	7.5.37	50		Group II.B.10.M.
		10.6.37	303	18.5.37	22		
9.	J. R.	10.2.36	312	12.6.36	12		Group II.C.4.M.
10.	J. P.	28.4.36	311	9.4.36 to	108	323	Group II.C.3.F.
		29.3.37	324	8.8.36			

In cases 3,4, 5 and 10 the effusion was secondary to an artificial pneumothorax.

The sodium content of the effusion did not correspond to that in the serum in two of three cases, being very much higher in the former. Little stress can be laid on these results, however, as great difficulty was encountered in the estimation, various analyses giving widely different results, as for example in case 7 the results for sodium in the effusion were 316,325 and 335 mgms.per 100 c.cm. The figure quoted is the average.

From this it can be calculated that in case 7 about 9.4 gms. of sodium were excreted into the effusion and in case 10, 10 gms.

This quantity is low when one remembers that the daily salt intake is 5 to 10 gms. and the loss of so small a quantity should be easily compensated. It may be that in the rapidly forming effusions there is a temporary upset in the sodium balance of the body thus producing a low reading for the serum sodium.

In case 10 a sodium estimation made when the effusion was no longer forming, showed an increase in serum sodium of 13 mgms per 100 c.cm.

These results neither confirm nor refute the findings of Sunderman, the number of cases being too small and in a recent case, not included in this series 212 ounces of fluid were aspirated within 14 days and the serum sodium estimation gave 323 mgms of sodium per 100 c.cm. of serum.

CORRELATION OF CLINICAL FEATURES AND SERUM SODIUM.

Several of the symptoms mentioned as occurring in Addison's disease were investigated and the incidence in Groups I and II noted.

PIGMENTATION.

None of the Group I patients showed any pigmentation, while this feature was present in eight patients in Group II. The degree of pigmentation was not comparable to that in a well-established Addison's disease nor was it so widely distributed. The hands and arms were deep brown in some not due to the sun, and of a lighter shade of brown on the face and neck and in the axillae and flexure of the elbows; in none was the buccal mucous membrane affected. In two of these cases amyloid disease was present.

MYASTHENIA.

Lassitude was present at some time or other in practically every patient but at the time of investigation in only 76, of whom 34 were in Group I and 42 in Group II. These numbers are practically the same, but when expressed as a percentage incidence for each group lassitude was present in 30% of Group I cases and 70% of Group II.

GASTRO-INTESTINAL SYMPTOMS.

These have been mentioned already Tables I and II. Of Group I cases 7 had diarrhoea and 5 vomiting while in Group II the incidence was 11 and 7. In almost every case there was a local lesion of the bowel as the most probable cause of the symptoms.

LOSS OF WEIGHT.

The amount of weight lost has not been recorded but was quite appreciable in 67 cases of which 31 were Group I and 36 in Group II. Calculated as a percentage this symptom occurred in 27% of patients with a high

serum sodium and in 60% with a low reading.

BLOOD PRESSURE.

A systolic pressure of 100 mm. of mercury was selected as the lowest limit of normal. 9 patients in Group I.had a low blood pressure and 26 in Group II. Many of the readings in the latter group were made within a few weeks of death.

It can be seen from the figures and percentages in the above groups that symptoms, similar to those in Addison's disease, were more frequent in Group II cases. Apart from the pigmentation they are symptoms common to many diseases and the gastro-intestinal ones were probably due to tuberculous lesions of the intestines. The degree of pigmentation was never comparable to that occurring in Addison's disease.

DETAILED EXAMINATION OF CASES.

Records in Appendix I and II.

Group I. A. Males.

In this group, namely those with serum sodium above 315 mgms. per 100 c.cm. it was hoped that a control series would be found, but in the majority who died the serum sodium was low at the first estimation or fell to the low level at a later period prior to death. In cases 3 and 7 it is felt that a later estimation would certainly have been low. At autopsy there was no evidence of any suprarenal lesion in case 3, while in case 7 although animal inoculation was positive for tubercle bacilli no lesion was seen in the sections.

It may be remarked here that in several cases animal inoculation was positive and pathological examination negative. The reason for this is probably a terminal dissemination of the bacilli with implantation in the suprarenal tissue death occurring before any reaction can occur. This probability is supported by the fact that in several other cases tiny areas of aggregations of small round cells may be seen in the suprarenal cortex, which are probably evidence of a commencing tuberculous focus.

In case 1. the sodium estimation, done 5 days prior to death, was 317 mgms per 100 c.cm. yet he had severe persistent vomiting and diarrhoea for several weeks previously. There was a septic focus in bone with amyloid degeneration and with such severe symptoms it was surprising to find so high a result. This is the only case in the group with a low B.P.

Of the other three cases in this group little can be said as they all died from accidents associated with operative interference, being clinically fairly fit at the time.

GROUP I. A. FEMALES.

Similarly in this Group the results are of little value. Case 2 died from Mitral stenosis with cardiac failure. Symptoms of vomiting and diarrhoea were severe in Case 1, and continued intermittently until death. A repeat result was not done in neither case 1 or in case 3.

GROUP II. A. MALES.

This group contains 15 cases in 8 of which the serum sodium was under 300 and in a further 3 was under 305. All showed profound asthenia and dehydration, emaciation and anorexia. The blood pressure was low in all save cases 4 and 15, only case 6 had a low sedimentation rate and in almost all the white cell ratio was of a 'septic' type.

The serum sodium estimation of cases 1 to 8 was done within six weeks of death from advanced pulmonary tuberculosis. They all ran a hectic temperature, but in cases 2 and 3 the temperature was subnormal for several days preceeding death. Animal inoculation was done from six of these (cases 3 to 8) and a positive result obtained in four (cases 3,4,6 and 8). In five of the eight serial section of the suprarenals showed evidence of a reaction to deposits of tubercle bacilli (cases 1,2,3,4, and 8), but in all except case 3 was of the small celled type already mentioned. Case 1,4, and 6 showed a positive bacilluria and at autopsy tuberculous deposits were found in the kidneys. This positive bacilluria according to Band and Munro[37] indicates a tuberculous lesion in the kidney and was obtained several weeks before death. This means that several weeks, it may have been months, before death tubercle bacilli were disseminated in the blood and deposited in the kidney. The suprarenal glands could have been involved at the same time, but in none of the cases was the suprarenal lesion as old as that in the kidney. The foci in the suprarenals are probably too small to cause any

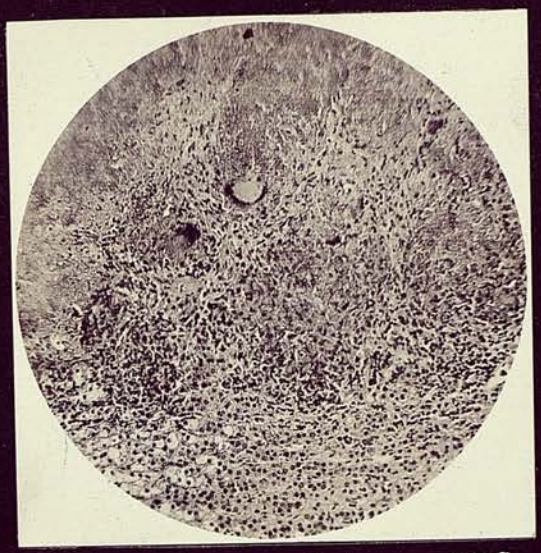

PLATE I x85

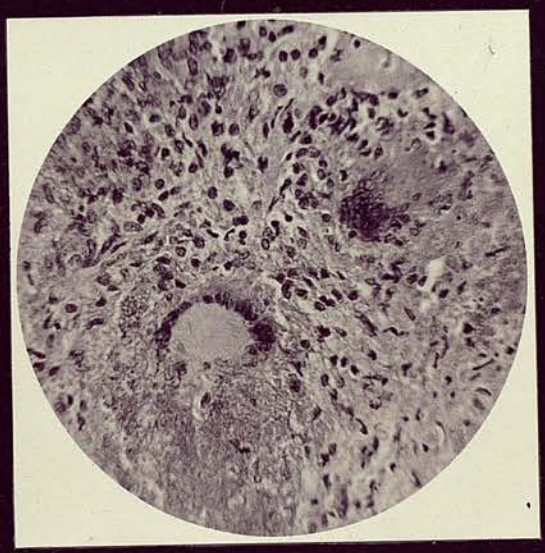

PLATE I x240

derangement of function in the glands, which may be excluded as the cause of the low serum sodium (case 3 vide infra). Symptoms known to cause a low serum sodium were present in none. There was pigmentation of the skin in cases 3 and 8 and in both the whole clinical picture, apart from the local pulmonary symptoms, was quite typical of Addison's disease. In case 8 animal inoculation was positive and small tuberculous foci were seen on section, but of insufficient degree to affect the function of the suprarenal glands. Case 3 on the other hand showed a well developed tuberculous lesion in the cortex of the left suprarenal in addition to a positive inoculation from the right. The lesion is shown in Plate I. Section of the remaining portion of the right gland showed a smaller lesion composed of lymphocytic infiltration situated in the cortex and round this focus the cortical cells were widely separated by blood cells. This was evidence of congestion of the gland and was much greater than is normally seen. The serum sodium was slightly decreased being 310 mgms., the B.P. very low 78/50, asthenia and emaciation marked, appetite poor, pigmentation definite and during the week preceeding death the temperature was subnormal, while respirations did not rise above 24 per minute. There was a state of coma for two days before death.

The significance of the various symptoms is not easily evaluated for the patient had extensive active pulmonary tuberculosis, but the mode of death is quite suggestive of suprarenal insufficiency. Pathologically there is evidence of tuberculous infiltration in the glands, definite, but not advanced, which may have been sufficient to derange the cortical secretion.

The only other markedly positive section was found in case 12.

No 2

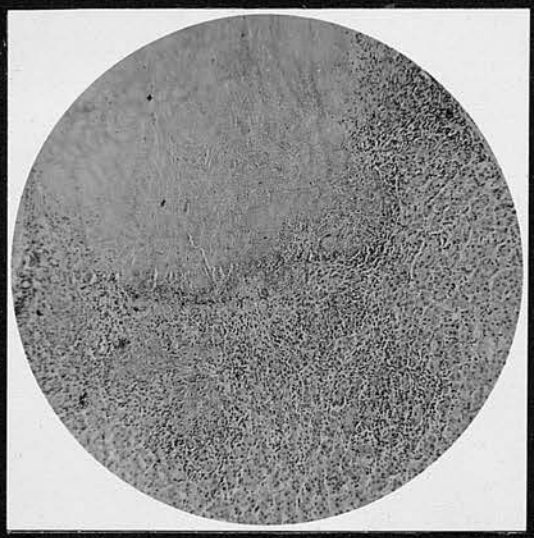

PLATE 2. X50

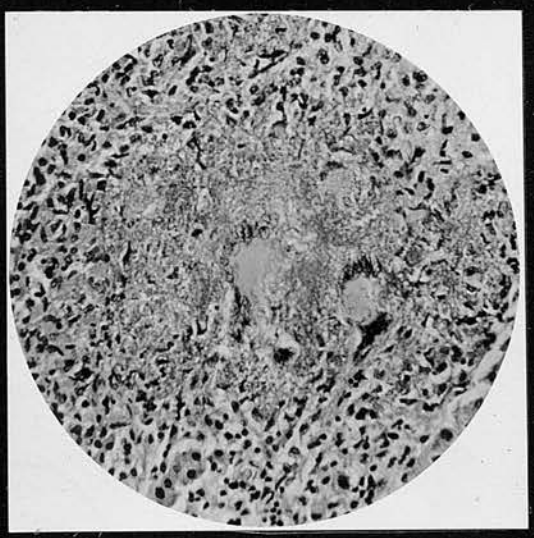

PLATE 2. X200

On admission in February 1936 the patient was ill with much cough and sputum, loss of weight, poor appetite and a low blood pressure. The serum sodium was 320 at this time, falling to 312 in July. During August patient first complained of headaches and periodic vomiting. These symptoms were present intermittently until October when patient died fairly suddenly from meningeal tuberculosis. Pigmentation of the face, neck, arms and hands was noted in August and it increased in degree. The serum sodium 9 days prior to death was 293 and the severe meningeal symptoms began 2 days after this estimation.

Animal inoculation of a piece of the right suprarenal was negative. On section there was a small area of lymphocytic infiltration in the right cortex with congestion between the cortical cells. Congestion was present in the cortex of the left suprarenal which in addition showed a well developed tuberculous lesion at one pole. Vide Plade II.

It seems probable that in this patient blood spread of the bacilli occurred sometime between February and August, some of the organisms implanted in the brain or meninges producing cerebral symptoms.

The lesion in the left suprarenal is obviously not recent and it is probable that deposits of the bacilli in the nervous system and suprarenal gland occurred at the same time, that is before August 1936. The symptoms suggestive of Addison's disease appeared after this, indicating insufficiency of cortical secretion yet at autopsy the lesions in the glands were small. They must have upset the secretion of cortical cells producing a case of early Addison's disease in which, but for the sudden death from meningeal complications, a typical picture would have developed.

