VOLUME XXXVII JULY, 1937 No. 3

THE SUPRARENAL GLANDS IN DIPHTHERIA

BY ALEX. MACLEAN, M.D., D.P.H.
Clinical Medical Officer, Glasgow Public Health Department; formerly Assistant Physician, Ruchill Fever Hospital, Glasgow

(With Plate II and 7 Graphs in the Text)

IN recent years, it has become apparent that lesions of the suprarenal glands occur more often in human disease than had formerly been suspected. The evident effect of such lesions is the production of profound general disturbances, which are seen in a chronic phase if the morbid process in the suprarenal tissue is slowly progressive, as, for example, in the ordinary case of Addison's disease, and in an acute phase if the lesion is of sudden onset, as in suprarenal haemorrhage, or if chronically diseased suprarenal tissue is subjected to sudden excessive demands, as in the critical stage of Addison's disease. In both phases, there is evidence to show that the best measures to employ in combating these disturbances, whether for prophylaxis or for therapy, consist of the administration to the patient of an extract of suprarenal cortex or, alternatively, of sodium chloride.

Experimental work on cases of diphtheria in Ruchill Hospital from May 1933 till April 1935 is detailed later in this article; it tends to support the belief that there is, in diphtheria, a series of changes which is attributable to deficiency of secretion of the suprarenal cortex. It will be of interest, however, if short notes on the known effects of suprarenal cortex deficiency in man and in animals is allowed to take precedence of this account, and for this purpose the writer, finding his own experience to be somewhat inadequate, has been compelled to draw largely on the scattered literature on the subject. Again, some indication will be made of the typical changes which follow the parenteral injection of the toxin of *Corynebacterium diphtheriae* in susceptible animals.

The subject-matter will, therefore, be treated under the following main heads:

A. Experimental suprarenal cortex deficiency in animals;
B. The effects of suprarenal cortex deficiency in human disease;
C. Diphtheria intoxication in susceptible animals;
D. Human diphtheria.

A. EXPERIMENTAL SUPRARENAL CORTEX DEFICIENCY IN ANIMALS

Many years ago, Brown-Séquard (see Refs. p. 367) observed that, if both suprarenal glands were completely destroyed, death followed after 8 hours in mice, 9 hours in rabbits, 13 hours in guinea-pigs and 14 hours in cats and dogs,

whereas, if only one suprarenal gland were destroyed, the period of survival was usually not less than 25 hours.

Hartman *et al.* (1932) found that when both suprarenal glands of an animal were removed a train of characteristic symptoms occurred in the following order:

(i) the animal tired easily and showed a disinclination for exercise;

(ii) there was loss of appetite with vomiting and, occasionally, haemorrhages;

(iii) there was a state of inertia akin to coma or the animal was irrational and easily irritated; then in turn there followed

(iv) coma,

(v) sudden collapse, and

(vi) death.

Further, they showed that the administration of extract of suprarenal cortex, at any point before the final stage, caused the symptoms to disappear, which they did in the reverse order of their appearance. Such an animal maintained normal health only when it received a daily ration of extract of suprarenal cortex.

Again, they observed that an animal kept in a state of suprarenal cortex deficiency by bilateral suprarenalectomy followed by administration daily of extract of suprarenal cortex in amounts which were insufficient to maintain normal health, presented the following features:

(i) extreme muscular weakness, anorexia, vomiting, diarrhoea and signs of lowering of the general bodily activity (e.g. fall of temperature, fall of blood pressure and diminution of the basal metabolic rate);

(ii) increased excretion of urea and chloride and decreased excretion of water in the urine (there was also reduced water intake);

(iii) increased concentration of the blood with increased blood-cell volume, increased erythrocyte count and decreased leucocyte count, distinctive changes in the chemical constitution of the blood plasma and serum (such as diminution of plasma total base, sodium, chlorine and bicarbonate and increase of plasma potassium, magnesium, inorganic sulphate and inorganic phosphate) and, finally, decrease of the blood sugar, increase of the blood non-protein nitrogen but no change in the blood calcium.

From similar observations, Britton & Silvette (1933, 1934) formed two conclusions, viz.

(i) that a suprarenalectomized animal with symptoms of suprarenal cortex deficiency showed an almost complete and, thus, very critical depletion of its circulating and reserve carbohydrate materials;

(ii) that, in the same state, there was no lack of water in the body of the animal because the loss of fluid from the blood stream was made good by increase of water in the hepatic and muscular tissues.

Harrop *et al.* (1933) found that suprarenalectomized dogs which received injections of solutions of sodium chloride survived longer than similar animals

which did not receive such injections. They regarded the concentration of the blood as the primary event in the sequence of symptoms when there was a state of suprarenal cortex deficiency, and the falls in plasma total base, sodium and chlorine with the increases in urinary sodium and chlorine as secondary features. They reached the conclusion that the suprarenal cortex normally exercised a regulatory influence over the excretion of water, sodium and chlorine and that when this influence was removed, the kidneys wasted those components not only from the blood plasma but also from the extravascular tissue fluids, the resulting dehydration being responsible for the symptoms and fatal ending in cases of suprarenal cortex deficiency. Pursuing this argument further, these authors surmised that, if the regulatory influence over the excretion of sodium and chlorine were lost after injections of extract of suprarenal cortex were stopped, the suprarenalectomized animal should go into a state of suprarenal cortex deficiency more readily on a salt-poor diet than on a normal diet and, conversely, that such an animal on a salt-rich diet should require less extract of suprarenal cortex than on a normal diet for the maintenance of perfect health; experimental evidence was later obtained supporting both conclusions. They showed also that suprarenalectomized animals on a bare maintenance dosage of extract of suprarenal cortex displayed the characteristic clinical, physiological and biochemical signs of deficiency of the suprarenal cortex secretion if placed on a salt-free diet and, if not allowed to sink too deeply, recovered after the administration of salt alone.

Study of this literature reveals, in the first place, that the main effects of deficiency of the secretion of the suprarenal cortex are (i) increase of the water content of the liver and of skeletal muscle, decrease of water in the circulating blood and diminution of excretion of water in the urine, (ii) decrease of sodium and chlorine in the circulating blood and increase in the excretion of sodium and chlorine in the urine, and (iii) decrease of carbohydrate in the circulating blood and of the carbohydrate reserve in the tissues, and, in the second place, that this condition of deficiency of the secretion of the suprarenal cortex in animals is best treated by injections of extract of suprarenal cortex, the most useful adjunct to this treatment being the administration of sodium chloride.

B. THE EFFECTS OF SUPRARENAL CORTEX DEFICIENCY IN HUMAN DISEASE

These effects will be studied in certain states in which damage to the suprarenal glands is known to occur.

(1) *Addison's disease*

Thomas Addison's description (see Refs. p. 367) of the symptomatology of the disease which is now known by his name remains unexcelled; it is summarized in his introduction to the lecture, in which he drew attention to the condition, as follows: "The leading and characteristic features of the morbid state to which I would direct attention are anaemia, a general languor and debility, a remarkable feebleness of the heart's action, irritability of the

stomach and a peculiar change of colour of the skin occurring in connexion with the diseased condition of the suprarenal capsule."

As a result of the discovery of efficient extracts of suprarenal cortex, much work has been done on Addison's disease in the last few years, and the tendency now is to distinguish clinically two main phases of the illness:

(*a*) a phase in which inexplicable weakness and exhaustion are followed by the typical syndrome with disinclination to any form of bodily activity;

(*b*) a phase in which there is collapse (the Addisonian crisis), characterized by prostration, nausea and vomiting (with signs of dehydration) or by coma.

In order of appearance, the most prominent symptoms in the first phase are asthenia and fatigue, pigmentation of the skin and mucous membranes, anorexia, nausea and vomiting, loss of weight, arterial hypotension, attacks of dizziness and syncope, and signs of dehydration and circulatory failure. The disease pursues a downward course broken, on the one hand, by periods of remission and, on the other, by exacerbations which may be severe enough to be regarded as crises. Signs of early dissolution are extreme asthenia, lowered bodily and surface temperature, collapse, protracted vomiting, systolic blood pressure of less than 70 mm. of mercury, blood urea of more than 60 mg. per 100 c.c., a short rapid course with little pigmentation, poor response to treatment and the presence of active tuberculosis.

The second phase may follow stress or strain, over-exertion, exposure, an acute infection, a surgical operation or the taking of a purgative or of any drug which increases the basal metabolism. It takes the form of an acute crisis, often heralded by sickness and by pain in the loins, back and abdomen which is usually dull and paroxysmal but may be intense and accompanied by abdominal rigidity; next, there follow insomnia, mental depression, poor judgement and failure of memory; later, there is coma ending in death. In some cases, sudden death occurs after a short period of excruciating lumbar and abdominal pain with dyspnoea and noisy delusions.

The first phase is associated with a morbid process of slowly progressive nature in the suprarenal glands. According to Rowntree (1933) (from whom this account is largely summarized), this process has been found to be tubercular in the majority of cases, the main lesion having been situated either in the middle layers of the cortex or in its deepest layer abutting on the medulla; other causes have been simple atrophy of the cortex (as a result of the necrotic action of some toxin with a specific affinity for the suprarenal cortex), a syphilitic lesion of the cortex and the effects of X-rays. The second phase occurs when chronically diseased suprarenal cortical tissue has sudden excessive demands made on it.

The treatment of the first phase consists of substitution therapy by means of injections of extracts of suprarenal cortex, the administration of sodium chloride or the use of either of these methods to the exclusion of the other; the treatment of the second phase requires the use of the same substances but in greatly increased quantities.

(2) *Suprarenal haemorrhage*

After an exhaustive search of the literature, Pearl & Brunn (1928) collected reports of twenty cases of bilateral suprarenal haemorrhage in adults and added one case of their own. The causes of the haemorrhage included thrombosis, capillary embolism, congestive diseases, infections and toxins, diseases of the solar plexus, surface burns and the haemorrhagic diathesis. The commonest and most characteristic symptom in all the cases was asthenia. Local symptoms varied from vague tenderness in the loins and epigastrium to severe abdominal pain with distension. Pearl & Brunn pointed out that the presence of severe abdominal symptoms with few physical signs in a patient who presented definite nervous manifestations, profound asthenia and gradual decline of blood pressure was suggestive of acute suprarenal disease; they stated that the prognosis was hopeless in marked bilateral cases but that small haemorrhages might be absorbed without the supervention of death; they were of the opinion that treatment was unsuccessful in severe cases but that the best results were obtained from injections of sodium chloride and extracts of suprarenal cortex.