There seems little doubt that in case 9, the intestinal lesion, the anorexia and the ileo-transverse colostomy caused the lowering of the serum sodium. The sodium intake was markedly reduced and absorption from the caecal region would be decreased by both the

tuberculous lesion and the short circuit operation.

In case 10 a low serum sodium was obtained on admission, symptoms other than local pulmonary and laryngeal were not prominent. Blood pressure was low. His condition gradually deteriorated and a serum sodium estimation done shortly after a profuse haemoptysis showed a definite rise. The patient was very collapsed at this time and had drenching night sweats. A blood count revealed only a slight microcytic anaemia. Unfortunately an autopsy was not granted. The reason the the original low result is not evident and the only cause I can suggest for the terminal increase is that there was haemoconcentration following the loss of blood.

A tentative diagnosis of Addison's disease complicating pulmonary tuberculous was made in case 11, but antopsy revealed no evidence of a suprarenal lesion. Suggestive symptoms were present such as asthenia, emaciation, low blood pressure 88/60 and a very low serum sodium of 285 mgms.

There was a moderate degree of anaemia and a 'septic' white count. Of all cases in the series this was the one most closely resembling Addison's disease yet no tuberculous lesion or atrophy was seen in the suprarenal glands. Cortical cells normally show great variation, but it was noted in this case that the cell nuclei and protoplasm stained poorly and toxaemia may have had some effect on the cells and produced a clinical picture of suprarenal insufficiency.

Cases 13 and 14 were not fully investigated.

In case 15 the serum sodium showed a marked fall when a pyothorax formed and during the time of a copious discharge from a sinus in the chest wall. The sodium content of this discharge was not estimated but doubtless he lost a large quantity by this route. The discharge continued until death, but a later result showed a rise in the serum sodium of 17 mgms. As in rapidly forming serous effusions, this pyothorax probably drained away some of the body sodium and

and upset the sodium balance but later compensation was attained and the serum sodium rose.

GROUP II. A. FEMALES.

This group contains 12 cases, in 5 of which the serum sodium was under 300 and under 305 in 10.

In 9 cases the blood pressure was low, being normal in cases 7, 11 and 12. Sedimentation rate high in all, and white count of the 'septic' type.

The serum sodium estimation in cases 1 to 4 was done within 6 weeks of death. All had intestinal tuberculosis, in addition to the pulmonary lesion, with severe persistent diarrhoea. Dehydration and emaciation were prominent features, one (case 4) showed pigmentation of the skin. In case 3 animal inoculation was positive being negative in the others. Section of the suprarenal glands was negative in all.

The level of serum sodium is similar to that obtained by McCance[32] in cases of persistent diarrhoea and this symptom is the most probable explanation of the low results. The relation of diarrhoea to the serum sodium has been discussed already and it was noted that some patients could apparently compensate for excessive sodium loss by this route. There is no evident reason for failure of compensation in these cases and in none was there any obvious suprarenal lesion to explain it.

A pyopneumothorax was present in case 5; the serum sodium was about normal but was not repeated during the last 3 months of life.

The two cases 6 and 7 are comparable in that both show a normal serum sodium at first with a marked fall following the onset of diarrhoea due to intestinal tuberculosis.

As a contrast to these two cases, case 8 illustrates how the level of serum sodium can be maintained despite the onset of equally severe gastro-

intestinal symptoms. Animal inoculation was positive.

The girl described in case 9 was ill throughout the period of investigation but was clinically improved in June, while in November there was dehydration, anorexia and vomiting.

Case 10 is an example of amyloid degeneration due to multiple tuberculous lesions with a septic focus in bone. The skin was smooth, dry and yellow in colour. The sections showed amyloid changes in the suprarenal glands but because of the many complicating factors it is difficult to ascribe any of the symptomsas due to suprarenal insufficiency. On admission case 12 showed a low serum sodium which rose to normal shortly before death. This girl had several severe haemoptyses. An interesting thing in this case was that a sister also showed a low serum sodium Group D. 1. This sister was clinically fit with a small quiescent lesion at one apex.

Case 11 was not fully investigated.

Of these 12 female cases only one was pigmented, animal inoculation of suprarenal tissue was positive in two, and of 10 autopsies only evidence of diseased suprarenal glands was seen in the sections of the case with amyloid degeneration.

SUMMARY OF GROUP A.

This group contains 37 cases and an autopsy was obtained in 25 of them. Of the ten deaths in group I three were acute due to reasons connected with operative treatment and one from a cardiac lesion. The remaining six died from chronic tuberculosis which for those in Group I gives a percentage mortality of 5.26%.

Symptoms were similar to those in group II cases but a low blood pressure was present in only one, one showed slight pigmentation, severe diarrhoea was present in three, and in one amyloid disease. Suprarenal section gave negative results

in all; in one of three inoculations a positive result was obtained.

In Group II there were 27 deaths; a mortality of 45%. Five showed pigmentation, nineteen a low blood pressure, and diarrhoea, vomiting or both in 10 cases. The low serum sodium estimation was obtained in sixteen within two months of death and was the only analysis made. A normal reading in five was low at a later period the decrease being attributed to severe gastro-intestinal symptoms.

Suprarenal tuberculosis was present in two cases and amyloid degeneration in one. Guinea pigs inoculated with suprarenal tissue revealed the presence of tubercle bacilli in Six. Serial section showed tuberculous lesions of the suprarenals in six, in four of minimal degree.

In two cases of haemoptysis the serum sodium taken shortly before death showed a rise to above 320 from the 300 level.

No detailed record of clinical data has been made of the remaining 137 patients but from the description of:- system affected, systemic upset, sedimentation rate and blood count a rough estimate can be made of the clinical condition and prognosis.

Any symptom or sign of particular importance will be mentioned as the cases are considered.

GROUP B. MALES.

The serum sodium is above 315 in 14 cases and below in 11. The table of averages (Appendix I) shows a similar blood pressure and sedimentation rate for both groups, but in Group I a better reaction of the white blood cells. Three in Group I had a low blood pressure, one a tuberculous bacilluria and one a serous effusion. Blood pressure was low in four Group II cases, a serous effusion present in two and a pyothorax in one. Systemic upset was present in most of the group B cases. In cases 3,5, and 14 Group I, sweating was complained of, drenching night sweats occurring in case 5. Cases 1,2 and 9

in Group II were also troubled with sweating. Pigmentation of the skin was not seen in any Group I case, but was present in cases 6 and 11 in Group II. In case 6 there is a deep brown pigmentation of the forehead, malar regions, axillae and hands. Patient has periodic attacks of anorexia, vomiting, generalised abdominal pain and diarrhoea. There is no evidence of intestinal tuberculosis, nutrition is moderate, blood pressure normal.

The second record of serum sodium was made during an exacerbation of symptoms, when vomiting and diarrhoea were severe yet the result had risen to above 315 mgms. This was considered as a case of early Addison's disease but unfortunately the patient elected to go home and his further progress has not been ascertained.

In case 11 the colour is more yellow than brown and effects the skin in all areas. The patient's condition has steadily deteriorated with loss of weight, asthenia, anorexia, severe cough, fall of blood pressure, increased sedimentation rate. Concurrently the serum sodium has steadily decreased and a recent reading not recorded in the tables, is down to 298 mgms. The very poor appetite suggests that diminished intake is the reason for the low results.

Of the other Group II cases, the patient in case I is very ill with a copious discharge from a pyothorax, through a sinus which followed rib resection.

The case resembles case 15 Group II,A. and it may be that sodium loss in the discharge forces the serum sodium down to a lower level. The constancy of this level has been shown by a more recent estimation which again was 311 mgms. Deficient intake was eliminated in this case by the use of a standard diet.

The very low result in case 7 was obtained while an effusion was collecting in the boy's abdomen.

The abdomen was distended, tympanitic round umbilicus but with a large quantity of fluid. The temperature rose in the evenings to 100° F and over.

The local condition settled spontaneously, the fluid was absorbed, the general condition improved greatly and the serum sodium rose to normal. Recently the boy was critically ill with consolidation at the left base, with a serous effusion from which tubercle bacilli were recovered and an estimation of serum sodium just after this settled gave a result of 309 mgms. In attempting to explain this low serum sodium three factors have to be considered.

1. The sodium content of the ascitic fluid was not ascertained, but from analogy with pleural effusions is is improbable that the total sodium content was high. On an adequate intake this would be compensated easily. The abnormal drain of sodium may have upset the sodium balance of the body.
2. Distention of the intestine was present and this may have produced a decreased sodium absorption. The intake was not unduly decreased as the child's appetite remained fairly good. There was no vomiting or diarrhoea. The serum sodium of 296 is much lower than that obtained by Gamble, Ross and Tisdale[34], in a fasting subject and while the sodium absorption may have been reduced it would be much above that absorbed during a fast.
3. The child's condition was definitely toxic and the toxaemia may have decreased the activity of the suprarenal glands.

No one of these causes will explain the very low result but the summation of the three acting concurrently may easily have done so.

On admission case 8 showed evidence of a local miliary spread in both lungs with a low serum sodium. He reacted well to treatment and the sodium level rose to normal. This man is very fond of salt, using about twice as much as normal. Estimation of sodium in the urine showed that he passes large quantities daily and his daily urinary output is about 2,500 c.cm.

Case 9 at first gave a normal reading, two months later a low one. This second record was made when patient was suffering with severe headaches and was considered as a probable meningitis. On lumbar puncture pressure was increased, cells, mostly lymphocytes, numerous, a trace of protein, no organism isolated. Patient was self-discharged shortly after and his further progress is unknown.

Case 10 has already been considered in reference to effusions. There is practically no clinical difference between these cases and those in Group I. B. In the latter group, Case I. had vomiting and diarrhoea, Case 5 night sweats, and marked anorexia was present in cases 6, 9, 11 and 14, Why these cases did not have a low serum sodium is not clear.

Of the female cases in group B, eight have a normal serum sodium and in three it is low. In both groups all have evening pyrexia, more marked in Group I. patients, most of whom are more acutely ill than the three in Group II. Of the latter, two have a low blood pressure, the average sedimentation rate is 48 and the white count shows that they are reacting to the infection. The reaction in Group I cases is less marked, being septic in two, the average sedimentation rate is 43, one has a low blood pressure. Of the cases in this group the first had anorexia nervosa, showing extreme emaciation with very slight pulmonary symptoms. So high a serum sodium was surprising in view of the reduced intake.

Case 2 has been mentioned already in connection with the complications of vomiting and diarrhoea. (Vide Tables I.2.) Despite the extreme severity of her symptoms the serum sodium has been maintained at a constant level near the lower limit of normal

The only other outstanding feature in Group I is the presence of a remittent temperature of 99° to 103° F. in Case 6.

In Group II. Case I. is an example of generalised tuberculosis due to the bovine bacillus, with commencing amyloid degeneration. Patient is thin, asthenia is not marked, appetite good, no vomiting or diarrhoea, pyrexia slight, and there are several discharging sinuses from vertebral lesions. The face is yellow, the fingers and hands brown, the skin smooth and thin. During 6 months of practically no change in general health, the serum sodium has risen from 298 to 314. 15 gms of sodium chloride was given daily for 10 days prior to the second estimation, but as the original level is unknown the record is of no value.

The patient in Case 2 showed great improvement during the five months interval between the first reading of 299 and the second of 324. She has a large cavity in the left upper lobe and on admission looked very toxic with a high swinging temperature. This gradually settled to normal, her general and local condition showing much improvement.

Case 3 is a girl of 14 years with an empyema of the right knee joint and a focus in the left lung. She is very thin and dehydrated but has no other abnormal symptoms.

There is nothingin any of these three patients to suggest suprarenal insufficiency.

SUMMARY OF GROUP B. CASES.

The Group contains 36 cases the serum sodium being above 315 in 22 and below in 14, four of whom have given a reading under 300.

None in Group I show pigmentation. Three have vomiting diarrhoea or both, one very severely, and in four the blood pressure is low.

In Group II three patients show slight pigmentation, one has gastro-intestinal symptoms, in six the blood pressure is low, three have serous effusions and three chronic purulent discharges.

Those cases with effusions and discharges gave the lowest values for serum sodium. It has been shown previously that an effusion is not always associated with a low serum sodium.

A diagnosis of early Addison's disease was made in one case but despite the continuation of symptoms a normal serum sodium level has been attained.

GROUPS C.AND D.

The remaining 101 patients may be considered collectively for in none were there any marked symptoms other than those referrable to the local lesion. The majority gave a normal serum sodium, 82 being in Group I and of the 19 in Group II, 5 subsequently were normal. Apart from the female (Group II.C.3.) already mentioned in discussing effusions, this increase of serum sodium was not associated with any marked clinical improvement. Is this their normal range of serum sodium? This seems improbable for in these groups results of 320 to 340 are much too constant to allow one to postulate so wide a range, even although the variation is only 5 to 6%. In none was there an obvious cause for a low serum sodium; there was no vomiting, sweating, pyrexia or diarrhoea.

One male and one female in Group I have a low blood pressure and two females in Group II. The average white count ratio shows evidence of a better reaction in Group II patients.

Sodium Balance.

The foregoing investigation has not considered the sodium intake, nor the quantity lost by normal routes such as sweat, urine and faeces. It was decided to investigate these points and for this purpose seven cases have been examined in detail. Unfortunately it has not been possible to estimate the sodium lost in sweat, a route through which large quantities of sodium may be excreted. It has been shown previously however, that patients with sweating did not have of necessity a low serum sodium.

METHOD OF INVESTIGATION.

A simple diet was chosen supplying about 3,500 calories daily and containing just over 5 grammes of sodium.

The following diet was given:-

Milk ℥ xl½ , Bread ℥ xx , Butter ℥ ℔

Cheese ℥ ℈ss , Eggs 4 , Apple 1

Sodium Chloride 2 gms, tea, sugar, jam as desired.

Unfortunately this diet did not suit all patients some being hungry on it, while others could consume only a fraction. Especially was this so with those who were very ill. All food returned was weighed, by subtraction the daily food intake obtained and the sodium content of this calculated.

The diet was given for five days, beginning on a Saturday. On Monday, Tuesday and Wednesday all urine excreted was collected for each 24 hours from 8 a.m. on Monday. The daily volume was measured and the sodium and chloride content of the urine estimated. On Wednesday morning blood was withdrawn for serum sodium estimation using the technique described previously.

On Monday morning a capsule of carmine alum lake was given before breakfast and another before

breakfast on Thursday morning. All faeces were collected from the first red stool until the first red stool from the Thursday dose, which was discarded. The sodium content of the stool was estimated. Only an infinitesimal quantity of sodium is normally lost in the faeces, but it was felt advisable to examine this, to exclude decreased absorbtion of sodium from the alimentary tract.

The sodium estimation in urine is done by a method similar to that for blood.

Urinary chloride was estimated as follows:-

To 5 c.cm. of urine add 100 c.cm. of distilled water and 10 c.cm. of 'silver nitrate solution'.

Titration against a thiocyanate solution until first salmon pink colour persists for a few seconds. The percentage is expressed in terms of chloride calculated as sodium chloride, the daily output as gms. of chloride.

SODIUM INTAKE.

An ordinary mixed diet contains from 5 to 10 gms of sodium, so that the above diet supplies an adequate quantity of sodium.

Experiments on fasting subjects by McCance[38], Gamble, Ross and Tisdall[34], show that the level of sodium in the serum can be maintained near normal on a greatly reduced sodium intake. Evidently the body could compensate for this reduced intake, but it should be noted that the period of investigation was short, under 14 days. Patients in the later stages of chronic pulmonary tuberculosis frequently have marked anorexia, with the result that for several months their sodium intake is reduced. Even in the worst cases this reduction is never comparable to that used in experimental fasts where only ·01 gm. of sodium daily may be given.

SODIUM EXCRETION.

On an ordinary mixed diet containing 7 to 10 gms. of sodium daily, the daily urinary loss is from 6 to 7 gms.

Experimenting on dogs Loeb et alia[8] found that 'balance studies show a striking loss of sodium from the body during the development of suprarenal insufficiency. This loss of sodium results from an increased excretion of sodium in the urine'. McCance[32] concludes 'that in the absence of cortical hormone the renal threshold to sodium falls.'

This suggests that if a low serum sodium is due to suprarenal insufficiency in cases in the previous series, then there will be an increased urinary sodium loss.

CONSIDERATION OF RESULTS.

Seven cases have been investigated and the results are recorded in Table V. P43. All of these cases are not included in the first series, but the three (cases 1,3 to 4) with a low serum sodium have been examined in detail already.

Case 1. W.J. is the boy of 12 years who had ascites and later a pleural effusion. During this examination his clinical condition was greatly improved, pulse and temperature quiet and no effusion present. Case 3. J.D. is the man with a sinus in his chest and a purulent discharge. This was slight during the investigation.

The clinical condition of G.D., Case 4, has deteriorated, his appetite is poor, he vomits a little each day and has night sweats.

The sodium intake in these cases was reduced to about half the normal value, but to balance this the urinary sodium excretion was low.

In case 4 with an intake varying from 2.15 to 2.81 the urinary sodium loss is 1.49, .513 and .664, This is certain evidence that there was an attempt to retain sodium, probably to compensate for the loss in vomitus and sweat. Case 1. also shows this reduced sodium excretion. This suggests that with a low serum sodium, the serum value falls below the normal renal threshold so that there is a diminished urinary excretion. It is probable, however, that the

renal threshold falls first and that the serum sodium level is adjusted to a lower level.

Case 4. has symptoms similar to those in Addison's disease, asthenia, low blood pressure, commencing pigmentation of the skin and a low serum sodium. Although there is a low sodium intake, and the reduction is not excessive, I am not willing to admit that even such a low excretion of sodium would be permitted in the presence of a low serum sodium, if the suprarenal glands were functioning normally.

Although Case 1. shows no suggestive symptoms of Addison's disease this argument still applies. In Case 3. despite the low serum sodium the kidneys continue to excrete most of the ingested sodium, which shows that there is no retention to raise the serum levels.

The sodium intake was normal in the other four cases and in cases 2,6 and 7 the daily urinary excretion is comparable to the intake. Their clinical condition is moderate, the only complication being a pleural effusion in case 2. During the month preceeding the investigation over 3 cc of serous fluid were aspirated from this man's chest and fluid is still gathering slowly. This case refutes the previous suggestion that a rapidly forming serous effusion causes a low serum sodium.

Case 5 has been recorded already as having night sweats. The low sodium excretion on the third day may have been to compensate for excessive sodium loss in the sweat, although patient said sweating had been no worse than usual on the previous nights. Despite this loss of sodium, the level in the serum remains high, indicating that his suprarenal glands are controlling the sodium balance in the body.

Ratio of Sodium to chloride excretion.

Loeb[8] states 'that' the behaviour of the chloride ion following adrenalectomy parallels that of the sodium ion'. The ratio $\frac{Na}{Cl}$ shows this to be true in

the urines examined, for it remains remarkably constant round 1/1·6.

This suggests that an easy way to assess the urinary sodium would be to estimate the daily chloride in the urine. This record divided by 1·6 would give a rough estimate of the sodium excreted.

FAECES

The normal faecal sodium loss varies from about ·03 to ·08 gms. per day and the above cases have not shown any evidence of increased loss. The loss is so small as to be negligible.

DISCUSSION.

In this investigation 174 tuberculous patients have been examined from the point of view of clinical features suggestive of Addison's disease, with special reference to the level of the sodium in the blood serum. In view of recent findings in Addison's disease, especially those of Loeb and Harrop it was felt that the serum sodium would be the best biochemical index of suprarenal deficiency. In Addison's disease the level of the serum sodium falls, this decrease being independant of anorexia, vomiting or diarrhoea.

The first difficulty was to decide the normal range for serum sodium, for that given in the literature was wide, but after due consideration of this and records obtained in control groups it was decided to assess the normal range as 315 to 350 mgms. sodium per 100 c.cm. of serum.

The patients were then divided into groups above and below the level of 315.

The/

The distribution of the two groups is of interest.

	Dead.	Ill	Moderate and Well.
Group 1 (above 315)	10	22	82
Group 11 (below 315)	27	14	19

for it shows that in Group 1 only 28% are dead or ill compared with 68.3% in Group 11. In this latter group the serum sodium estimation in 15 was made within two months of death and is a record of a terminal condition. Omitting these cases the percentage dead or ill is still high, namely 43.3%. This indicates that in most cases a low serum sodium is of serious prognostic significance.

Examination of these low results shows that the serum sodium is under 305 in 32 cases, in 17 of which a record under 300 was obtained. These results are very different to those obtained by Sunderman[36] whose lowest was 317 in a case of miliary tuberculosis, mostly pulmonary; the level of sodium in the serum is comparable to that in Addison's disease.

Is a low serum sodium evidence of Addison's disease? A priori the answer is no, for in many other conditions the serum sodium falls. Vomiting, diarrhoea and sweating are symptoms known to produce such a result. Such symptoms are common in tuberculous patients and they were investigated in an attempt to assess their effect.

In many cases it seemed that these symptoms did cause a fall in serum sodium, but in others despite equally severe symptoms the normal level was maintained. Apparently some could compensate for an excessive sodium loss, while others failed to do so.

Certain cases with a pleural effusion or a purulent discharge give low serum sodium records, and it was thought at first that rapidly forming effusions temporarily upset the sodium balance in the body. In view of the findings in a more recent case this theory cannot be upheld.

Any of the symptoms just mentioned may contribute in the production of ~~the~~ a low serum sodium, but obviously they are not the whole cause. Some other factor must be present enabling certain patients to compensate abnormal sodium loss.

There are three important factors which influence the sodium metabolism.

1. Low intake of sodium.
2. Increased excretion of sodium in the urine.
3. Failure to absorb sodium from the gut.

This last factor was thought to be important only in one case in the series and during the balance studies estimation of sodium in the faeces showed no evidence of deficient absorbtion. Unfortunately intake and excretion were not assessed during the main portion of the thesis, and deductions must be drawn by analogy to the later cases.

During the terminal stage of pulmonary tuberculosis anorexia is usually extreme and was present in most of the 15 cases examined during the last two months of life.

In the balance series it is seen that the case with a very low serum sodium has a diminished sodium intake, loses sodium in vomit and sweat and to compensate decreases the urinary excretion. As already stated this does not explain the low serum sodium, for with a normal sodium control, excretion would be even further decreased to allow the serum level return to normal. If the suprarenals have as one of their functions the control of serum sodium level, and one cannot question that at present, then continued sodium loss, however small, in the face of a low serum sodium, means suprarenal damage. This factor is probably the main cause of a low serum sodium, even in those cases with vomiting, anorexia, etc. Of the cases with anorexia I feel sure that the sodium intake never fell below a level adequate for normal sodium metabolism.

The cause of this suprarenal damage has not been clearly demonstrated and in only three cases did autopsy findings confirm a diagnosis of suprarenal insufficiency.

The two factors most liable to damage the suprarenal cells in these tuberculous patients are:-

a. Toxaemia

b. Suprarenal tuberculosis.

(a) Toxaemia.

The high percentage of dead and ill in the low serum sodium group suggests that their condition was highly toxic, which is undoubtedly true, but in the normal group, apart from the four cases of sudden death, patients dead or ill were equally toxic. This is evident on examining the sedimentation rate and white blood cell ratio.

Toxaemia might influence sodium metabolism in many ways, by causing anorexia, vomiting or sweating, by its action on the cells of the suprarenal glands. Of all the glands examined by section, in none could it be said that there was definite evidence of degeneration of the cortical or medullary cells.

It should be noted that in 19 cases with a low serum sodium there was no evidence of toxaemia. The fall was slight in these cases, the general average being 310 mgms and in several a later estimation was normal.

There is no evidence to support the contention that in these cases the low value was obtained because of a tuberculous lesion of the suprarenal glands, which at a later date healed. In none of the sections examined was there evidence of a healed tuberculous lesion, although the presence of calcification which is known to occur is evidence that a lesion in the gland can heal.

The three cases with amyloid disease may be included in this toxaemia group. Two are dead, in one autopsy revealed infiltration of amyloid into the cortex. In the other no autopsy was

obtained. The patient still alive has symptoms suggestive of suprarenal involvement and the serum sodium is low.

This evidence does not prove that toxaemia produced suprarenal damage in these tuberculous patients, but although autopsy evidence was inconclusive, no cellular degeneration being detected, toxaemia cannot be completely excluded.

b. Suprarenal Tuberculosis.

In ten cases evidence was obtained that the suprarenal glands contained tubercle bacilli, such cases occurring, with one exception, in those with a low serum sodium. In all save two of these cases the deposit of bacilli was considered terminal. The two definitely positive showed clinical evidence of suprarenal insufficiency and were diagnosed as cases of early Addison's Disease.

A similar diagnosis was made in two other patients, one of whom is untraced and the other had no evidence of suprarenal disease at autopsy.

The number of cases with a low serum sodium proved to have a pathological suprarenal lesion is thus low, but it is thought that the glands function might easily be upset without showing a definite lesion on section. The factor causing this upset of suprarenal function has not been detected. Symptoms suggestive of suprarenal insufficiency predominated in those with a low serum sodium, while the most striking symptom, namely pigmentation of the skin, was present only in this group.

In conclusion it may be stated, that in the absence of factors such as severe vomiting, or diarrhoea, a low level of sodium in the blood serum is suspicious evidence of suprarenal insufficiency.

SUMMARY.

1. Evidence of suprarenal insufficiency has been sought in 174 patients with tuberculosis.

Clinical features have been examined and the

level of sodium in the blood serum investigated.

2. Serial sections of glands obtained at autopsy showed suprarenal abnormality in eleven patients.
Serum sodium above 315.

Three autopsies.