The literature contains a number of reports of cases of suprarenal haemorrhage in children. For example, Rabinowitz (1923) reported two cases which were in a state of marked drowsiness and collapse and had a generalized purpuric eruption; post-mortem, the only significant findings apart from the skin condition were, in the one case, diffuse infiltration of both suprarenal glands with bright red blood-clots, and, in the other, a haemorrhagic sac in the left suprarenal gland and an intensely haemorrhagic infiltration of the right suprarenal gland. He concluded that the action of toxins on the walls of the capillaries in the skin and in the suprarenal glands was responsible for the diapedesis of blood into these tissues in the cases he quoted.

Thomson (1925) stated that bleeding into one or both suprarenals was often found in new-born children as the result of a birth injury, that it sometimes occurred in children of a few days old from septicaemia and that it occasionally happened in children in the first year of life as part of a rapidly fatal illness, the onset of which was sudden with severe abdominal pain, high fever, sometimes vomiting, diarrhoea, and scattered purpuric spots over the surface of the body; he found that there were commonly convulsions with quick pulse and respiration, general collapse and, usually, death within 24 hours of the onset; treatment was without effect.

(3) *Acute infections*

Lucke *et al.* (1919) made a detailed study of 126 fatal cases of influenza in the United States during the pandemic outbreak of 1918. The principal symptoms in these cases during life were marked asthenia and prostration. Among the most important post-mortem findings were changes in the suprarenal glands. In twenty cases there were no gross changes; in three instances, there were macroscopic haemorrhages in the suprarenal substance; in the other 103 cases

definite changes were noted as follows: (*a*) to the naked eye, the gland was pinkish brown in surface colour and haemorrhagic on section, the outer zone of the cortex being narrowed and changed in colour from deep orange-yellow to pale greyish yellow, the intermediate zone of the cortex being deep reddish brown in colour from exudation of blood and the medulla being reddish grey or deep red in colour; (*b*) histologically, the medulla and intermediate zone of the cortex showed extreme congestion and numerous small haemorrhages with cloudy swelling of the parenchymatous cells of the cortex and decrease of their lipoid material and with oedema of the interstitial cells of the cortex; in a few cases, there were areas of focal necrosis with small round cell infiltration and, very occasionally, there was diffuse infiltration with polymorphonuclear cells suggestive of acute inflammatory suprarenalitis.

Rubinztejn (1934) recorded eight cases of typhoid fever in which, he stated, there was involvement of the suprarenal glands, manifested by the presence of the typhoid state, prostration, low blood pressure and such symptoms as hypothermia and pseudo-perforation.

Peters & Gunn (1930) found that in fulminating cases of cerebrospinal fever the suprarenal glands were enlarged, soft and resembled blood-clot both in colour and consistence; they regarded this observation as characteristic of the post-mortem findings in the epidemic with which they dealt, the Glasgow outbreak in 1929. It is noteworthy that the less fulminating cases described by these authors were confused at first with such illnesses as acute appendicitis and pneumonia (perhaps because of abdominal pain) and influenza (perhaps because of general symptoms of asthenia) and that at the onset vomiting occurred in 70 per cent and coma as an early symptom in 10 per cent of the cases. Suprarenal haemorrhage in cerebrospinal fever was noted also by MacLagan & Cooke (1916) and by Burton & Chalmers (1930).

To summarize the symptomatology in these cases, in which involvement of the suprarenal cortex was found, it may be said that the most characteristic observation was of asthenia and that there was a distinct tendency to a fulminating condition with sudden death.

C. Diphtheria intoxication in susceptible animals

The effect of the subcutaneous injection of a culture of *C. diphtheriae* is so typical that it was formerly used as a test to complete the investigation of the characters of that organism. It was considered that virulence of the organism was established only if haemorrhages were found in the suprarenal glands of the injected animal.

More recently, Thaddea (1935) has shown that the changes, caused by the injection of diphtheria toxin into an animal, affect both the morphology and the chemical constitution of the suprarenal cortex; necrosis and haemorrhages are found in the cortex and there is also a disappearance from the cortex of lipoid material in greater or less amount according to the degree of intoxication.

He has also observed that the changes produced in guinea-pigs by experimental intoxication with diphtheria toxin can be mitigated by treatment with extract of suprarenal cortex if combined with large doses of ascorbic acid (which is normally present in the cortex).

Thus, it is evident that diphtheria toxin has a specific affinity for the suprarenal cortex to cause damage to it, and that at least one of the known methods of treatment of deficiency of the suprarenal cortex, viz., injection of extract of suprarenal cortex, is of value in minimizing the effects of the injury produced.

D. HUMAN DIPHTHERIA

The subject of this section will be treated in those aspects which have a bearing on the points emphasized in the preceding sections.

(1) *Symptomatology*

Several features of the clinical state in diphtheria are reminiscent of that in a case of suprarenal cortex deficiency, particularly of that acute phase of Addison's disease which is often known by the name of the Addisonian crisis.

Thus, pyrexia in the acute stage of diphtheria is seldom high; indeed Ker (see Refs. p. 367) may be quoted as saying that "in a pure diphtheria, if it has any relation to the local condition of the throat at all...the worse the lesion the lower the temperature," and, again, that "in septic cases...it would seem that the depressing effect of the diphtheria toxins does much to counteract the tendency of the septic infection to cause high temperature". In the acute phase of Addison's disease the temperature is subnormal.

Many observers, notably Rolleston (1925), have shown that the blood pressure tends to be subnormal in diphtheria and that the extent and duration of the depression are usually in direct relation with the severity of the local lesion. Lowering of the blood pressure is a typical finding in conditions of deficiency of the suprarenal cortex.

A state of lassitude and asthenia is characteristic of the early stages of diphtheria as of states of suprarenal cortex deficiency. Syncopal attacks in the acute stage of diphtheria are feared so much that clinicians insist on patients in that stage maintaining a horizontal posture; similar attacks are encountered in cases of suprarenal cortex deficiency.

Nausea and vomiting, which are well known in suprarenal cortex deficiency, occur in the early stages of diphtheria, apart from the phenomena of serum reaction; for example, a blood-sugar test may be rendered invalid by the sickness of the patient, if the test sugar has been given by mouth; protracted vomiting in a case of diphtheria is a sign of poor prognosis. Pains of varying severity in the lumbar region and abdomen (distinct from the precordial pain of a failing heart which may also be present) are frequently complained of by patients suffering from severe diphtheria, in whom death is imminent; in one case of my experience the patient a few hours before death

had a dull ache in his right loin—at autopsy later, small haemorrhages were found in the right suprarenal gland. Vague pains in the small of the back and in the abdomen are present in the Addisonian crisis.

In conversation with diphtheria patients, when they have improved after having been very ill, it may be noted with some surprise that they do not remember unpleasant happenings such as needle punctures and that they have lost all sense of time. Failure of memory is often a feature of suprarenal cortex deficiency.

On the other hand, pigmentation is a feature of Addison's disease but not of diphtheria nor yet of recorded cases of suprarenal haemorrhage. This, however, is comprehensible if we regard pigmentation, whatever its true significance may be, as an index of chronicity in disease of the suprarenal cortex; we should, therefore, not expect to find it in an illness of short duration like diphtheria.

It appears, therefore, that there are numerous points of similarity between the symptoms of the acute stage of diphtheria and those of conditions characterized by deficiency of the suprarenal cortex.

(2) *Pathological changes in the suprarenal glands*

Writers on diphtheria have realized for a long time that changes occur in the suprarenal glands in this disease, but it is doubtful if any great significance has been accorded to these observations. Thus, Muir (1924) has noted that poisoning with diphtheria toxin is associated with marked congestion and minute haemorrhages of the suprarenal glands, and Ker (see Refs. p. 367) has stated that the suprarenal glands may show degeneration in diphtheria and that haemorrhages are not infrequently observed in their substance. On the other hand, Rolleston (1925) has written that in contrast with the well-marked haemorrhagic lesions of the suprarenals in the guinea-pig which has died of experimental diphtheria, these organs in the human subject rarely show any gross naked-eye changes, and that even microscopic lesions, such as cell-degeneration and necrosis, small haemorrhages and necrosis, described by some writers, are not constant.

The present writer's own conclusions from experience of autopsies in fatal cases of diphtheria may be summarized as follows:

Like other organs, the suprarenal glands suffer from the presence in the body of diphtheria toxin. In cases in which intoxication is at a minimum, e.g. cases of membranous croup, there is either no visible change or there is at most only a small amount of haemorrhage between the fasciculi of the zona reticularis of the cortex (see Pl. II, Fig. 1). If intoxication is greater, the suprarenal lymphatic glands along the suprarenal vein are inflamed (see Fig. 2), haemorrhages are found in all three layers of the cortex and in that region of the medulla which is in proximity to the cortex, and cloudy swelling of varying degree affects the parenchymatous tissue of the cortex; the haemorrhages and cloudy swelling are most intense in the zona reticularis and the inner part of

the zona fasciculata (see Fig. 3). In the worst cases, haemorrhages in one or other suprarenal gland are of such extent as to be apparent on the surface of the organ (see fig. 4).

In some cases the cloudy swelling and haemorrhage appear to have a focal distribution in the suprarenal cortex.

It appears likely that the part of the suprarenal tissue which is affected first in diphtheria is the zona reticularis of the suprarenal cortex, that the lesion, as it affects the suprarenal parenchyma, is of the nature of cloudy swelling and that, associated with this, there is haemorrhage from damage to the capillary walls.