One positive inoculation for tubercle bacilli.

Serum sodium below 315.

Twenty-two autopsies.

Seven positive on inoculation for tubercle bacilli.

Serial sections.

Two definite tuberculous lesions.

Four small tuberculous foci.

One amyloid degeneration.

3. Suprarenal insufficiency was diagnosed in four patients, two showed tuberculous lesions of the suprarenals, in one there was no evidence of disease in the glands, while the other is untraced.

4. The normal range of sodium has been assessed as 315 to 350 mgms per 100c.cm. of serum.

5. In 114 cases the level of serum sodium was normal.

In 60 cases the level of serum sodium was low.

6. A low serum sodium indicates a bad prognosis.

7. Such suprarenal lesions as were found, occurred, with one exception, in Group with low serum sodium.

8. Pigmentation of the skin was present only in the group with a low serum sodium.

9. Cases with pyrexia, sweating, diarrhoea or vomiting did not have of necessity a low serum sodium.

10. There is no proof that serous effusions or purulent discharges can drain away sufficient sodium to account for the low level, nor that they upset the sodium balance.

11. There is no evidence that cases with a low serum sodium had a low enough sodium intake to explain the decreased serum level.

12. Even with a low sodium intake there is an appreciable loss of sodium in the urine.

13. In the presence of a low serum sodium continued excretion of sodium in the urine suggests suprarenal damage, even with a low intake.

14. In the absence of factors such as severe vomiting or diarrhoea a low serum sodium is suspicious evidence of suprarenal insufficiency.

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REFERENCES.

1. FISHBERG, M. : PULMONARY TUBERCULOSIS,4th ED. VOL. II.P. 219
2. BAUMON,E. J. & KURLAND, S. : JONR. BIOL. CHEM. 1926 LXXI. 281.
3. MARINE , D. & BAUMAN,E. J. : AMER. JONR. PHYSIOL. 1927, LXXI. 86
4. STEWART, J.M. & ROGOFF, J.M. : IBID. 1928. LXXXIV. 649
5. SWINGLE, W.W. & Pfiffiner, J.J. : SCIENCE LXXI, 321.
6. BRITTON, S.W. & SILVETTE, H. : AMER. JONR. PHYSIOL. 1931. XCIX. 15.
7. LOEB, R.F. : SCIENCE 1932. LXXVI. 420.
8. " " : JONR. EXP. MED. 1933. LVII. 775.
9. ROWNTREE, L.G. : JONR. AMER. MED. ASSOC., 1925, LXXXIV. 327.
10. HARROP, G.A. ET ALIA : IBID. 1933. C. 1850.
11. GUTTMAN, P.H. : ARCH. PATH. 1930 P.742.
12. CLARK, R. & ROWNTREE, G. : ENDOCRINOLOGY 18
13. COLTON, W. A. : AMER. REV. TUB. 1935. XXXI, 333
14. SIMPSON, S. Levy : BRIT. MED. JONR. JAN. 1937, 229.
15. SPENCE, A.W. : IBID. FEB. 1937, 279
16. FISHBERG, M. : PULMONARY TUBERCULOSIS, 4th ED. Vol. I. P. 219.
17. NOLAN, L. E. : MED. BUL. VETERANS ADMINISTRATION 1932.
18. COREY, E.L. & BRITTON, S.W. : AMER. JONR. PHYSIOL. 1932. 102.
19. ALLOTT, E.N. : THE LANCET, JUNE 1936. 1406.
20. SIMPSON, S. LEVY. : QUART. JONR. MED., 1932. 25. 121
21. LOEB, R.F. ET ALIA : JONR. AMER. MED. ASSOC. 1935. CIV. 2149.
22. BUTLER & TUTHILL : JONR. BIOL. CHEM. 1931. XCIII. 171.
23. ROLLESTON, H. : THE LANCET, 1933 i. 519.
24. WESTERGREN : BRIT. JONR. TUBER. 1921. XV. 72
25. TRAILL, R.R. : THE LANCET, Mar. 11th 1933.
26. FLINN, J.W ., & R.S. : AMER. REV. TUBERC. 1929 . 347.
27. SABIN, F.R. : BULL. JOHN HOPKINS HOSP. SEPT. 1923.
28. MEDLAR, E.M. : AMER. REV. TUBERC. 1929 XX, 312.
29. DAILY : JONR. BIOL. CHEM. 1931. XCIII. 51
30. GUTTMAN, P.H. : JONR. CLIN. INVEST. 1936. 15, 475.
31. KEYS : JONR. BIOL. CHEM. 1936. CXIV. 449
32. McCANCE, R.A. : THE LANCET, 1936 ; i. 708
33. ROURKE, D. : JONR. BIOL. CHEM. LXXVIII. 337
34. GAMBLE, J.L., ROSS & TISDALL : IBID LVII 633
35. KERR & LENDRUM : BRIT. JONR. SURG. 1935-36 615
36. SINDEMAN, AUSTIN & CAMACHE : JONR. CLIN. INVEST. 1928, 6., 37
37. BAND, D. & MUNRO, W.T. : EDIN. MED. JONR. 1935. XLII, 162
38. McCANCE, R.A. : THE LANCET, 1936; i. 826.

TABLE V.

No.	Name	Date	Sodium Intake grms	Serum Sodium mgms/ /100c.m.	Daily Volume of urine c.cm.	Specific Gravity	Cl. as Na.ce inurine %	Daily Excretion of chloride gms.	Sodium in Urine %	Daily excretion of sodium gms.	Ratio $\frac{Na}{Cl}$	Faecal sodium in gms.
6	O.M.	24.9.37	5 gms		870	1023	.86	4.54	.327	2. 85	1/1.58	
	do.	25.9.37	daily		1185	1020	.82	5.9	.3065	3.63	1/1.6	.016
	"	26.9.37		315	915	1023	1.07	5.936	.405	3.71	1/1.6	.016
7.	J.T.	24.9.37	5 gms		1265	1019	.86	6,604	.325	4.11	1/1.6	
	"	25.9.37	daily		1580	1013	.61	5.85	.242	3.7	1/1.58	
	"	26.9.37		325	1555	1016	.78	7.363	.292	4.5	1/1.63	.026.

TABLE V

No.	Name	Date	Sodium Intake gms	Serum Sodium mgs. /100c.cm	Daily Volume of urine c.cm.	Specific Gravity	Cl. as Na. cl. % in urine	Daily excretion of chloride gms	Sodium in Urine. %	Daily excretion of sodium gms	Ratio $\frac{Na}{Cl}$	Faecal sodium in gms	Ref. App.I
1.	W.J.	17.9.37	2.8		485	1010	.47	1.387	.173	.84	1/1.65		
	"	18.9.37	to		1055	1016	.59	3.775	.221	2.32	1/1.63	lost	Gr.II M
	"	19.9.37	3.6	309	970	1016	.59	3.462	,197	1.91	1/1.8	.04	B.7.
2.	G. M.	17.9.37	5 gms		1470	1018	.74	6.604	.268	3.945	1/1.66	.043	
	"	18.9.37	daily		1170	1022	.805	5.917	.30	3.51	1/1.62	.013	
	"	19.9.37		323	1265	1022	.905	6.944	.338	4.28	1/1.62	lost	
3.	J.D.	17.9.37	2.8		990	1015	.59	3.544	.256	2.53	1/1.4	lost	Gr.II M
	"	18.9.37	to		1355	1014	.56	4.601	.2116	2.87	1/1.6	.028	B.1.
	"	19.9.37	3.3	311	905	1015	.61	3.35	.218	1.97	1/1.7	.050	
4.	G.D.	17.9.37	2.15		1250	1012	.31	2.367	.119	1.49	1/1.58	.050	Gr.II M
	"	18.9.37	to		960	1010	.215	1.177	.053	.513	1/2.29	lost	B II
	"	19.9.37	2.81	298	950	1010	.2	1.153	.069	.664	1/1.7	.016	
5.	W.F.	24.9.37	5 gms		1470	1014	.55	4.907	.206	3.03	1/1.6		Gr. I M
	"	25.9.37	daily		1340	1016	.62	5.038	.218	2.93	1/1.7	.069	B.5.
	"	26.9.37		333	620	1017	.73	2.743	.2515	1.56	1/1.75	.089	

APPENDIX I.

RESULTS.

GROUP I. MALES.

Serum Sodium above 315 mgms per 100 c.cm. of serum.

Subgroup A. Dead, - 7.

No.	Name.	System	Date	Serum Sodium	B.P.	S.R.	Red Blood Count	White Count	Ratio	Reference Appendix II
1.	J.A.	S. Spine+amyloid		317	80/50					Case 23
2.	A.G.	L_3		336						Air Embolus
3.	J.A.	L_3S + U		317	110/76	45	R.BC.-3,700,000 H6-74%.C.I.1.	23,400	75:1.8	Case 24
4,	R.M.	L_3		327						Air Embolus
5.	A.F.	L_3		330	116/76	9				Spont. Pneumo.
6.	W.B.	L_3S + Effusion		318	128/80	46				
7.	F.J.	L_3S + Arthritis		327	124/90	48				Case 26.

GROUP I. MALES.

Subgroup B. Ill,- 14.

No.	Name	System	Date	Serum Sodium	B.P.	S.R.	Red Blood Count	White Count	Ratio
1.	W.M.	L_3S		317	96/73	50	R.B.C.-5,300,000 H6-9%.C.I.:83	24,800	3:4
2.	J.G.	L_3S		329					
3.	P.S.	L_3S		324	104/76	29	R.B.C.-5,080,000 H6-82%.C.I.:8	16,800	3.8:1.4
4.	R.E.	L_3S		321	82/62	26	R.B.C.-5,760,000 H6-101%.C.I.:88	12,000	1.2:6.3
5.	W.F.	L_3S	10.2.36	321	105/75	34		11,600	3.4:3.5
			23.5.37	320	102/64	46			
6.	J.P.	L_3S		328	98/64	41	R.B.C.-4,780,000 H6-81% C.I:86	10,000	2.7:3.
7.	H.B.	Knee		318	104/68	60		17,800	.74:9.
8.	A.H.	L_3S+U+Glands		325	110/74	33		10,200	2.6:5.
9.	J.G.	L_3S		323	100/75	30		12,600	2.8:3.5
10.	T.McG.	L_3S		325	118/72	28		17,700	1.8:5.5
11.	G.M.	L_3S		321	112/80	36			
12.	R.I.	L_3S+ Effusion		322	115/85	44		24,200	3.3:4.4
13.	D.C.	L_3S		321	108/78	39			
14.	C.McF.	L_3S	13.5.37	317	116/71	44	R.B.C.-5,430,000 H6-94%.C.I.:9	15,800	1.5:7.4

GROUP I. MALES.

Subgroup. C. Moderate,- 18

No.	Name	System	Date	Serum Sodium	B.P.	S.R.	RED BLOOD COUNT	White Count	Ratio
1.	J.J.	L_3S + Knee		333	120/74	35	R.B.C.-5,030,000 H6-94%.C.I.94	8,400	5.7:2.3
2.	D.K.	L_3		337	140/72	16	R.B.C.-5,310,000.H6-100%.C.I.93	8,200	4.6:1.6
3.	J.P.	L_3		317	122/74	28	-	-	-
4.	A.A.	L_3		333	100/70	20	R.B.C.-5,960,000,H6-98%.C.I.83	15,600	5:2.7
5.	G.McK.	L_3 + U		325	115/62	25	+	-	-
6.	H.W.	L_3 + Glands		324	128/72	23	-	19,800	1.3:2.
7.	G.B.	L_3S+ Glands		347	102/76	9	-	9,400	1.7:7
8.	A.W.	L_3		315	124/76	16	-		
9.	J.S.	L_3s		317	152/68	16	R.B.C.-4,010,000 H6-94%.C.I.7	21,600	2.3:4
10.	H.C.	L_3		324	110/70	25		16,000	
11.	J.D.	Glands		326	114/74	11		12,800	2:4
12.	J.B.	L_3		323	124/74	24		10,800	3:2.5
13.	W.MacR	Hip		319	104/68	36		14,000	2:4
14.	T.L.	L_3		331		17		11,500	2:6.5
15.	J.W.	L_3		329		18		10,600	2.7:4
16.	B.McQ	L_3		320					
17.	T.G.	L_3		332 326	82/50	8 9	R.B.C.-4,840,000 H6-96%.C.I.1.	8,000	
18.	T.T.	Spine + Kidney		339	118/82	27			

GROUP I. MALES.

Subgroup D. Well,- 35.