(3) *Water excretion*

The amount of water excreted by the kidneys in a number of cases of diphtheria was investigated by means of the following test:

On the day preceding the test, intake of water is restricted and after 9 p.m. is stopped; at 9 p.m., the bladder is emptied and the urine discarded. From 9 p.m. till 9 a.m. on the day of the test, all urine is kept, the final quantity being passed at 9 a.m.; the volume and specific gravity of this, the night urine, are measured. At 9 a.m. the patient drinks 30 oz. of water; urine is passed at 10 a.m., 11 a.m., 12 noon, 1 p.m., 2 p.m. and 3 p.m. and the volume and specific gravity of each specimen are measured. Normally, under the conditions of the test, the night urine does not exceed 20 oz. and its minimum specific gravity is 1025, and during the day the entire 30 oz. of water, drunk at 9 a.m., are excreted in 5 hours, the first 15 oz. being excreted in 2 hours, and the maximum specific gravity not exceeding 1003. Renal impairment is shown by poor concentration of the night urine (excretion of more than 20 oz. of urine of which the specific gravity is less than 1025), by failure to excrete the test dose of water in 5 hours, by persistence of a specific gravity of 1010 or more in successive hourly specimens and by equality in the quantities of the hourly specimens. This test was employed at weekly intervals in thirty-two cases of mild and moderately severe diphtheria (more severe cases were not included as restriction of water was considered to be too rigorous a measure for them). The deficiencies of excretion at 2 hours (calculated as a percentage of 15 oz.) and at 5 hours (calculated as a percentage of 30 oz.) after the drinking of the test quantity of water were estimated; the smaller of these two deficiencies was taken as a measure of the deficiency in water excretion because that figure was less likely to be affected by mechanical difficulties in the excretion of urine.

Three cases (one of which was a healthy carrier) did not show deficiency of water excretion; in a fourth case the initial test was rendered invalid by menstruation. In each of the remaining twenty-eight cases there was some deficiency of water excretion in the acute stage of the illness.

That the deficiency of water excretion was not due to kidney damage, such as might be presumed to result from the action of diphtheria toxin in the

circulating blood, was suggested by the fact that in three cases only did the night urine exceed 20 oz.; in one of these there was no deficiency in the day urine and, presumably, no kidney damage existed; in the other two, the specific gravity of the night urine was less than 1025. In two other cases there was transient albuminuria, possibly due to kidney damage.

Discounting the five cases in which there was a suspicion of kidney damage, the case in which menstruation interfered with the results, and the carrier case, there remained twenty-five cases in which the presence of kidney damage was not proved and, of these, only two cases failed to show deficiency of water excretion in the acute stage of the illness. Hence twenty-three cases out of twenty-five, or 92 per cent, had diminution of water excretion in the acute stage.

Further, of these twenty-five cases, twelve, or 48 per cent, had diminished water excretion 1 week after admission, five, or 20 per cent, had diminished water excretion 2 weeks after admission and two, or 8 per cent, had diminished water excretion 3 weeks after admission; all had normal water excretion at the time of dismissal.

It is thus evident that diminution of excretion of water through the kidneys occurs in the acute stage of diphtheria.

Details of illustrative cases are appended (see Cases 1–5).

Case 1. E.O., female, 12 years. Severe diphtheria.
Admitted 12. v. 33, the third day of illness. Normal course without paralysis.
Dismissed well 4. vii. 33.
The test shows deficiency in the excretion of water on admission.

Date ...	24. v. 33		31. v. 33		7. vi. 33		14. vi. 33	
Time	Quantity oz.	Specific gravity	Quantity oz.	Specific gravity	Quantity oz.	Specific gravity	Quantity oz.	Specific gravity
9 p.m.–9 a.m.	5	1046	10	1040	10	1034	10	1032
10 a.m.	3	1042	12	1002	12	1002	4	1000
11 a.m.	1	1024	20	1000	16	1000	26	1000
12 a.m.	1·5		0	—	2·5	1008	0	—
1 p.m.	0	—	0	—	0	—	2	1012
2 p.m.	1	1024	0	—	2	1008	0	—
3 p.m.	0	—	3	1020	0	—	0	—
Quantity: 2 hours	4 oz.		32 oz.		28 oz.		30 oz.	
Deficiency: 2 hours	11 oz.		0		0		0	
% deficiency	73		0		0		0	
Quantity: 5 hours	6·5 oz.		32 oz.		32·5 oz.		32 oz.	
Deficiency: 5 hours	23·5 oz.		0		0		0	
% deficiency	78		0		0		0	
Minimum deficiency %	73		0		0		0	

(4) *The blood sugar*

It is now well known that abnormal variations in the blood sugar occur in diphtheria. Schwentker & Noel (1930) found that, in the early part of the acute stage of the illness, hypoglycaemia and reduction of the store of glycogen in the liver and muscles occurred as a result of increased breakdown of that glycogen and of increased utilization of circulating carbohydrate; while, at a later period in the acute stage, they found that increasing difficulty in the assimilation of glucose from the blood occurred with resulting hyperglycaemia.

Donato (1930), Polandowski (1932) and Lereboullet (with his collaborators, 1931) found that hypoglycaemia, increase of blood urea, diminution of blood chloride and initial decrease, followed later by increase, of blood cholesterol occurred in diphtheria. Benn *et al.* (1932) observed that in the acute stage of

Case 2. J. R., female, 19 years. Moderately severe diphtheria.

Admitted 25. v. 33, the third day of illness. Mild cardiac paralysis noted from the beginning of the third week till the middle of the fourth week of residence.

Dismissed well 5. viii. 33.

The test shows deficiency in the excretion of water until after the end of the second week of treatment.

Date ...	26. v. 33		2. vi. 33		9. vi. 33		21. vi. 33		28. vi. 33	
Time	Quantity oz.	Specific gravity	Quantity oz.	Specific gravity	Quantity oz.	Specific gravity	Quantity oz.	Specific gravity	Quantity oz.	Specific gravity
9 p.m.–9 a.m.	12	1040	20	1020	9	1030	12	1036	16	1026
10 a.m.	0	—	0	—	0·5	—	0	—	22	1000
11 a.m.	0	—	0	—	14·0	1002	23	1000	5	1010
12 a.m.	0	—	8	1018	0	—	15	1000	6	1010
1 p.m.	0	—	0	—	0	—	0	—	1	1010
2 p.m.	0	—	2	1018	2·5	1020	0	—	1	
3 p.m.	5	1032	1·5	1004	0	—	0	—	1·5	1006
Quantity: 2 hours	0		0		14·5 oz.		23 oz.		27 oz.	
Deficiency: 2 hours	15 oz.		15 oz.		0·5 oz.		0		0	
% deficiency	100		100		3·0		0		0	
Quantity: 5 hours	4·2* oz.		10 oz.		17 oz.		38 oz.		35 oz.	
Deficiency: 5 hours	25·8 oz.		20 oz.		13 oz.		0		0	
% deficiency	86		67		43		0		0	
Minimum deficiency %	86		67		3		0		0	

* By estimation.

Case 3. M.J., female, 9 years. Moderately severe diphtheria.

Admitted 25. v. 33, the third day of illness. Normal course without paralysis.

Dismissed well 14. vii. 33.

The test shows deficiency in the excretion of water until after the end of the first week of treatment.

Date ...	26. v. 33		2. vi. 33		9. vi. 33		16. vi. 33	
Time	Quantity oz.	Specific gravity	Quantity oz.	Specific gravity	Quantity oz.	Specific gravity	Quantity oz.	Specific gravity
9 p.m.–9 a.m.	9	1040	14	1022	6	1024	16	1026
10 a.m.	1·25	1030	2	1006	4	1012	14	1002
11 a.m.	1·5		2·5	1004	14	1000	10	1000
12 a.m.	1	1032	1·5	1018	2	1004	5	1006
1 p.m.	1		·75		0	—	0	—
2 p.m.	0·75	1030	1·25	1020	1	1020	2·5	1010
3 p.m.	1		1		1		2	1012
Quantity: 2 hours	2·75 oz.		4·5 oz.		18 oz.		24 oz.	
Deficiency: 2 hours	12·25 oz.		10·5 oz.		0		0	
% deficiency	82		70		0		0	
Quantity: 5 hours	5·5 oz.		8 oz.		21 oz.		31·5 oz.	
Deficiency: 5 hours	24·5 oz.		22 oz.		9 oz.		0	
% deficiency	82		73		30		0	
Minimum deficiency %	82		70		0		0	

diphtheria the blood-sugar curve after intravenous injection of glucose was of similar form to that seen in cases of diabetes. Brems (1932) noted that the blood-sugar curve following ingestion of glucose was of the diabetic type in the acute stage of diphtheria and for a period of two to three weeks afterwards. Begg (see Refs. p. 367), more recently, also noted the abnormalities in the glucose

tolerance curves and quoted experimental evidence which suggested that a close relationship existed between the type of blood-sugar curve and the degree of cardiovascular failure in the early stages of diphtheria; he also showed that

Case 4. W.P., female, 12 years. Moderately severe diphtheria.

Admitted 8. xi. 33, the third day of illness. Albuminuria was present on the first 2 days in hospital. The further course of the illness was normal, without paralysis.

Dismissed well 27. xii. 33.

The test shows deficiency in the excretion of water until after the end of the first week of treatment.

Date ...	10. xi. 33		17. xi. 33		24. xi. 33		1. xii. 33		8. xii. 33	
Time	Quantity oz.	Specific gravity	Quantity oz.	Specific gravity	Quantity oz.	Specific gravity	Quantity oz.	Specific gravity	Quantity oz.	Specific gravity
9 p.m.–9 a.m.	11	1022	6	1035	9·5	1028	14·5	1024	8	1030
10 a.m.	2·25	1022	3·5	1010	11	1006	8	1014	10	1001
11 a.m.	2·75	1012	5·5	1002	12	1002	15	1003	11	1000
12 a.m.	2·5	1011	1·75	1022	3·5	1010	3·5	1014	7	1000
1 p.m.	2	1016	0	—	2·75	1020	2·5	1020	4	1002
2 p.m.	2	1020	0	—	2·0	1022	1·75	1022	1	1018
3 p.m.	1·5	1022	2·75	1026	2·75	1024	1·75	1024	1	1020
Quantity: 2 hours	5 oz.		9 oz.		23 oz.		23 oz.		21 oz.	
Deficiency: 2 hours	10 oz.		6 oz.		0		0		0	
% deficiency	67		40		0		0		0	
Quantity: 5 hours	11·5 oz.		10·75 oz.		31·25 oz.		30·75 oz.		33 oz.	
Deficiency: 5 hours	18·5 oz.		19·25 oz.		0		0		0	
% deficiency	62		64		0		0		0	
Minimum deficiency %	62		40		0		0		0	

Case 5. J.P., female, 15 years. Moderately severe diphtheria.

Admitted 28. xii. 33, the eighth day of illness. Albuminuria was present on admission and until 3. i. 34; it was not associated with menstruation. Recovery was retarded by the development of cardiac paralysis of a mild type on 9. ii. 34.

Dismissed well 28. ii. 34.

The test shows deficiency in the excretion of water on admission and again a fortnight later but not after one week's residence in hospital.

Date ...	30. xii. 33		8. i. 34		15. i. 34		22. i. 34		29. i. 34	
Time	Quantity oz.	Specific gravity	Quantity oz.	Specific gravity	Quantity oz.	Specific gravity	Quantity oz.	Specific gravity	Quantity oz.	Specific gravity
9 p.m.–9 a.m.	1	1026	17	1014	6	1028	8	1040	12	1028
10 a.m.	11	1025	14	1010	10	1012	6	1014	12	1008
11 a.m.	1·5	1020	3·5	1008	0	—	10	1004	10	1002
12 a.m.	1·5	1030	11·25	1020	8	1010	4·25	1010	6	1004
1 p.m.	1·5	1028	3	1018	0	—	2	1020	1·5	1016
2 p.m.	1·5	1022	1	1022	4·5	1020	1·5	1022	1·5	1018
3 p.m.	1·25	1018	2		0	—	1	—	1	—
Quantity: 2 hours	12·5 oz.		17·5 oz.		10 oz.		16 oz.		22 oz.	
Deficiency: 2 hours	2·5 oz.		0		5 oz.		0		0	
% deficiency	17		0		33		0		0	
Quantity: 5 hours	17 oz.		32·75 oz.		22·5 oz.		23·75 oz.		31 oz.	
Deficiency: 5 hours	13 oz.		0		7·5 oz.		6·25 oz.		0	
% deficiency	43		0		25		21		0	
Minimum deficiency %	17		0		25		0		0	

the administration of insulin with glucose to diphtheria patients did not give better results than that of glucose alone.

In the present study, making use of Herbert & Bourne's (1931) modification of the Folin-Wu method of blood-sugar estimation, it was found that the mean fasting blood sugar of thirty-one cases of diphtheria on admission was 80·4 mg.

per 100 c.c. and 4 weeks later 84·1 mg. per 100 c.c. In fifteen cases, blood-sugar curves were plotted after the ingestion of 20 g. of glucose; in these, at admission, the curves took the form that has frequently been called the "lag" curve, whereas, 4 weeks later, the curves were of the recognized normal form or were approaching that state. In five cases, galactose was the test sugar; on admission, the blood-sugar curves in two cases conformed to the normal curve after galactose, in one case resembled a normal blood-sugar curve after glucose and in two cases were of the "lag" type. In eleven cases, laevulose was the test sugar; on admission, in five cases the blood-sugar curves were of the form normally found after laevulose, in one case similar to the normal curve after glucose and in five cases resembled a "lag" curve. Of these last sixteen cases, repetition of the curves after 4 weeks' treatment of the patients revealed normal results in all but two patients, in whom the curves were of normal shape but the individual readings were somewhat high.

Hence, in the early stages of diphtheria, it would appear from the few cases quoted here that there is a state of hypoglycaemia during fasting. Again, as Benn *et al.* (1932), Brems (1932) and Begg (see Refs. p. 367) have already shown, glucose tolerance curves in the acute stage of diphtheria tend to approximate to the "lag" form, which suggests that there is practically no impairment of the power of absorption of glucose from the alimentary tract into the blood but that there is diminution of the power of assimilation of glucose by the tissues from the blood. The blood-sugar curves after galactose and laevulose were abnormal in eight cases or 50 per cent of the whole, which would give rise to the surmise that, as the liver is known to be entirely responsible for the assimilation of galactose and laevulose from the blood, the sugar-absorbing power of the liver could be at fault in only half of the cases of diphtheria in the acute stage. Therefore, there is some evidence in favour of the belief that the particular form of blood-sugar curve found in the acute stage of diphtheria after the ingestion of glucose is mainly due to diminished assimilation of glucose from the blood not by the liver but rather by the peripheral tissues. Further support for this view was obtained by the finding that in twenty-five cases of diphtheria, samples of blood were tested by the van den Bergh method for the investigation of bile pigment and in no case was there found an increase of bile pigment in the blood serum, which suggested that the liver was, in one of its other functions, acting normally.

Typical blood-sugar curves are appended (see Cases 6–12).

(5) *Serum sodium, serum chlorine, serum potassium*

The sera of samples of venous blood taken from a number of patients, who were at least 7 years of age and for the greater part over 10 years of age (thus allowing for ease of repeated venous puncture), on admission, at the end of 1 week, at the end of 2 weeks and on the day before dismissal, were examined for their contents of sodium, chlorine and potassium. The methods employed were those advocated by Peters & van Slyke (1932), who state that the normal

values, in milli-equivalents per litre, are 138 and 105, 5, respectively, for serum sodium, serum chlorine and serum potassium.

In eighty-four cases of diphtheria investigated as above and in which, ultimately, complete recovery took place it was found that in the acute stage, at the time of admission to hospital, the mean serum sodium was 121·05, the mean serum chlorine 101·83 and the mean serum potassium 7·16 milli-equivalents per litre, the probable errors of the individual values in each series being $\pm 4{\cdot}51$, $\pm 2{\cdot}89$ and $\pm 1{\cdot}57$ respectively. There were thus a considerable fall in the serum sodium, a slight fall in the serum chlorine and a slight rise in the serum potassium from the accepted normal values.

Fifty-five of these cases received an extra quantity of sodium chloride, either by mouth, per rectum or intravenously, during the first 3 weeks of their treatment. Twenty-nine cases received no extra sodium chloride. The findings in each series are summarized in Table I, which shows that with treatment there is a gradual approach of the mean values for serum sodium, serum potassium and serum chlorine towards normal but that there is no quicker return to normal in the one series than in the other.

The coefficient of correlation between the serum sodium and the serum chlorine values in the eighty-four cases at the time of admission was $0{\cdot}3433 \pm 0{\cdot}0650$, which showed that there was positive correlation of medium grade and of definite significance between the serum sodium and the serum chlorine. Similarly between serum sodium and serum potassium the coefficient of correlation was $-0{\cdot}1520 \pm 0{\cdot}0719$, suggesting that here there was poor correlation of negative sign and insignificant value; again, between serum chlorine and serum potassium the coefficient of correlation was $-0{\cdot}1751 \pm 0{\cdot}0713$, leading to the same conclusion. Hence it appears that the considerable decrease in serum sodium in the acute stage of diphtheria was mirrored by a decrease in serum chlorine which was not coextensive with it, and by an increase in serum potassium which had very little relation to it, but before any true conclusions could be drawn from these findings it would be essential to know what the behaviour was of the other serum constituents.

The coefficients of variation (calculated as one hundred times the quotient of the standard deviations and the means under the same conditions as in Table I) are given in Table II which shows that the variabilities of serum sodium and chlorine are much less than the variability of serum potassium and that for all values the variabilities decrease as the patients progress towards recovery.

In four cases of diphtheria which proved fatal the mean serum sodium on admission was 118·47 and shortly before death 100·85 milli-equivalents per litre. The similar values for serum chlorine were 93·09 and 80·44 respectively and for serum potassium 8·35 and 11·66 respectively (in the latter case the mean serum potassium shortly before death was calculated in only two cases because insufficient serum was collected in the other two cases to enable the estimation to be made—the mean serum potassium on admission of the two

cases in which final estimations were made was 8·29). Hence it would appear that severe falls in serum sodium and serum chlorine precedes death in cases which ultimately prove fatal.

Table I. *Showing the means (M) and the probable errors* (P.E.) *of the individual values for sodium, chlorine and potassium in the blood serum in milli-equivalents per litre at different periods in the treatment of two series of cases*

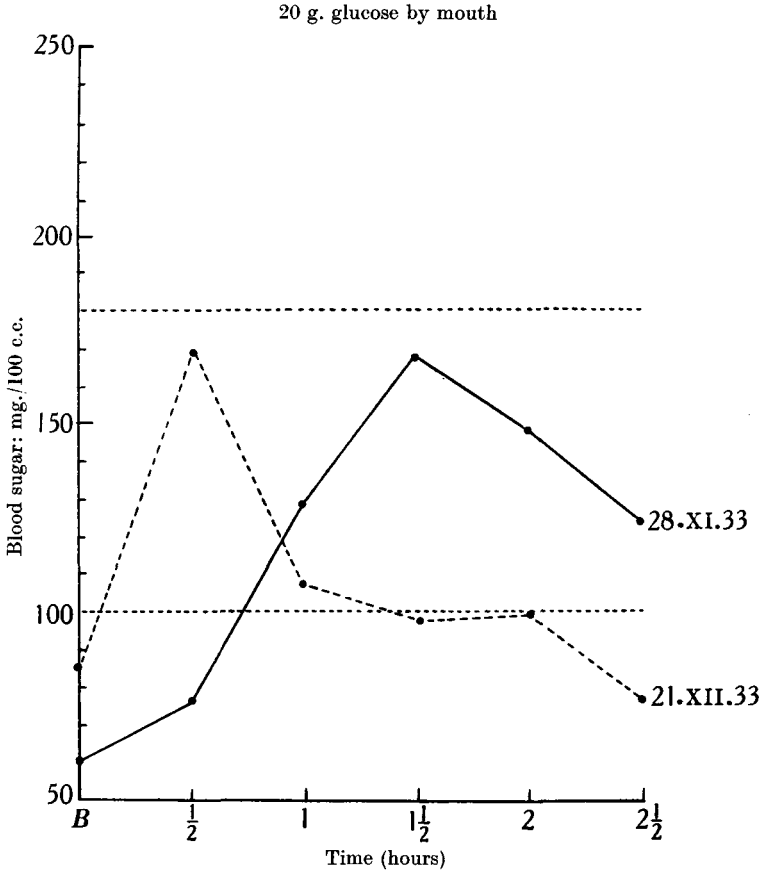
	First series 55 cases receiving extra sodium chloride						Second series 29 cases not receiving extra sodium chloride					
	Sodium		Chlorine		Potassium		Sodium		Chlorine		Potassium	
Day in hospital	*M*	P.E.	*M*	P.E.	*M*	P.E.	*M*	P.E.	*M*	P.E.	*M*	P.E.
First	121·74	±4·72	101·76	±2·86	6·98	±1·69	119·77	±3·83	101·95	±2·81	7·49	±1·29
Eighth	122·25	±5·33	101·76	±3·80	6·96	±1·70	124·49	±3·90	102·28	±2·63	6·81	±1·17
Fifteenth	123·44	±5·53	103·23	±2·12	6·68	±1·55	124·00	±4·41	103·47	±1·81	6·17	±1·13
Last	131·61	±3·44	104·75	±2·26	6·13	±1·30	130·19	±2·99	103·98	±1·70	5·34	±1·10

Case 6. T.R., male, 13 years. Mild diphtheria.