No.	Name.	System	Serum Sodium	B.P.	S.R.	Red Blood Count	White Count	Ratio.
1.	J.C.	L_3	325	116/70	10	R.B.C.-5,880,000 H6-105%.C.I.·9.	10,100	7.4:1.6
2.	W.B.	L_3	317	100/72	3.5	R.B.C.-6,380,000 H6-104%.C.I.·82	9,800	2.2:3.6
			333		2.5			
3.	H.M.	L_3	330	122/78	8	R.B.C.-6,060,000 H6-96%.C.I. ·8	17,600	1.6:3.5
4.	A.McD	L_3	333	118/82	4	R.B.C.-6,090,000,H6-106%.C.I·88	9,000	
5.	J.R.	L_3	325	120/84	1	R.B.C.-5,530,000,H6-103%.C.I.93	16,200	2.2:2.8
6.	G.M.	L_3	322		11	R.B.C.-6,230,000,H6-98%.C.I. ·8	8,200	2.5:1.2
7.	D.McN	Tarsus	331		2.5			
8.	A.C.	L_3	335	120/70	4	R.B.C.-5,530,000,H6-104%.C.I·94	15,200	3:4
9.	Wm.S.	L_3	340	124/84	9			
10.	J.G.	L_3	334	130/80	16	R.B.C.-5,950,000,H6-103%.C.I.·88	8,200	1.6:2
11.	A.McK.	L_1	322	138/90	1.5	R.B.C.-5,630,000,H6-100%.C.I.·9	11,600	2.7:1.5
12.	F.C.	L_2	320	136/84	6		8,600	1.2:2.5
13.	F.M.	L_3 + Effusion	320	116/70	10	R.B.C.-5,000,000,H6-100%.C.I.1.	9,000	1.7:8.7
14.	T.H.	L_2	317	152/84	6		17,000	2:3.7
15.	G.L.	L_3	325	126/78	12	R.B.C.-5,540,000,H6-96%.C.I.·87	9,600	1.9:2.5
16.	J.A.	L_2	321	105/70	11		10,400	2.3:2.6
17.	J.S.	L_1	329	124/74				

Forward

Group I.Males. Subgroup D. Well-35. (Continued.)

No.	Name.	System		Serum Sodium	B.P.	S. R.	Red Blood Count	White Count	Ratio.
18	T.B.	Glands		322		9		9,600	1.2:4.
19.	J.G.	L_3		327	118/68	19	R.B.C.-5,770,000 H6-98%.C.I. ·86	10,400	2.3:4
20.	I.McE	L_3		335	130/70	4	R.B.C.-5,760,000 H6-104% C.I.·94	7,800	2.2:5
21.	J.W.	L_3		334	115/64	11	R.B.C.-5,300,000 H6-105% C.I. 1	5,800	2.2:2.8
22.	A.W.	L_3		325	115/70	9	R.B.C.-5,100,000 H6-95% C.I. ·93	6,200	1.4:6.3
23.	R.McV	L_3 + U		324	110/80	23		12,200	2.8:3.5
24.	W.P.	L_2		329		8		20,800	3.6:2.5
25.	R.McM	L_3		324	110/76	6		14,800	3.2:3.
26.	J.O'N.	L_3		322	110/84	5		8,800	2:4.4
27.	M.S.	L_3		332		10		18,600	3.7:3.3
28.	W.S.	L_3		325					
29.	D.T.			321					
30.	C.S.			319					
31.	W.T.			321					
32.	W.G.			328					
33.	R.W.	L_3 + U		333					
34.	J.S.			328					
35.	J.H.	L_3		340					

GROUP II. MALES.

Serum Sodium below 315 mgms per 100 c.cm. of serum.

Subdivision A. Dead-15.

No.	Name	System	Date	Serum Sodium	B.P.	S.R.	Red Blood Count	White Count	Ratio	Ref. Appendix I
1.	J.C.	L_3S + U	8.1.36	313						1
2.	P.C.	L_3S	15.1.36	298	85/68					2
3.	Wm.F.	L_3S	16,6.36	310	78/50	49		16,000	7:2.	3.
4.	J.T.	L_3S + U	29.6.36	305	115/84	61				4.
5.	J.D.	L_3S	"	305	100/64	44		20,000	7:1.	5.
6.	J.G.	L_3S + U	6.7.36	296	90/60	5				6
7.	J.G.G	L_3S + U		297	94/70	33				7
8.	A.M.	L_3S		306	92/66	56		11,200		8
9.	F.McG.	Hyperplastic	21.1.36	328	82/60	18	R.B.C.-4,300,00,H6.85%.C.I:98	4,200	3.3:1	
		Caecum S	15.9.36	284	75/52	18		3,000	1.3:3	16
10.	M.McI	L_3S	21.3.36	303	92/60	37				
			2.11.36	330	86/60	63	R.B.C.-4,500,000 H6.75% C.I:83	20,000	5.3:5	17
11.	F.D.	L_3S	25.1.37	285	88/60	56	R.B.C.-3,550,000 H6-70% C.I. 1	9,600	11:1.6	18
			22.2.37	296		52				
12.	M.McD.	L_3S+Meningitis	10.2.36	320	98/70	50				
			17.7.36	312		34	R.B.C.-4,930,000 H6-90% C.I. .9	13,600	2:6.2	19
			5.10.36	293	<.....>		C.S.F.Sodium.318 mgms/100cc.			

Continued/

GROUP II.- MALES

Subdivision A.- Dead.-15... (CONTINUED)

No.	Name	System	Date	Serum Sodium	B.P.	S.R.	Red Blood Count	White Count	Ratio	Ref. Appendix II
13.	R.K.	L_3S		312						No.P.M
14.	A.N.	L_3S		300						No P.M
15.	J.McB.	L_3S +	9.3.36	313	104/68	25	R.B.C.-4,870,000 H6-78% C.I.8	8,600	2:4	Case 27
		Pyothorax	25.1.37	291		50		16,000	7.5:1.8	
			10.6.37	308						

GROUP II. MALES.

SUBGROUP B. III.- 11.

No.	Name.	System	Date	Serum Sodium	B.P.	S.R.	Red Blood Count	White Count	Ratio.
1.	J.R.D.	L_3S+Pyoth: arax	23.11.36	309	98/72	52		17,600	7:2
			24.5.37	311	110/72	46	R.B.C.-4,720,000 H6-82%C.I.·87.	11,200	8.5:2
2.	T.R	L_3S		306	102/64	39	R.B.C- 4,590,000 H6-90%.C.I. 1·	6,600	4.5:1.8
3.	D.B.	L_3S +Effusion		300	110/70	26		9,600	2.4:2.6
4.	D.S.	L_3S		313	120/70	60			
5.	R.T.	L_3S		313	110/72	57	R.B.C.-4,290,000 H6-82%.C.I. ·98		
6.	R.R.	L_3S	25.1.37	306	110/72	35	R.B.C.-5,680,000 H6-105% " ·93	13,600	2.7:2.2
		L_3S	24.5.37	317	do.	34			
7.	W.J.	Abdomen+S	5.3.37	296	96/78	43		11,500	1: 7.6
		No S	3.5.37	320	do.	26	R.B.C.-5,290,000 H6-98%C.I. ·94	12,200	1:12.
8.	P.R.	L_3	9.3.37	309	148/90	23		16,200	3:1.6
		L_3	19.4.37	319		5		13,600	2:4
9.	Wm.S.	L_3S	10.2.36	324	120/78	50	R.B.C.-6,270,000 H6-83%C.I. ·7	16,200	1.8:13.
			28.4.36	313	98/72	49			
10.	J.P.	L_3S+Effusion	23.5.37	304		35	R.B.C.-4,470,000 H6-71%C.I. ·8	11,100	2.8:5
			10.6.37	303					
11.	G.D.	L_3S	9.6.36	324	134/90	54		15,200	1.6:1.3
			15.3.37	312	86/54	60		24,600	6:1.6
			24.5.37	301		64	R.B.C.-4,300,000 H6-81%C.I. ·94	13,800	4:1:2.6

GROUP II. MALES

Subgroup C. Moderate. 5.

No.	Name	System	Date	Serum Sodium	B.P.	S.R.	Red Blood Count	White Count	Ratio
1.	H.B.	Abdominal Glands		304	106/74	5		8,100	1.2:11
2.	J.T.	Genito-urinary		302	132/86	6			
3.	A.G.	L_3		314	120/74	34		16,200	2.3:2.5
4.	J.R.	L_3 + effusion		312	106/78	35		15,800	1.5:7.
5.	D.K.	L_3		311	114/75	28		8,800	2:5.8

Subgroup D. Well. 5.

1.	R.McK.	L_2		312	-	-	-	-	-
2.	Mm.B.	L_1		313	152/84	4.5	R.B.C.5,360,000,H6-93%.C.I.:88	14,600	1.7:6.
3.	T.N.	L_3	22.2.37	305	122/82	5		9,700	1.1:4.7
			10.6.37	330		5			
4.	J.I.	L_3	22.1.36	305	106/66	9	R.B.C.5,180,000,H6-97% C.I.:95	8,200	1.9:2.8
			17.3.36	343		7			
5.	J.McD.	L_3	24.2.36	309	120/80	1	R.B.C.-5,420,000 H6-104%.C.I:96	8,800	1.7:3.6
			2.6.36	338		1			

GROUP I. FEMALES.

Serum Sodium above 315 mgms per 100 c.cm. of serum.

Subdivision A. - Dead. 3.

No.	Name.	System	Date	Serum Sodium	B.P.	S.R.	Red Blood Count	White Count	Ratio	Ref. Appendix II.
1.	Mrs J.	L_3S+U+Abdomen		321	110/75	43	R.B.C,-4,740,000 H6-93%,C.I.98	15,800	2:6	No P.M.
2.	Mrs H.	L_3 +U+Mitral Stenosis		324	95/70	-	-	-	-	No P.M.
3.	M.A.	L_3S+U		318	110/78	35	R.B.C.-4,970,000 H6-100% C.I.1+	26,000	7:4	Case 25
		Subgroup B.		III - 8						
1.	C.P.	L_3S		332	100/64	40	R.B.C.-3,700,000-H6-70%C.I..94	6,600	2:4	
2.	H.W	L_3S + U +	9.3.36	318	105/75	68		17,800	6.7:2	
		Abdomen	29.3.37	317		72				
3.	Mrs F.	L_3S+U		330	82/60	45	R.B.C.-4,670,000 H6-77%C.I.·83	18,800	6:2.8	
4.	H.M.	L_3S		318	108/74	32	R.B.C.-4,960,000 H6-100% C.I. L	11,200	3.7:3.3	
5.	J.D.	L_3S		318	130/80	38		21,800	2:4	
6.	M.W.	LS + Abdomen		332	120/80	12	R.B.C.-4,200,000 H6-93% C.I. 1·1	8,100		
7.	D.F.	L_3S		318	118/76	38	R.B.C.-4,980,000 H6-100%C.I. 1·	14,600	2.5:4.5	
8.	J.M.	L_3S		320						

GROUP I. FEMALES.

Subgroup C. Moderate..13.

No.	Name	System	Date	Serum Sodium	B.P.	S.R.	Red Blood Count	White Count	Ratio.
1.	R.M.	Glands + U		319	122/72	16	R.B.C.-5,630,000 H6-95% C.I.·85	14,400	2.7:1.5
2.	I.E.	L_3+ U		326					
3.	R.W.	L_3		318	124/84	38			
4.	Mrs A.	Kidney		321	132/90	24			
5.	Mrs B.	L_2S+ Effusion		318	152/90	14		10,600	3.2:3.1
6.	M.D.	L_3		333	128/80	8		15,800	2.8:3.4
7.	M.M.	L_3S + U		323	130/76	15		16,600	1.6:4.3
8.	M.M.	L_2		318	102/68	11		15,000	2:8
9.	I.McF	Bilateral renal T.B.		328	118/78	14		6,800	.77:9.
10.	Mrs F.	L_3		326		16			
11.	Mrs R.	L_3		317		8			
12.	Mrs A.	L_3		320	124/80				
13.	M.L.	Glands		322	95/72			8,800	2:5.8

GROUP I. FEMALES.

Subgroup D. - Well ...16.

No.	Name	System	Date	Serum Sodium	B.P.	S.R.	Red Blood Count	White Count	Ratio
1.	B.N.	Spine		318	102/64	18			
2.	M.W.	L_3		338					
3.	M.W.	L_3		330	112/70	11	R.B.C-5,300,000 H6-103%.C.I.·98	8,000	1.6:3.5
4.	Mrs A.	L_3 + Effusion		318	90/74	27	R.B.C-4,580,000 H6-90%. C.I. 1·	9,200	.85:3
5.	J.F.	L_3		319	118/72	11	R.B.C.-5,440,000 H6-114%C.I.-1 +	12,200	1.2:5
6.	M.T.	L_3		330	118/86	6			
7.	Mrs M.	L_3		322	104/70	11			
8.	J.McN.	L_3+effusion		317	118/72	6	R.B.C.-5,210,000 H6-96%.C.I.·95	11,000	2:3
9.	J.K.	L_3		329	106/74	12	R.B.C-4,710,000 H6-93%.C.I. ·98	11,600	2,1:3.2
10.	B.B.	L_3		318	118/90	4	R.B.C-5,220,000 H6-110%.C.I.1+	16,500	2.7:3
11.	E.S.	L_3		329	110/73	5		13,800	1:5
12.	J.S.	Abdomen		322		4			
13.	Mrs A.	L_3 + U		320	105/65	23			
14.	Mrs M.	Abdomen		320	120/82	2		10,100	2.8:8.6
15.	J.S.	L_1 + Abdomen		319	110/68	3		9,900	1.7:18.
16.	Mrs M.	Pyo+salpinx		323	126/78	5		9,400	2.8:2

GROUP II. FEMALES.