Admitted 26. xi. 33, the fifth day of illness. Normal course without paralysis.

Dismissed well 5. i. 34.

Blood-sugar curve, after glucose, on 28. xi. 33 shows initial hypoglycaemia and has a "lag" form; on 21. xii. 33, the fasting blood sugar is normal and the curve has a normal form.



https://doi.org/10.1017/S0022172400035099 Published online by Cambridge University Press

Table II. *Showing the coefficients of variation for serum sodium, serum chlorine and serum potassium at different periods during the treatment of the two series of cases*

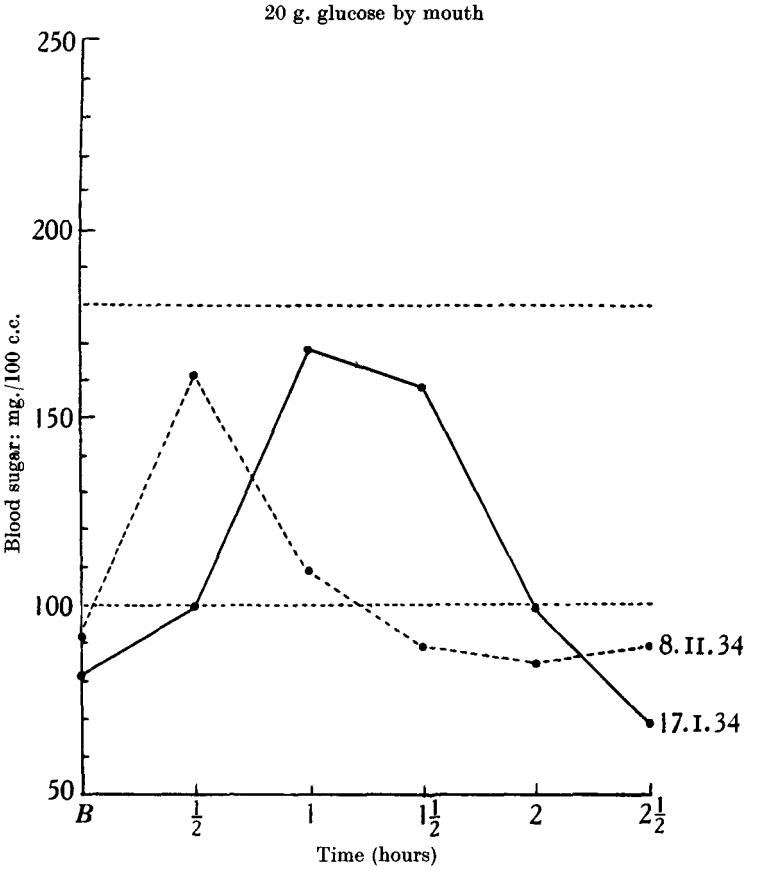
Day in hospital	First series 55 cases receiving extra sodium chloride			Second series 29 cases not receiving extra sodium chloride		
	Sodium	Chlorine	Potassium	Sodium	Chlorine	Potassium
First	5·75	4·17	35·89	4·74	4·09	25·53
Eighth	6·46	5·54	36·14	4·64	3·81	25·54
Fifteenth	6·64	3·03	34·44	5·27	2·59	27·08
Last	3·88	3·20	31·39	3·41	2·45	30·49

Case 7. J.L., male, 14 years. Moderately severe diphtheria.

Admitted 16. i. 34, the fourth day of illness. Slight albuminuria present from admission till 2. ii. 34. Paralysis not noted.

Dismissed well 2. iii. 34.

Blood-sugar curve, after glucose, on 17. i. 34 showed a normal fasting blood sugar but a tendency on the part of the curve to approximate to the "lag" form; on 8. ii. 34, the curve was normal.



The complete results in all the cases, as regards serum sodium, serum chlorine and serum potassium, are given in Tables III–VII.

https://doi.org/10.1017/S0022172400035099 Published online by Cambridge University Press

Case 8. J.B., female, 12 years. Mild diphtheria.

Admitted 7. xi. 33, the fourth day of illness. Recovery uneventful except for the presence of extra systoles from 23. xii. 33 till 27. xii. 33 inclusive.

Dismissed well 2. i. 34.

Blood-sugar curve, after galactose, on 8. xi. 33 showed a low fasting blood sugar; otherwise the curve was normal. On 5. xii. 33, the curve was normal.

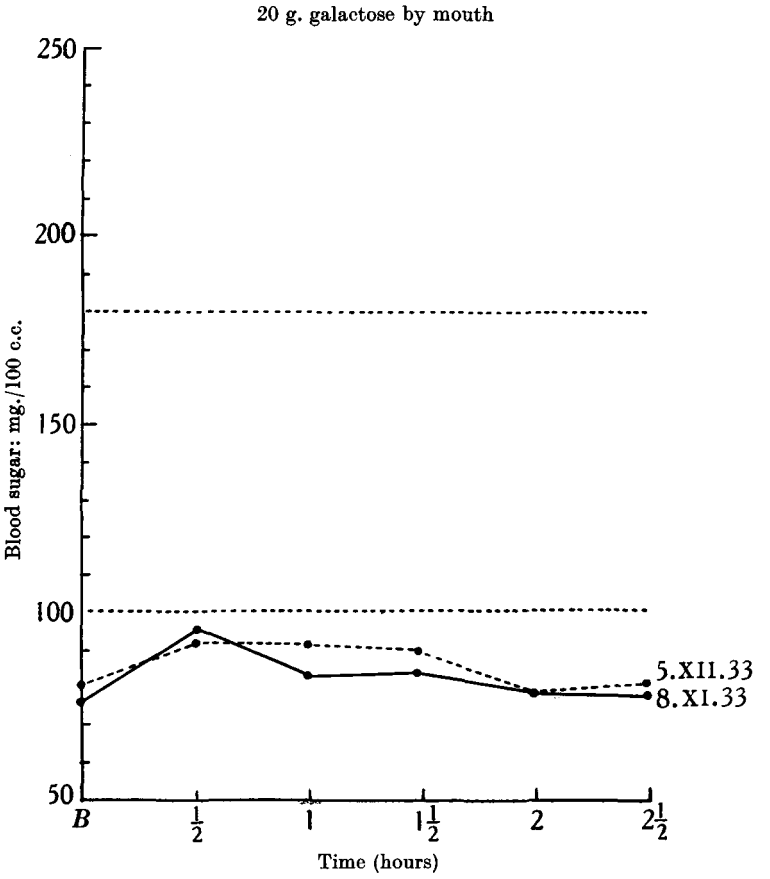


Table III. *Cases of mild diphtheria receiving extra sodium chloride*

Serum sodium (Na), serum chlorine (Cl) and serum potassium (K) in milli-equivalents per litre

	Day in hospital ...	First			Eighth			Fifteenth			Last		
Patient	Type of recovery	Na	Cl	K	Na	Cl	K	Na	Cl	K	Na	Cl	K
MAS	Normal	128·73	104·39	12·69	132·48	98·82	12·60	134·00	101·31	10·23	129·95	106·28	5·25
MDY	Normal	126·85	101·04	5·98	126·35	102·48	6·82	129·20	105·12	13·36	132·65	99·51	10·40
MBS	Normal	120·71	100·71	6·55	118·99	104·48	5·64	122·29	105·96	4·69	133·73	108·29	5·57
MMY	Normal	119·10	101·79	6·57	125·89	98·99	5·24	107·64	103·13	9·91	125·59	102·92	8·46
RDH	Normal	118·26	103·40	5·18	128·24	107·02	3·02	122·29	106·59	2·06	121·20	95·79	4·04
RCR	Normal	119·38	99·97	9·35	119·90	107·58	9·82	117·19	104·40	8·46	134·68	106·82	4·42
JBT	Normal	115·10	105·38	7·04	125·27	95·36	6·31	121·23	98·76	12·22	118·73	103·35	7·57
JHD	Mild paralysis	115·59	105·05	3·99	114·32	101·68	9·73	118·75	99·49	9·80	135·08	107·04	6·20
JYG	Mild paralysis	130·80	105·54	3·27	118·30	98·99	6·65	121·81	98·00	5·70	138·01	101·86	6·82
EJN	Delay in dismissal	127·26	99·77	11·15	132·01	104·98	15·27	125·39	98·98	8·02	126·50	101·70	4·38
EKS	Normal	128·25	105·44	11·98	129·49	105·98	7·72	135·08	103·68	8·80	127·90	99·51	4·56
JHY	Normal	122·55	105·82	3·47	120·65	104·42	6·88	130·99	108·70	5·24	140·59	107·99	7·44
JME	Normal	136·23	106·95	5·16	129·20	106·09	9·23	135·76	103·97	6·82	132·23	108·83	7·18
MSH	Normal	114·30	105·38	4·99	119·61	92·13	4·22	106·89	103·91	3·91	133·12	105·09	3·91
ECD	Normal	118·15	105·68	8·14	136·25	107·33	6·98	123·72	106·87	4·39	124·04	108·36	4·55
MAR	Normal	128·22	105·63	6·74	131·83	101·19	4·86	124·99	101·05	4·93	129·79	101·27	5·12
FCW	Normal	126·44	101·72	6·67	115·10	100·66	4·20	104·31	101·32	7·98	127·64	102·93	8·06

Table III (*continued*)

Cases of mild diphtheria not receiving extra sodium chloride

Serum sodium (Na), serum chlorine (Cl) and serum potassium (K) in milli-equivalents per litre