Serum Sodium below 315 mgms per 100 c.cm. of serum

Subdivision A. Dead 12.

No.	Name	System	Date	Serum Sodium	B.P.	S.R.	Red Blood Count	White Count	Ratio	Ref. App. II.
1.	H.M.	L_3S + U	22. 1.36	301	70/50					Case 9
2.	R.W.	L_3S	24.2. 36	301	75/50					Case10
3.	C.C.	L_3S + U	2.3. 36	301	78/58		R.B.C.-4,630,000 H6-47%.C.I.·5	19,400	5.6:0	" 11
4.	Mrs McA	L_3S	28.4. 36	286	82/60	60				" 12
5.	Mrs D.	L_3S + U	23.11.36	314	90/74	26		15,800	11:1.6	" 13
6.	J.A.	L_3S + U	24. 2.36	330	100/70	67	R.B.C.-3,810,000 H6-75%.C.I.·95			
			2.11.36	282	96/60	68		20,600	4:6	" 14
7.	Mrs B	L_3S + U	2. 3.36	326	110/72	33				
		- Abdomen	13. 7.36	300						" 15
8.	A.G.	L_3S + U	13. 7.36	315	90/66	50	R.B.C.-4,030,000 H6-72%.C.I.·9			
		- Abdomen	2.11.36	312	85/64	64		6,000	2.5:1.8	" 20
9.	E.McF.	L_3S + U	2. 3.36	297	94/68	35	R.B.C.4,180,000-H6-94%.C.I.1+			
			2. 6.36	321		23		16,000	4:4.5	
			2.11.36	293		44				" 21

Continued.

Group II. Females. (Continued.)

Subdivision A. - Dead 12. (Continued.)

No.	Name	System	Date	Ser. Sod.	B.P.	S.R.	Red Blood Count	White Count	Ratio	Ref. App. II.
10.	A.McK	Mandible + U+	2.3. 36	322						
		Abdomen+Spine	4.5. 36	305	84/60	84	R.B.C.-2,150,000 H6-44%.C.I. 1+			
		Amyloid + S	25.5.36	312				7,400	1:3.7	
			9.6.36	302						Case 22
11.	A.M.	L_3S		304	105/80					No P.M.
12.	J.B.	L_3S	6.4.36	300	110/72	55	R.B.C.-5,410,000 h6-93%.C.I.·9			No P.M.
	B to A		13.5.37	320		35		7,800	2.8:2.5	

GROUP II. FEMALES.

Subgroup B. III - 3.

No.	Name	System	Date	Serum Sodium	B.P.	S.R.	Red Blood Count	White Count	Ratio.
1.	E.M.	Spine, Abdomen	21.4.36	298	97/68	61	R.B.C.-3,640,000 H6-61%.C.I. ·84	13,200	2.6:4
		Kidney, Lung	25.5.36	309	104/68				
		Amyloid	5.10.36	314	96/68	56			
2.	L B.	L_3S	2.11.36	299	105/68	58	R.B.C.-4,400,000 H6-86%.C.I. ·97	7,500	2.3:4
		L_3	26.4.37	324	do.	50		13,200	
3.	E.R.	Knee + L_1S		306	96/64	18	R.B.C.-5,000,000 H6-90%.C.I. ·9	14,000	3.8:4
			Subgroup C.-		Moderate.-6				
1.	M.Y.	L_3		313	102/12	14	R.B.C.-5,060,000 H6-93% C.I. ·93	14,000	2.1:4.3
2.	E.J.	L_3 + U	16,3.36	313	112/60	7	R.B.C.-4,890,000 H6-94%.C.I. ·98	9,200	1.7:4
			29.3.37	325	92/62	5		10,000	2:4
3.	J.P.	L_3+effusion	28.4.36	311	84/64	15	R.B.C.-5,190,000 H6-91%.C.I. ·89	12,200	2:3
			29.3.37	324	98/64	4		14,000	1.2:7
4.	B.B.	Abdominal Glands		309	104/70	26		8,600	1.7:3.2
5.	Mrs P.	L_3		310	100/66	28		14,800	1.9:6.6
6.	J.S.	L_3		304	114/68	13		15,400	3.1:4.6

Continued.

GROUP II- FEMALES. (Contd.)

Subgroup D. - Well, 3.

No.	Name	System	Date	Serum Sodium	B.P.	S.R.	Red Blood Count	White Count	Ratio
1.	A.B.	L_1		309	122/78	6	R.B.C.-4,850,000,H6-96% C.I. 1-	9,600	1.5:4
2.	A.G.	L_3		314	128/84	5		7,200	1.4:8
3.	M.K.	L_3		313	110/70	6		11,000	2:8

AVERAGES.

Males:-

Group:I. Serum Sodium above 315 mgms per 100 c.cm. of serum.

Total:- 74.

Subgroup	Total Number	Serum Sodium	B.P.	S.R.	Ratio
A.	7	324	112/74	37	. . . .
B.	14	322	105/72	36	2.4:4.8
C.	18	327	117/71	20	2.8:3.8
D.	35	327	121/76	8	2.5:3.4

Group II. Serum Sodium below 315 mgms per 100 c.cm. of sodium.

Total:- 36.

Subgroup	Total Number	Serum Sodium	B.P.	S.R.	Ratio.
A.	15.	301	90/64	43	5.3:3.
B.	11.	306	107/71	44	4.3:2.9
C.	5.	309	116/77	22	1.9:6.6
D.	5.	309	125/78	49	1.6:4.3

AVERAGES.

Females. :-

Group I. Serum Sodium above 315 mgms per 100 c.cm. of sodium.

Total.- 40.

Subgroup	Number	Serum Sodium	B.P.	S.R.	Ratio
A.	3	321	108/76	39	4.5:5
B.	8	323	109/74	43	3.8:3.3
C.	13	322	122/79	16	2.1:5
D.	16	323	110/74	10	1.8:5.8

Group II. Serum Sodium below 315 mgms per 100 c.cm. of serum.

Total - 24.

Subgroup	Number	Serum Sodium	B.P.	S.R.	Ratio
A.	12	302	89/64	49	4.8:2.8
B.	3	305	104/69	47	2.8:3.6
C.	6	310	105/65	17	2.25:4.3
D.	3	312	113/77	6	1.6:6.6

APPENDIX II

CASE REPORTS

CASE I

J.C. Male. Age 29 years.

Admitted - 23. 3. 35.

Died - - 10. 1. 36.

History,-

Always fit as a school child.

First began to feel unwell in 1928 when he was more easily tired than usual and lost weight.

In 1929 forced to leave police force because of severe cough with sputum.

In a sanatorium from 1930 to 1931.

Recently not so well, easily tired, short of breath on exertion, severe cough with sputum.

Indigestion with loss of weight.

Examination,-

Sputum T.B. -/-/-

Tall, spare, hollow cheeks

cyanosed.

Extensive disease of left lung with cavitation in upper lobe.

Infiltration with breaking down on right.

Course. Disease slowly progressive with much cough, and sputum, fast pulse and hectic temperature.

Gradually increasing asthenia.

Asthenic death.

8. 1. 36. Serum Sodium 313 mgms per 100 c,cm

Autopsy.

No animal inoculation.

Pathological Examination.

Area of small celled infiltration in right suprarenal.

CASE 2.

P.C. Male Age 27 years.
Admitted - 12. 8. 35.
Died - 10. 2. 36
History,-

Always well until 1933 when off work with influenza.

No cough after it.

In March 1935 more easily tired than usual.

Cough with sputum began then, he had a small haemoptysis at this time and cough rapidly became worse.

Night sweats began at this time.

Lost over 2 stones in weight recently.

Examination,-

Sputum T.B. +++

Pale and thin. Looks ill.

Extensive active disease throughout right lung and in left upper lobe.

B.P. - 85/58

15.1.36 Serum sodium - 298 mgms per 100 c.cm.

Course. Progressive emaciation.

Severe cough and much sputum.

Hectic temperature.

Asthenic death with subnormal temperature for ~~at~~ least few days.

Antopsy.

No animal inoculated.

Pathological Examination.

Three small foci of small celled infiltration in cortex of right suprarenal.

CASE 3.

Wm.F. Male Age 32 years.
Admitted - 10.6.36.
Died - 3.7.36

History,-

Admitted in extremis.
Very weak and voice almost gone.
Cough with sputum for many years.
Dysphagia recently.

Examination, Sputum T.B. +/+/+

Skin of face, arms and trunk yellow brown colour.

No pigmentation of mucous membrances.
Marked emaciation, clubbed fingers.
Exudative disease throughout both lungs.
B.P. - 75/50.

16.6.36 Serum Sodium - 310 mgms per 100 c.cm.
S.R. - 49 mm
W.B.C. - 16,000
Polymorphs-82%. Lymphocytes-12%
Hyalines - 6%
Ratio - 7:2

Course.

Increasing emaciation and asthenia.

For 7 days preceeding death subnormal temper-:ature.

Respirations remained at about 24.

Asthenic death.

Autopsy.

Guinea pig positive from right.

Pathological Examination.

Left adrenal had a tuberculous focus in the cortex. ·4 mm. by ·2 m and was present in 18 sections.

Central necrosis, with endothelial and giant cells round about and a small celled infiltration.

Neighbouring cortical cells swollen and nuclei stain poorly.

Two other areas of small celled infiltration.

CASE 4.

J.W.T. Male. Age 49. years.

Admitted - 20.6. 36.

Died. - 15.7. 36.

History.

Sailing Engineer for 30 years and save for winter colds has always been healthy.

In December 1935 attack of influenza with cough and sputum.

Cough persisted and during January 1936 his voice became rough, and later hoarse and weak.

In May a biopsy on larynx and tuberculosis diagnosed.

Dysphagia ever since, all symptoms being much worse, cough increased, some sputum.

Increasing languor, dyspnoeic, night sweats and loss of 18 lbs in 6 weeks.

Examination.

Pale, ill looking.

Unproductive, bovine, cough.

Marked systemic upset.

Old lesion in left upper lobe and miliary spread throughout both lungs.

Ulceration of arytenoids and both vocal cords.

Epiglottis swollen.

Sputum T.B +++

Urine T.B. +

29.6.36 B.P. - 115/84

" Serum sodium- 305 mgms per 100 c.cm.

" S.R. - 61 mm.

W.B.C. - —

Course.

Hectic temperature.

Rising respiratory rate and broncho-pneumonic consolidation .

Contd.

Case 4 (Continued.)

Antopsy.

Animal inoculation positive.

Pathological Examination.

Area of small celled infiltration in right suprarenal cortex.

Large tuberculous mass in right kidney.

CASE 5.

J.D. Male. Age 16 years.
Admitted - 8.6.36.
Died - 14.7.36.

History.

Always healthy as a child.

Started work in coal mines age 14 years.

3 months ago an attack of pleurisy on left side of chest and was off work for 9 weeks.

No cough, no night sweats then but felt very tired.

Worked for 2 weeks but stopped because of severe cough.

Now dyspnoeic, voice hoarse.

Night sweats and loss of weight.

Examination.

Emaciated, pale, worn and tired looking.

Dyspnoeic, some cyanosis.

Dry, parched tongue and cracked lips.

Hectic temperature.

Broncho-pneumonic lesion of left lower lobe.

Sputum T.B. +++

29.6.36 B.P. - 100/64
" Serum sodium - 305 mgms per 100 c.cm.
S.R. - 44 mm.
W.B.C. - 20,000
- Polymorphs-78%.Lymphocytes-11%.
Hyalaines- 11%
Ratio - 7 : 1

Course.

Extent of lesion increased with spread to right.

Died after a spontaneous pneumothorax of left.

Autopsy.

Guinea-pig inoculation negative.

Pathological Examination.

Nil abnormal in adrenal sections.

CASE 6

J.G. Male. Age 30 years.
Admitted - 4.7. 36.
Died - 11.7. 36.

History.

Too ill for history but pleurisy four times.
Pale, dyspnoeic, very thin.

Examination.

Gross cavitation of left lung.
Active infiltration on right.
Swelling of left ankle.
Hectic temperature.
Sputum T.B. +++

Course.

Rising pulse and respirations.
Broncho-pneumonic consolidation.

6.7.35. B.P. - 90/68
" Serum sodium- 296 mgms per 100 c.cm.
S.R. - 5 m.m.

Autopsy.

Guinea-pig inoculation positive.

Pathological Examination.

Negative for tuberculous lesions.

CASE 7.

J.G.G. Male Age 47 years.
Admitted - 20.7.36
Died - 13.8.36

History.

Always well until war, when wounded in chest.

In 1930 first had cough and sputum and felt out of sorts. Radiographed and told 'marks on plate' but no treatment recommended.