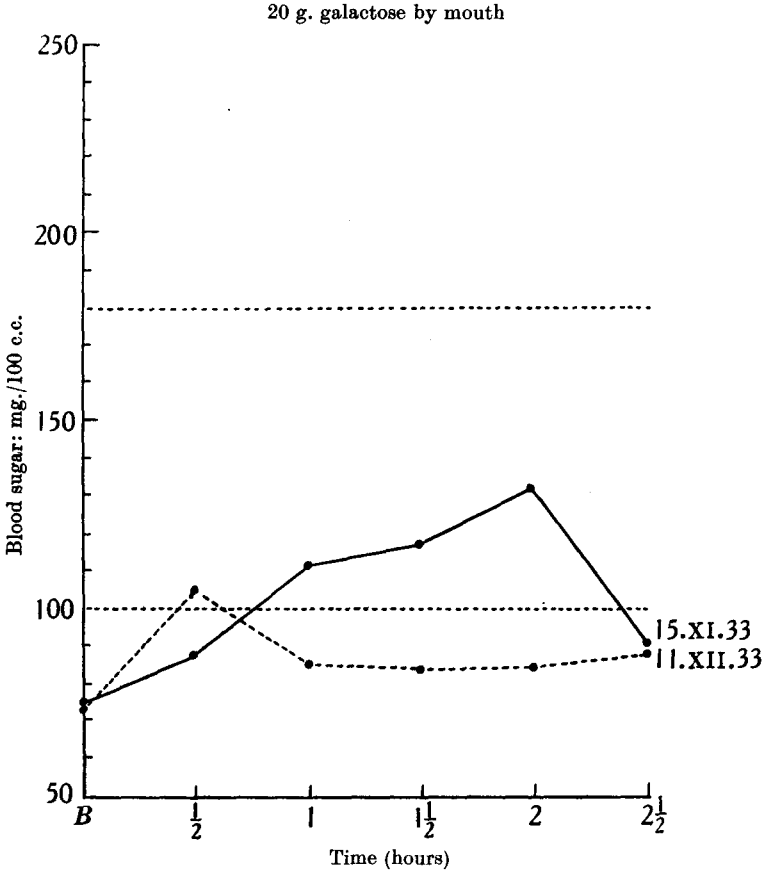
Day in hospital ...		First			Eighth			Fifteenth			Last		
Patient	Type of recovery	Na	Cl	K	Na	Cl	K	Na	Cl	K	Na	Cl	K
JNL	Normal	117·72	93·94	8·87	120·29	94·94	9·38	121·87	99·64	7·24	122·21	102·94	6·0
MDY	Normal	126·46	104·47	6·50	129·29	102·03	6·30	129·14	101·14	5·12	130·19	106·79	5·4
AMR	Normal	125·94	102·07	7·04	124·55	106·07	6·11	127·48	109·81	6·50	135·52	106·42	4·8
RHY	Normal	125·56	98·29	7·21	127·23	99·10	5·05	125·33	102·91	5·75	126·96	98·89	5·8
HOL	Normal	122·46	104·94	8·49	138·66	94·03	9·23	123·34	99·71	7·85	123·58	103·71	6·0
SZO	Normal	130·91	102·78	6·54	132·38	99·85	6·07	134·42	104·61	5·16	132·16	103·95	7·2

Case 9. M. A., female, 19 years. Mild diphtheria.

Admitted 14. xi. 33, the third day of illness. Acute tonsillitis noted on 24. xii. 33; otherwise, normal course without paralysis.

Dismissed well 11. i. 34.

Blood-sugar curve, after galactose, on 15. xi. 33 showed a fasting hypoglycaemia and a "lag" form. On 11. xii. 33 apart from fasting hypoglycaemia the curve was practically normal in shape.



https://doi.org/10.1017/S0022172400035099 Published online by Cambridge University Press

Case 10. M. McK., female, 12 years. Very severe diphtheria.

Admitted 17. xi. 33, the second day of illness. Mild cardiac paralysis from 22. xi. 33 till 18. i. 34; when first allowed up there was a very stiff gait.

Dismissed well on 3. iii. 34.

Blood-sugar curve, after laevulose, on 20. xi. 33 showed a normal fasting blood sugar and a "lag" form. On 31. i. 34 the curve was normal.

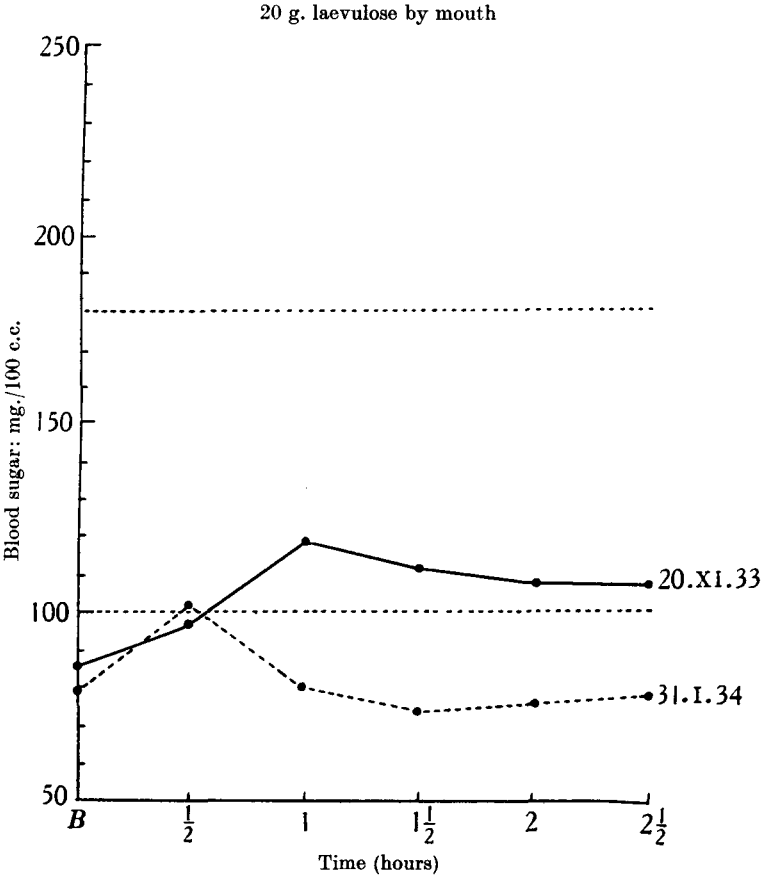


Table IV. *Cases of moderately severe diphtheria receiving extra sodium chloride*

Serum sodium (Na), serum chlorine (Cl) and serum potassium (K) in milli-equivalents per litre

	Day in hospital ...	First			Eighth			Fifteenth			Last		
Patient	Type of recovery	Na	Cl	K	Na	Cl	K	Na	Cl	K	Na	Cl	K
SNT	Normal	130·15	103·01	4·52	110·20	106·67	3·81	135·74	105·50	9·82	135·08	105·89	12·03
MPS	Normal	124·45	100·77	5·42	121·60	104·98	4·61	137·22	105·50	7·14	132·99	107·36	7·24
IST	Normal	124·18	99·57	4·35	104·29	101·95	5·73	128·44	106·18	10·07	130·09	105·82	5·86
MHY	Normal	123·20	109·25	7·93	117·16	102·04	8·27	139·86	107·28	4·09	135·95	103·21	3·15
SBE	Normal	125·07	101·48	5·74	125·03	97·11	5·41	123·43	99·33	6·23	132·01	102·36	7·78
MKY	Normal	119·54	109·25	6·05	132·04	106·88	6·69	124·63	96·37	7·52	134·53	104·70	8·31
MBD	Normal	124·20	102·37	6·34	140·86	103·59	5·82	116·29	98·47	4·68	133·63	109·38	3·18
WTN	Delay in dismissal	117·89	95·70	5·26	115·56	87·88	4·93	119·90	102·60	6·40	138·46	102·77	3·41
GMY	Normal	110·00	102·02	4·37	112·00	93·14	5·72	130·27	102·57	4·96	143·25	107·59	5·06
SWT	Normal	115·29	97·64	7·09	121·38	101·59	8·93	117·41	100·59	6·44	125·40	103·29	6·38
MMY	Normal	111·26	102·60	3·32	116·85	103·29	9·04	129·68	110·32	6·20	129·69	108·00	8·46
SDN	Mild paralysis	113·54	93·64	6·78	121·51	103·37	7·93	123·37	104·86	7·61	127·78	110·05	5·04
MFY	Normal	112·79	99·99	10·86	121·37	105·38	6·19	118·13	102·62	9·55	130·08	108·20	6·22
DME	Normal	132·03	104·35	6·00	121·10	97·46	7·10	128·24	101·54	6·92	134·03	108·75	6·30
MTN	Normal	124·50	96·06	14·13	116·48	102·31	6·04	114·86	104·95	8·74	136·37	107·97	5·66
EAN	Normal	118·47	104·97	3·95	120·33	108·01	4·65	128·97	105·15	4·66	120·03	97·68	5·79
MRS	Normal	112·14	91·79	3·27	121·17	93·07	6·43	114·03	98·49	4·37	134·62	102·47	4·89
MGN	Normal	122·58	102·12	7·59	128·17	109·32	5·18	124·01	100·70	6·40	133·00	107·53	5·04

Table IV (*continued*)