In 1932 voice first husky and has been so ever since.

Sent to Ear, Nose & Throat Dept. 22.6.36 and diagnosed as tuberculosis. Cough troublesome and fair amount of sputum.

Examination.

Sputum T.B. +++
Thin, gaunt, sallow complexion.
Looks very ill.
Extensive cavitation in both lungs.
Tuberculous teno-synovitis.
Larynx nodular, ulcerated epiglottis.
Arytenoids & post. part of cords ulcerated.

9.8.37. B.P. - 94/70
Serum sodium - 297 mgms per 100 c.cm.
S.R. - 33 mm.
Urine - T.B. +

Course.

Hectic temperature.

Pneumonic condition with terminal cardiac failure.

Antopsy.

Animal inoculation negative.
Suprarenal section showed no abnormality.

CASE 8

A.M. Male Age 27 years.
Admitted. 2.12.36
Died. 1. 2.37.

History.

Always healthy in army.

In February 1935 two haemoptyses but told not due to tuberculosis.

Since then has had cough and sputum, has been easily tired and lost weight but worked until November 1936 when was so done could not carry on.

Examination.

Very ill, thin, short of breath.

Face, axillae and hands pigmented.

No pigmentation of mucous membranes.

Voice weak.

Extensive disease in both lungs.

4.12.36. B.P. - 92/66
Serum sodium- 306 mgms per 100 c.cm.
S.R. - 56 mm.
W.B.C. - 11,200

Course.

Fast pulse, hectic temperature.

Progressive asthenia with death.

Autopsy.

Animal inoculation positive.

Pathological Examination.

No abnormality seen in the suprarenal sections.

CASE 9.

H.M. Female Age 22 years.

Admitted - 1.8.35.
Died - 27.2.36

History.

In Glenlomond in 1926 for eight months with lesion of left upper lobe.

Left to work in London as a domestic and fit save for three months in West Middlesex Hospital in 1931 with pleurisy.

Cough then but not at other times.

Acute appendix in March 1934. Drain inserted.

Cough began after operation, present ever since, streaked at times.

Losing weight, night sweats, anorexia and diarrhoea.

Examination.

Sputum T.B. +++

Looks ill, lips grey, emaciated.

Fingers clubbed.

Extensive lesion on left with cavitation.

Less on right.

Marked systemic upset.

22.1.36. B.P. - 70/50

Serum sodium - 301 mgms per 100 c,cm.

Urine - T.B.+

Course.

Appendix scar broke down and copious discharge.

Diarrhoea persistent.

Hectic temperature. Progressive asthenia.

Autopsy.

No animal inoculation.

Suprarenal sections.

No evidence of tuberculosis.

CASE 10.

A.W. Female Age 14 years.

Admitted - 18.2.36.

Died - 3.3.36

History.

Bad family history a brother dying of pulmonary tuberculosis in 1933 and a brother and sister have T.B + sputum.

Child always thin, never played about like other children.

Easily tired. Cough recently.

Examination.

Very emaciated.

Cyanosed and dyspnoeic.

Extensive disease in both lungs with cavitation.

Voice hoarse.

Has diarrhoea and there is a tender mass in R.I.F.

Sputum T.B. ++++

24.2.36 B.P. - 75/50

Serum sodium-301 mgms per 100 c.cm.

Course.

High swinging temperature.

Progressive asthenia.

Autopsy.

No animal inoculated.

Pathological examination.

No tuberculous disease found in the suprarenals.

CASE 11.

C.C. Female Age 21 years.

Admitted - 12.9.35.

Died - 21.4.36

History.

Frequent winter cough while at school.

In June 1935 pain in left side of chest, worse in deep breathing,

Too ill to be moved then.

Cough now very bad. Voice hoarse.

Sweats at night. Anorexia.

Losing weight.

Examination.

Very pale and thin.

Marked systemic upset.

Extensive exudative disease in left lung.

Slightly less on right.

Sputum T.B. +++

2. 3. 36. B.P. - 78/58

Serum Sodium - 301 mgms per 100 c.cm.

W.B.C. - 19,400

- Polymorphs - 85%, Lymphocytes, 15%

- Arneth shift to left.

R.B.C. - 4,630,000. H6-47% C.I.- .5

Course.

Swelling and pain in abdomen with a tender mass in R.I.F.

Diarrhoea severe.

Cyanosed and breathlessness increased.

Asthenic death.

Autopsy.

Guinea-pig inoculated. T.B. positive.

Pathological Examination.

No tuberculosis in suprarenal sections.

CASE 12.

Mrs McA. Age 32 years.

Admitted - 27. 4. 36.

Died. - 18. 5. 36.

History.

'Cold' in chest in December 1935 with cough and sputum.

Easily tired and unfit for work, with shivering attacks and night sweats.

Severe thirst and diagnosed as a diabetic.

Cough continued to be troublesome.

Became dyspnoeic on exertion and had palpitation.

Progressive loss of weight.

Anorexia: attacks of diarrhoea.

Examination.

Critically ill, marked systemic upset.

Cyanosed and dyspnoeic.

Deep brown pigmentation of skin.

Extensive disease in right lung with cavitation in upper lobe.

Left upper lobe involved.

Tender swelling in L.I.F.

Sputum T.B. ++++

28. 4. 36 B.P. - 82/60

Serum sodium- 286 mgms per 100 c.cm.

S.R. - 60 mm.

Course.

Diarrhoea and abdominal pain.

Increasing dyspnoea and emaciation.

Intermittent temp.

Asthenic death.

Antopsy. Guinea pig died suddenly on second day. No. repeat.

Pathological Examination.

No tuberculosis present in suprarenal glands.

CASE 13.

Mrs E.D. Age 29 years.
Admitted. - 16.11.36
Died. - 11. 3.37

History.

Easily tired in 1929 and had attacks of pain in left side of chest.

Cough with sputum shortly after, recurrent attacks of pleurisy.

Night sweats later and first admitted in June 1935 with infiltration in left upper lobe with moderate cavity.

A.P. of left started and good collapse being obtained when patient left at her own request.

In January 1936 easily tired, bad cold with 'catarrh in chest'.

Some pain across back.

Symptoms has become worse.

Cough and sputum.

Splashing in chest in July.

Examination.

Pale and malar flush and cyanosed lips.

Tongue dry and furred.

Brown pigmentation of palate. Fingers clubbed.

Large cavity in left upper lobe and pyo-pneumothorax of left.

Infiltration in right upper lobe.

23.11.36. B.P. - 90/74.

Serum sodium-314 mgms per 100 c.cm.
S.R. - 26 mm.
W.B.C. - 15,800.
-Polymorphs-86%.Lymphocytes.8%
Hyalines-6%
Ratio - 11:1.3
Urine - T.B. -/-

Course.

Pus/

Case 13 (Continued)

Course.

Pus aspirated from left side of chest. Fluid T.B. ++

Olive Oil and gomenol 10% injected which was coughed up.

Mild pyrexia at first, later hectic.

Progressive toxaemia and death.

Autopsy.

Inoculation and sections negative.

CASE 14.

J.A. Female. Age 23 years.

Admitted - 29.5.35
Died - 9.11.36

History.

In January 1935 noted was much more easily tired than usual.

Complained of cough and sputum.

Examination.

Very thin, pale and ill looking.

Sputum T.B. +++

Active disease in both lungs.

24. 2.36 B.P. - 100/70

Serum sodium- 330 mgms per 100 c.cm.

S.R. - 67 mm.

W.B.C. - 20,600.

- Polymorphs-77%; Lymphocytes-20%
Hyalines - 3%

Ratio- 3.8:6.6

R.B.C. - 3,810,000 H6-75%. C.I. .95.

2.11.36. Serum sodium - 282 mgms per 100 c.cm.

S.R. - 68 mm.

B.P. - 96/60

Urine T.B. +

Course

Continued for over a year with cough and sputum, fast pulse and hectic temperature.

Emaciated, hectic malar flush, cyanosed and dyspnoeic.

In September 1936 onset of diarrhoea and vomiting.

Abdomen distended and tumid to palpation.

Oedema of ankles in October.

Progressive asthenia and death.

Autopsy. Animal inoculation negative.

Pathological Examination.

No evidence of tuberculosis in the suprarenal sections.

CASE 15.

Mrs A.B. Age 35 years.
Admitted - 29. 3. 35
Died - 4. 8. 36

History.

In December 1934 in bed for two weeks with 'pneumonia';cough and sputum present but cleared up. Began working after this but felt easily tired, cough re-appeared in February 1935 and sputum was stained during March.

Night sweats. Voice hoarse.

Examination.

Thin, colour fairly good.
Troublesome cough, sputum T.B. +++
Thorax narrow and flattened on right side.
Expansion poor. Note impaired apex to base.
Breath sounds bronchial with many râles.
Pulse and temperature quiet.

2.3.36 B.P. - 110/72
" Serum sodium - 326 mgms per 100 c.cm.
13.7.36 Serum sodium - 300 mgms per 100 c.cm.
16.5.36 S.R. - 33 mm.
Urine T.B. +-

Course.

Artificial pneumothorax tried but poor space obtained so abandoned.

Spread on opposite side. Cavitation of right upper lobe.

Fast pulse and high swinging temperature.

Abdomen became swollen and partial obstruction developed.

Mass in R.I.F. Large liver.

Night sweats, attacks of diarrhoea.

Frequency of micturition.

Terminal cardiac failure.

Autopsy.

Animal inoculation and suprarenal sections negative.

CASE 16.

F. McG. Male Age 26 years.
Admitted - 7.5.35
Died - 20.9.36

History.

In January 1935 did not feel well, having sickness and vomiting.

18 months before this swelling of glands on right side of neck.

Now has abdominal discomfort and attacks of diarrhoea.

Slight cough. Glands in neck enlarged.

Examination.

Sallow complexion, axillae pigmented.

Discrete palpable glands on both side of neck in both anterior and posterior triangles.

No evidence of softening.

Infiltration in right upper lobe.

Nil abnormal in abdomen.

Sputum T.B. -/

Barium meal. Filling defect in caecum.

Course.

Improved at first and symptoms disappeared.
2.12.35. Complained of severe abdominal cramps and constipation.

Tender fixed mass in R.I.F. and cord like caecum palpable.

Tip of spleen palpable.
18.5.36. Periodic attacks of diarrhoea.

Appetite poor.

Distended abdomen with large tender mass in R.I.F.

No free fluid.

High intermittent temperature.

Glands small.

Nil abnormal in chest.

These symptoms continued and on 1.8.36 abdomen opened, and tuberculous hyperplasia of caecum found. Fixed and unsuitable for resection.

Case 16 (Continued)

Ileo-transverse anastomosis done.

Rallied after operation, but diarrhoea continued appetite very poor.

Fast pulse and high intermittent temperature.

Increasing dehydration and pigmentation of face and arms increased.

Terminal cardiac failure.

27.1.36.	Serum sodium	- 328 mgms per 100 c.cm.
	B.P.	- 82/60
	S.R.	- 18
4.5.36	W.B.C.	- 4,200.
		- Polymorphs-62%; Lymphocytes-19%. Hyaline-19%
		- Ratio 3.3:1
	R.B.C.	4,300,000 H6-85% C.I. ·98
18.7.36	W.B.C.	3,000
		- Polymorphs 50%. Lymphocytes.37%. Hyaline. 13%
		Ratio 1.3:3.
15.9.36	Serum sodium	- 284 mgms per 100 c.cm.
	B.P.	- 74/52
	S.R.	- 10

Autopsy.

Animal inoculation and suprarenal section negative.

CASE 17.

M. McI. Male Age 18 years.

Admitted - 18. 3. 36

Died. - 3. 1. 37

History.

Always fit at school and until January 1935 when he was off work with right sided pleurisy with cough and sputum.

Off work for three months but felt very fit afterwards.

In December noticed was very easily tired, cough severe and pain in chest returned.

Has been present ever since.

Much sputum now. Night sweats at this time.

Voice husky for eight weeks.

No haemoptysis.

Appetite good.

Examination.

Sputum T.B. ~~++~~

Pale, looks ill, nutrition fair.

Profuse axillary sweating.

Extensive disease in right lung with upper lobe cavitation. Infiltration out from left root.

Course.

Unsuccessful attempt at A.P. on right.

Later spread of lesion on left.

Systemic upset and cough increased.

23.9.36. Haemoptysis of ~~℥ xxxv~~

Continued in a collapsed condition with hectic temperature.

Drenching night sweats.

21.12.36 Haemoptysis ~~℥ xi~~

23.12.36 ~~℥ ix~~ and ~~℥ iv~~

Broncho-pneumonia ∴ death.

21.3.36 Serum sodium - 303 mgms per 100 c.cm.
B.P. - 92/60
S.R. - 37 mm.

Case 17 (Contd.)

23.10.36 R.B.C.-4,500,000 H6-75% C.I..83
W.B.C. - 20,000
-Polymorphs,82%; Lymphocytes-15%;
Hyalines.-3%
Ratio: - 5.3: 5

2.11.36 Serum sodium - 330 mgms per 100 c.cm.
B.P. - 86/60
S.R. - 63,mm.

No autopsy.