Cases of moderately severe diphtheria not receiving extra sodium chloride

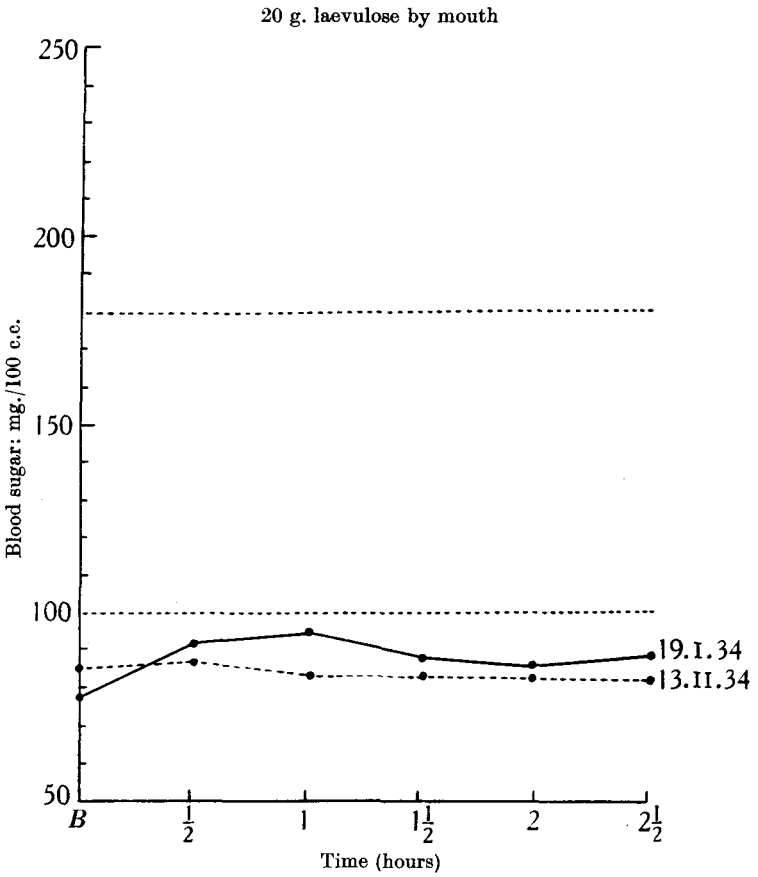
Serum sodium (Na), serum chlorine (Cl) and serum potassium (K) in milli-equivalents per litre

Day in hospital ...		First			Eighth			Fifteenth			Last		
Patient	Type of recovery	Na	Cl	K	Na	Cl	K	Na	Cl	K	Na	Cl	K
MPN	Normal	118·31	101·87	10·47	116·60	106·68	11·27	107·43	102·02	7·14	132·59	103·39	6·09
MHN	Normal	115·42	103·70	8·50	120·53	108·44	7·79	109·62	105·77	8·10	122·95	97·83	4·90
MGT	Normal	118·09	104·42	6·72	127·20	106·06	4·31	129·35	98·37	5·15	134·63	103·71	3·87
JME	Normal	113·12	101·17	8·18	121·62	102·27	6·43	120·66	105·31	6·74	127·22	105·61	4·31
HOL	Normal	120·36	106·68	7·41	126·36	102·14	6·03	132·24	102·59	5·85	135·68	98·90	3·48
JMY	Normal	119·56	104·65	6·60	122·04	106·19	6·40	124·63	103·52	3·02	126·78	106·87	3·46
DWE	Normal	110·18	106·99	8·50	116·20	101·14	6·91	122·04	103·49	3·32	126·94	101·69	3·51
EMD	Normal	113·59	108·35	6·76	119·49	99·75	7·14	126·04	102·82	7·88	131·54	103·16	6·92
EMY	Normal	114·45	104·44	7·04	120·79	101·74	9·83	123·12	103·41	7·20	129·70	106·66	3·15
HME	Normal	122·23	103·26	6·37	119·29	99·86	6·76	126·00	108·24	7·07	137·41	105·57	3·50
CDY	Normal	119·08	100·09	3·66	129·85	101·19	6·06	126·08	104·90	6·37	128·53	104·92	6·31

Case 11. H. V., female, 11 years. Very severe diphtheria.

Admitted 15. i. 34, the fourth day of illness. Palatal paralysis present from 17. i. 34 till 18. ii. 34 inclusive; cardiac paralysis of severe type from 28. i. 34 till 26. ii. 34 inclusive; pharyngeal paralysis from 18. ii. 34 till 28. ii. 34; albuminuria in first 4 weeks of treatment. Positive throat cultures and a succession of attacks of acute tonsillitis caused delay in dismissal till 28. v. 34.

Blood-sugar curves, after laevulose, on 19. i. 34 and 13. ii. 34 were both normal with the exception that there was fasting hypoglycaemia on the former date.



https://doi.org/10.1017/S0022172400035099 Published online by Cambridge University Press

Case 12. F. McI., female, 15 years. Moderately severe diphtheria.
Admitted 28. i. 34, the third day of illness. Normal course without paralysis.
Dismissed well 14. iii. 34.

Blood-sugar curve, after laevulose, on 29. i. 34 was similar to a normal curve after glucose; there was slight fasting hypoglycaemia. The curve was more nearly normal on 21. ii. 34.

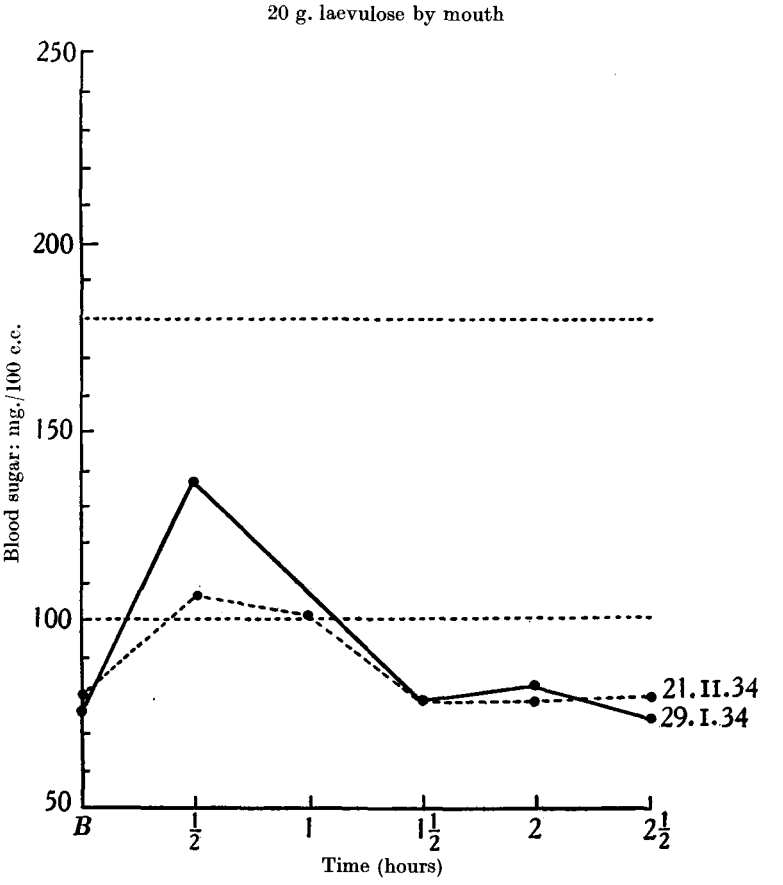


Table V. *Cases of severe diphtheria receiving extra sodium chloride*

Serum sodium (Na), serum chlorine (Cl) and serum potassium (K) in milli-equivalents per litre

Day in hospital ...		First			Eighth			Fifteenth			Last		
Patient	Type of recovery	Na	Cl	K	Na	Cl	K	Na	Cl	K	Na	Cl	K
JSH	Normal	137·75	107·19	5·04	135·86	108·15	7·65	123·98	102·09	9·23	126·03	102·44	3·81
MST	Normal	120·50	104·44	9·22	118·46	103·32	7·53	120·16	98·79	5·04	138·69	105·01	9·30
CWE	Normal	113·31	102·56	9·51	117·60	102·25	7·09	115·90	103·29	4·60	133·98	105·98	8·58
JTH	Normal	122·36	94·56	8·54	109·89	89·91	7·63	112·16	106·31	7·01	123·43	103·37	5·11
GJE	Normal	120·80	108·82	6·98	120·02	106·88	6·59	105·51	104·93	6·37	133·25	107·32	6·98
MBE	Normal	120·81	99·17	7·69	130·31	106·83	7·33	129·69	106·34	6·80	135·18	105·63	7·88
CCE	Normal	110·96	91·09	7·93	112·64	105·49	6·72	124·71	105·79	5·95	130·63	109·49	4·89
DME	Normal	130·01	106·06	11·15	122·54	106·31	15·73	123·87	106·59	8·90	129·49	100·07	4·99
MMN	Normal	121·44	101·06	6·87	131·24	102·67	9·10	133·19	101·92	7·61	131·18	103·97	9·58
EMW	Normal	122·21	96·13	9·03	129·04	99·57	6·64	136·00	97·28	3·78	130·62	99·28	5·23
MDM	Normal	111·90	97·29	9·97	117·10	93·31	6·05	117·99	106·70	5·60	138·88	104·36	4·23

Table V (*continued*)

Cases of severe diphtheria not receiving extra sodium chloride

Serum sodium (Na), serum chlorine (Cl) and serum potassium (K) in milli-equivalents per litre

	Day in hospital ...	First			Eighth			Fifteenth			Last		
Patient	Type of recovery	Na	Cl	K	Na	Cl	K	Na	Cl	K	Na	Cl	K
MMR	Mild paralysis	134·19	'102·10	5·21	113·99	103·68	8·51	114·30	106·06	4·34	123·19	105·00	4·68
CSS	Normal	125·03	104·17	5·28	117·62	98·01	5·61	133·32	106·13	4·55	132·64	103·72	7·16
WAN	Normal	113·26	95·41	6·35	121·48	102·36	5·04	122·11	102·96	5·32	126·45	101·70	5·21
RWE	Delay in dismissal	111·90	94·63	11·28	123·11	94·93	8·00	114·08	102·04	7·16	132·47	107·21	11·22
EMN	Normal	114·93	93·90	9·59	121·55	105·11	7·13	118·62	107·21	5·49	126·00	104·14	4·04
PGL	Normal	119·89	107·68	6·92	126·13	100·54	5·04	126·74	100·98	5·73	134·73	101·31	6·60
LSH	Mild paralysis	127·31	104·99	5·47	135·59	106·62	3·86	117·50	103·03	6·85	133·48	106·95	4·56
MPN	Normal	121·80	105·18	7·83	127·56	106·34	5·22	128·04	105·90	5·85	133·34	105·16	4·27

Table VI. *Cases of very severe diphtheria receiving extra sodium chloride*

Serum sodium (Na), serum chlorine (Cl) and serum potassium (K) in milli-equivalents per litre

	Day in hospital ...	First			Eighth			Fifteenth			Last		
Patient	Type of recovery	Na	Cl	K	Na	Cl	K	Na	Cl	K	Na	Cl	K
CDF	Mild paralysis	116·70	99·64	9·17	118·41	92·32	7·68	110·96	102·93	4·52	134·13	103·04	8·02
ELE	Normal	132·32	106·79	7·09	115·90	103·03	6·51	125·27	99·84	6·31	132·64	109·48	4·18
EBN	Mild paralysis	128·76	99·52	7·04	123·54	97·96	5·16	126·64	105·47	4·76	130·36	105·61	4·37
JTR	Mild paralysis	109·82	98·66	10·00	119·90	108·30	9·02	126·83	103·43	6·61	134·59	103·79	5·53
DLK	Severe paralysis	119·82	97·60	4·29	122·08	89·51	4·41	126·87	102·02	3·06	139·73	107·62	5·66
JDT	Severe paralysis	126·64	93·67	4·56	112·05	90·61	3·37	134·28	107·71	3·72	135·50	108·17	6·79
ESN	Normal	112·11	101·06	5·85	109·41	108·64	7·25	111·26	102·02	6·40	127·55	106·09	8·18
FMN	Normal	134·13	104·30	4·65	142·11	107·91	3·27	120·08	103·53	4·40	127·55	99·33	3·41
MKN	Severe paralysis	125·88	106·95	7·23	123·98	107·52	10·51	127·72	106·28	8·36	126·50	100·44	6·82

Cases of very severe diphtheria not receiving extra sodium chloride

Serum sodium (Na), serum chlorine (Cl) and serum potassium (K) in milli-equivalents per litre

	Day in hospital ...	First			Eighth			Fifteenth			Last		
Patient	Type of recovery	Na	Cl	K	Na	Cl	K	Na	Cl	K	Na	Cl	K
CBR	Mild paralysis	122·55	103·62	6·20	134·49	107·21	5·53	125·88	103·89	7·44	139·34	106·53	5·11
ATS	Normal	112·45	100·45	11·09	127·38	106·64	8·70	124·49	101·00	8·51	128·03	106·59	4·91
AMR	Delay in dismissal	115·83	95·21	11·80	122·29	104·69	8·41	131·61	104·20	6·62	131·80	104·74	6·93
JAN	Delay in dismissal	118·87	97·14	5·58	128·64	98·31	5·41	130·46	99·08	5·49	129·57	101·33	5·31

Table VII. *Cases of very severe diphtheria with fatal results (extra sodium chloride not given)*

Serum sodium (Na), serum chlorine (Cl) and serum potassium (K) in milli-equivalents per litre

	Period ...	On admission			Shortly before death		
Patient	Time of death	Na	Cl	K	Na	Cl	K
RB	7th day	112·23	90·10	9·34	98·64	75·37	—*
JW	11th day	124·31	97·55	7·46	97·72	77·78	—*
MG	17th day	116·20	88·23	8·97	107·49	86·15	11·08
JM	8th day	121·14	96·47	7·61	104·53	82·44	12·23

* Insufficient serum obtained for proper estimation of potassium.

CONCLUSION

When due consideration has been given to the points made in the foregoing parts of this article, it cannot be doubted that there is a large amount of evidence in favour of the view that lesions of the suprarenal glands must play a considerable part in the production of the typical symptomatology of diphtheria. Moreover, it has already been shown (Maclean, 1936) that the administration of sodium chloride (one of the accepted methods of treating deficiency of the suprarenal cortex) is of distinct value in promoting improved results in the treatment of diphtheria, an observation which is added proof in aid of the contention already made.

This article is published with the permission of Dr W. M. Elliott, Physician-Superintendent of Ruchill Hospital.

REFERENCES

ADDISON (1903). A collection of the published writings of the late Thomas Addison, *Practitioner*, **71**, 472.
BEGG & HARRIES (1935). *Lancet*, i, 480.
BENN, HUGHES & ALSTEAD (1932). *Lancet*, i, 281.
BREMS (1932). *Acta Med. Scand.*, 14 Dec., p. 1.
BRITTON & SILVETTE (1933). *Amer. J. Physiol.* **104**, 399.
—— —— (1934). *Ibid.* **107**, 190.
BROWN-SÉQUARD. Quoted by RABINOWITZ (1923). *Amer. J. Med. Sci.* **166**, 516.
BURTON & CHALMERS (1930). *Lancet*, i, 296.
DONATO (1930). Thèse de Paris, No. 323.
HARROP, WEINSTEIN, SOFFER & TRESCHER (1933). *J. Exp. Med.* **58**, 1.
HARTMAN, BROWNELL & LOCKWOOD (1932). *Endocrinology*, **16**, 521.
HERBERT & BOURNE (1931). *Brit. Med. J.* i, 94.
KER, C. B. *Infectious Diseases* (revised by Rundle, 1929).
LEREBOULLET, GOURMAY & DONATO (1931). *Ann. de Méd.*, May, p. 547.
LUCKE, WIGHT & KIME (1919). *Arch. Int. Med.* **24**, 19.
MACLAGAN & COOKE (1916). *Lancet*, ii, 1054.
MACLEAN (1936). *Lancet*, ii, 129.
MUIR, R. (1924). *Text-Book of Pathology.*
PEARL & BRUNN (1928). *Surg., Gyn. & Obstet.*, Sept., p. 393.
PETERS & GUNN (1930). *J. Hygiene*, **30**, 420.
PETERS & VAN SLYKE (1932). *Quantitative Clinical Chemistry*, vol. ii, pp. 737, 751, 835.
POLANDOWSKI (1932). Thèse de Paris, No. 35.
RABINOWITZ (1923). *Amer. J. Med. Sci.* **166**, 516.
ROLLESTON, J. D. (1925). *Acute Infectious Diseases.*
ROWNTREE (1933). Article on Addison's disease in *Text-Book of Medicine by American Authors*, 3rd ed., edited by Russell L. Cecil, p. 1249.
RUBINZTEJN (1934). Thèse de Paris, No. 134.
SCHWENTKER & NOEL (1930). *Bull. Johns Hopkins Hosp.*, June, p. 358.
THADDEA (1935). *Klin. Woch.*, 7 Sept. (Annotation in *Brit. Med. J.* 1935, ii, 1003.)
THOMSON, JOHN (1925). *The Clinical Study and Treatment of Sick Children*, 4th ed., p. 461.

EXPLANATION OF PLATE II

Fig. 1. Section of suprarenal gland from a case of laryngeal diphtheria, showing normal appearance of the suprarenal tissue.

Fig. 2. Kidney and suprarenal gland from a case of faucial diphtheria, showing enlarged lymphatic glands at hilus of the suprarenal gland.

Fig. 3. Section of suprarenal gland from a case of faucial diphtheria, showing cloudy swelling and haemorrhages in the cortical tissue.

Fig. 4. Kidney and suprarenal gland from a case of faucial diphtheria, showing extensive haemorrhage on the surface of the left suprarenal gland which is also greatly enlarged.

(*MS. received for publication* 30. XII. 1936.—Ed.)

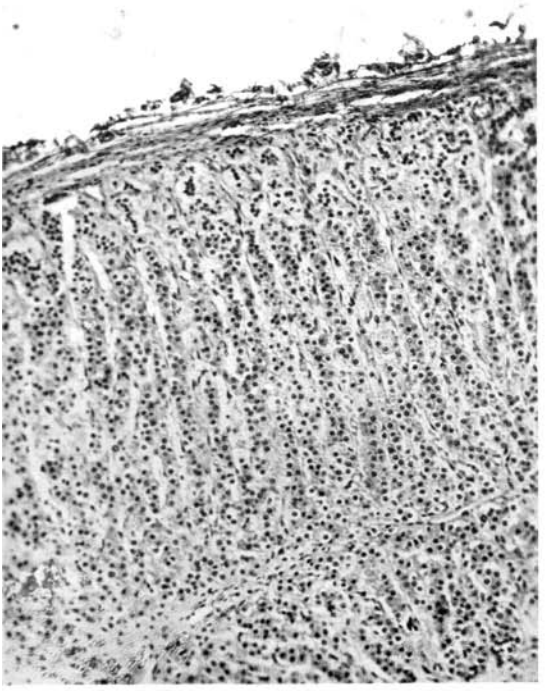


Fig. 1.

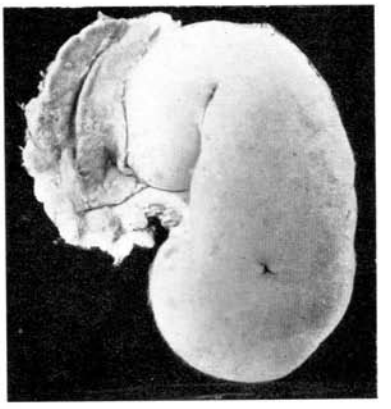


Fig. 2.

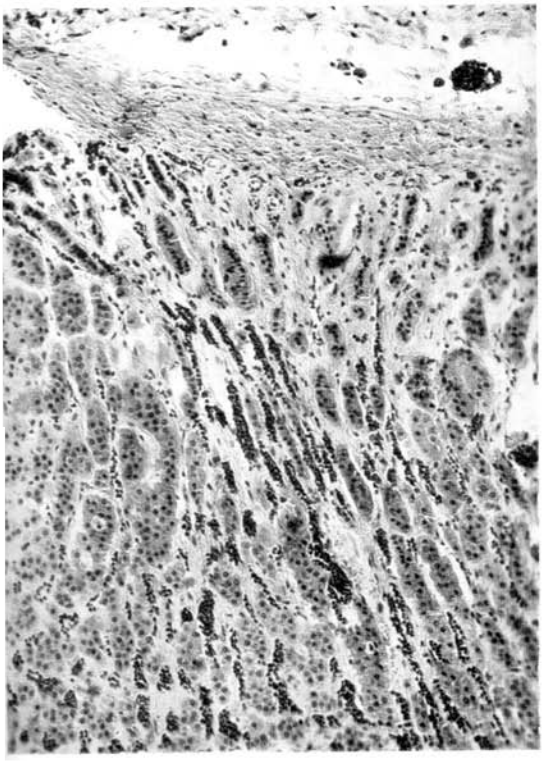


Fig. 3.

Fig. 4.

https://doi.org/10.1017/S0022172400035099 Published online by Cambridge University Press