CASE 18.

F.D. Male. Age 35 years.

Admitted: 20.1.37.

Died : 20.3.37.

History.

In September 1936 pain in right side of chest worse on deep breathing.

Cough and sputum at this time.

Smoker's cough for three months before this.

In June 1936 had cold shivers and felt very exhausted.

Always troubled with winter colds and coughs with sputum.

Examination.

Extremely ill, tired, haggard and breathless.

Skin a dirty brown muddy colour.

Lips and ears cyanosed.

Marked systemic upset.

Mass of glands on right side of neck.

Old standing disease in left lobe with upper lobe cavities.

Infiltration in right upper lobe.

Many rhonchi and râles on both sides.

T.B. +++

Course.

Slight improvement in first month but pulse fast and temperature high.

Colour of skin darkened. No pigmentation of mucous membrane.

16.2.37 Sputum offensive.

Gangrene of lung, ensued.

25.1.37 Serum sodium-285 mgms; 22.2.37-296 mgms per 100 c.cm.

" B.P. -88/60 " -

" S.R. -56 " 52.

R.B.C. -3,550,000 H6-C.I. 1-

W.B.C. - 9,600; Polymorphs-87%; Lymphocytes-8%; Hyalines-5%

Ratio - 11:1.6.

Autopsy. Animal inoculation negative.

No evidence of tuberculosis on section of the suprarenal glands.

CASE 19.

M.McD. Male Age 23 years.

Admitted - 3.2.36

Died -14.10.36.

History.

Off school repeatedly with influenza and run down.

Age 17 years off work for 6 weeks because run down.

Age 20 years influenza, never fit since, cough with sputum, have persisted.

Sputum stained several times in last few months.

Sweating at nights.

Hoarseness for two years.

Examination.

Thin pale & worn.

Extensive bilateral disease with cavitation in right lung.

Sputum T.B. +++

10.2.36 Serum sodium -320 mgms per 100 c.cm.
S.R. -50 mm.
B.P. -98/70

13.7.36 Serum sodium -312 mgms per 100 c.cm.
S.R. -34 mm.

5.10.36. Serum Sodium -293 mgms per 100 c.cm.
Sodium in C.S.F. - 318 mgms per 100 c.cm.

20.8.36 R.B.C.-4,930,000 H6-90%. C.I.- .91
W.B.C. - 13,600
-Polymorphs-64%.Lymphocytes-31%;
Hyalines-5%
Ratio : 2: 6.2

Course.

Fast pulse and hectic temperature.

4.8.36. Onset of periodic headaches.

Occasionally vomited after meals

Pigmentation of face, neck, forearms and hands appeared and increased in degree but never marked.

8.10.36/

Case 19. (Contd.)

8.10.36. Suddenly vomited, unconscious, divergent squint and tremor of arms and hands.
Typical meningitis there-after.

Autopsy.

Animal inoculation negative.

Suprarenal section.

Tuberculous mass in pole of left suprarenal.
caseation and giant celled systems present.
Lesion seen in 25 sections.
Congestion in cortex.
Cortex congested on right round an area of lymphocytic infiltration.

CASE 20.

A.G. Female Age 22 years.
Admitted - 13.7.36
Died - 17.1.37

History.

Frequent colds and headaches as a child.

In February 1936 voice first hoarse; had cough and sputum then but felt quite fit.

Since April has been easily tired, cough and sputum increased.

Dyspnoeic on exertion. Severe night sweats.

Recently pains in left side of chest.

Loss of weight.

Examination.

Sputum T.B. -/-/-

Looks ill, pale and tired, lips cracked.

Voice weak and hoarse.

Breathless while talking.

Infiltration throughout left lung and in right upper lobe.

Ulceration of vocal cords.

Pulse fast, temperature raised.

Urine T.B. -/-

13.7.36 Serum sodium- 317 mgms per 100 c.cm.
B.P. - 90/66
S.R. - 64

2.11.36 Serum sodium-312 mgms per 100 c.cm.
B.P. - 90/60
S.R. - 50

19.8.36 R.B.C.-4,030,000; H6-72% C.I. - .9
W.B.C.- 6,000
-Polymorphs,-61.5%; Lymphocytes-25%;
-Hyalines-13.5%
Ratio: 2.5:1.8

Course.

Progressive asthenia with swinging temperature.

24.9.36 Onset of vomiting and diarrhoea.
Tender mass in R.I.F.

Autopsy. Animal inoculation gave positive result for tubercle bacillus.

Suprarenal sections were negative.

CASE 21

E.McF. Female Age 18 years.
Admitted - 25.1.36
Discharged- 28.11.36
Died - End of December.

History.

Bad family history 1 brother dying of tuberculosis in infancy and a sister of pulmonary tuberculosis in 1934.

Patient was always well at school and was rarely off work as a domestic.

In November 1935 complained of not feeling well and always tired.

"Bronchitis" in December 1935 with cough and sputum.

Always been thin.

Examination.

Patient looks ill, cyanosed, muscle tone poor.

Extensive active lesion in both lungs.

Sputum T.B. +++

Urine T.B. +

2.3.36 Serum sodium -297 mgms per 100 c.cm.
B.P. - 94/68
S.R. - 35

3.6.36 Serum sodium -321 mgms per 100 c.cm.
B.P. - _
S.R. - 23

2.11.36 Serum sodium -293 mgms per 100 c.cm.
S.R. - 44

5.5.36 W.B.C. - 16,000
-Polymorphs-68%; Lymphocytes-18%.
Hyalines .4%

Ratio 4:4.5

R.B.C. -4,180,000 H6-94% C.I. 1+

Course. Fast pulse with slight pyrexia until mid June, after which high intermittent temperature.

Diarrhoea started in July and shortly afterwards vomiting.

Progressive emaciation, severe cough and sputum.

Discharged at own request and died about 4 weeks later.

No autopsy.

CASE 22.

A.McK. Female. Age 8 years.
Admitted 3.1.33
Died 27.10.36.

History.

Little history recorded.
Complaint of pain in left hip for a month.

Examination.

Thin and pale with cyanosed cheeks.
Respirations shallow and laboured.
Many palpable cervical lymph nodes.
Fluid at base of right side of thorax.
Abdomen tense, tympanitic with dullness in flanks.
No thrill.
Nil abnormal noted in hip joints.
Pulse and temperature raised.

Course.

At first child improved.

16.1.34. Abscess over manubrium sterni which was aspirated.

February 1934. Abscess of mandible on right and developed a discharging sinus into mouth.
Later foul sanious discharge.
Abdominal distension, fluid present, liver enlarged.
Smooth yellow waxy appearance of face.
Hectic temperature.
Attacks of diarrhoea.
Terminal oedema of ankles and legs.
Urine T.B. +

2.3.36 Serum sodium-322 mgms per 100 c.cm.
B.P. - 84/60
S.R. - 84

4.5.36. Serum sodium-305 mgms -do-

25.5.36. -do- 312 mgms -do-

9.6.36 -do- 302 mgms -do-

27.4.36 W.B.C. - 7,400
-Polymorphs-44%. Lymphocytes-44%
Hyalines-12%
Ratio- 1: 3.7

continued

Case 22 (Continued)

27.4.36 R.B.C.-2,150,000 H6-44% C.I. 1+

Autopsy.

Animal not inoculated.

Pathological examination.

Amyloid degeneration of the cortex of both suprarenal glands.

CASE 23

J.A.S. Male Age - 44 years.

Admitted - 18. 3.35

Died - 22. 1.36

History.

Complained of lumbago for several years and in September 1934 noticed a swelling on right side of back.

This was incised at home and later admitted to hospital where further incision made, track followed to 9th and 10th dorsal vertebral. Necrosed bone removed, track cleaned, fixed in plaster. Plaster removed because of discomfort in back and copious discharge from two sinuses.

Course.

Continued discharging from sinuses.

Slowly developed typical amyloid disease.

Novr, 1935. Diarrhoea. Abdomen distended,

Jany. 1935 Vomiting and diarrhoea persistent.

Generalised oedema.

Subnormal temperature for 18 days before death.

15.1.36 Serum sodium- 317 mgms per 100 c.cm.

B.P. - 80/55

No autopsy.

CASE 24.

J.A. Male Age 22 years.
Admitted - 9.7.35
Died - 22.8.36

History.

Influenza in January 1935 and has been unfit for work since April. Easily exhausted.
Cough troublesome, some sputum.
Never fat but has lost weight.
Hoarseness since 1934.
Bad family history.

Examination.

Looks ill, nutrition fair, colour poor.
Active disease in both lungs.
Slit-like epiglottis, lustreless cords.
Sputum T.B. ++
Urine T.B. +

Course.

Cyanosed, breathless, progressive loss of weight.
Hectic temperature at first.
For 3 months prior to death temperature rarely above normal and subnormal for last 5 days.
Pulse always above 100.
Severe diarrhoea and mass felt in R.I.F.
Cachectic death.

3.4.36. Serum sodium - 317 mgms per 100 c.cm.
B.P. - 110/76
S.R. - 45
W.B.C. - 23,400.
- Polymorphs-83%.Lymphocytes-11%; Hyalines-6%
Ratio - - 7.5:1.8.

Autopsy.

Animal inoculation negative.
Suprarenal section negative.

CASE 25.

M.A. Female Age 18 years.
Admitted 11.6.35.
Died. 17.10.36

History.

In November 1933 pain in left side of chest with cough and off work for 6 weeks.

Worked until May 1934 when cough very severe and so easily tired that forced to stop.

Off work since and slowly losing ground.

Voice hoarse for 2 years.

Bad family history.

Examination.

Hectic flush. Breathless.

Extensive disease in both lungs.

Larynx: ulcer at posterior part of right cord.

Pulse over 100. Temperature varies.

Sputum T.B. +++

Urine T.B. +

6.7.36 Serum sodium - 318 mgms per 100 c.cm.
B.P. - 118/78
S.R. - 35
W.B.C. - 26,000
R.B.C. - 4,970,000 H6-100% C.I. 1+
- Polymorphs-85%. Lymphocytes-12%.
- Hyalines-3%
Ratio: 7: 4

Course.

Died of congestive heart failure.

Autopsy.

Animal inoculation negative.

Suprarenal section negative.

CASE 26.

F.J. Male Age 29 years.
Admitted 27.7.29
Died 29.4.37

History.

A case of old standing pulmonary tuberculosis with gradual deterioration during the seven years residence in the sanatorium.

Both lungs were extensively involved on admission and the lesion slowly progressed.

Chronic arthritis affecting almost all joints. This developed after typhoid fever in 1920.

During the period of investigation disease active in both lungs. Sputum T.B. ++

Great emaciation. Colour fairly good.

Appetite poor.

Asthenic death with a subnormal temperature during last five days.

Blood.

3.2.36 Serum sodium -327 mgms per 10^0 c.cm.
B.P. - 124/90
S.R. - - 48

Autopsy.

Animal inoculation positive for tubercle bacilli.

Suprarenal section showed no evidence of tuberculous disease.

CASE 27.

J.McB. Male. Age 14 years.
Admitted - 25. 2.36
Died. - 27. 6.37

History.

Scarlet Fever when aged 12, when was in hospital for 15 weeks. At this time developed an empyaema on his right side and a rib resection was done. At this time had a cough which has been present since. Sinus in chest healed up at end of 1934. Shortly after an ischio-rectal abscess developed and is still discharging.

Fairly well during 1935 but at beginning of 1936 felt very tired with troublesome cough and some sputum.

Recent night sweats.

No loss of weight. Appetite good.

Examination.

Thin; colour fairly good.

P.N. impaired down right side of chest, with bronchial breathing and many râles. Scar at angle of right scapula.

Prolonged expiration over right apex and root, but there are no moist sounds.

Sputum T.B. +

Progress.

In June 1936 first noted that left lung showed active disease and since the disease has progressed in both lungs.

In February 1937 dullness at right base. Pus containing staphylococci and tubercle bacilli was aspirated.

Old scar broke down followed by profuse discharge.

Continued degeneration, very emaciated, much cough and sputum. Hectic temperature.

Larynx now involved.

Asthenic death.

continued

Case 27 (continued)

Blood.

9.3.36 Serum sodium - 313 mgms per 100 c.cm.
S.R. - 25
R.B.C.-4,870,000;H6-78%.C.I.·81.
W.B.C. - 8,600
Polymorphs-60%
Lymphocytes-32%; Hyalines- 8%
Ratio - 2: 4
B.P. - 104/68

25.1.37. Serum sodium - 291 mgms per 100 c.cm.
S.R. - 50
W.B.C. - 16,000
Polymorphs - 83%; Lymphocytes-11%;
Hyalines - 6%
Ratio:- 7.5:1.8

10.6.37 Serum sodium- 308 mgms per 100 c.cm.
S.R. - 60

Autopsy.

No evidence of tuberculosis in the suprarenal glands.