OEDEMA ASSOCIATED WITH ENTERITIS IN CHILDREN

Thesis submitted for degree of M.D., Edin.

by

ALLAN GEORGE HAMILTON,

M.B., Ch.B.

March 1912.

The extraordinarily long hot summer of 1911 was responsible for an extremely severe epidemic of gastro-enteritis in children, the Registrar General's reports showing that the mortality in London from that disease was the highest recorded since 1897.

From the beginning of June to the end of October, no less than 3118 cases of diarrhoea or diarrhoea and vomiting were treated at the East London Hospital for Children. Twenty-five of these cases were of special interest, in that they had developed that unusual form of oedema which I intend to describe. Oedema associated with or following upon an attack of gastro-enteritis is by no means common, and the condition is so striking, the clinical type so definite, the literature concerning it so scanty and many of its features so interesting that a further study of the disease seems desirable.

The cases resemble one another so closely that it will be convenient to give a summary of them all and then record the detailed notes of three of them. I then propose to discuss the etiology, pathology, diagnosis, prognosis and treatment of the condition.

Twenty-four of the children were patients in the East London Hospital and the majority lived in the poorest houses of the East-end. Their ages ranged from /

from three months to five years; only two being under one year, thirteen between one and two, while the remaining ten were between two and five years old.

With the exception of one, all the cases had a history of diarrhoea or diarrhoea and vomiting, varying from two weeks to three months. In the exceptional case the mother said that there had been no diarrhoea. When the child was admitted to hospital, however, she had loose offensive stools which contained a considerable amount of mucus. It is worth noting that in almost every instance the child was brought to hospital on account of the swelling of the face, hands and feet: and not on account of the diarrhoea. With the one exception mentioned above, the enteritis had lasted two or more weeks before the oedema began to appear. The late Dr. Coutts, under whom many of these children were admitted to the East London Hospital, used to lay stress on the fact that the oedema frequently began after the diarrhoea had stopped, (i.e. when the stools were no longer frequent) and after analysing the notes of my series it was found that nine belonged to this class.

The child is usually drowsy and irritable. His face is pale and swollen, the complexion often muddy, and the whole picture suggests an intense toxaemia. The /

The oedema is usually most evident in the face, hands and feet but in many cases extends well up the limbs and is marked in the lumbo-sacral region. It varies with the position of the child and pits well to pressure. In Case No. XXIV. the swelling was most marked in the face, lumbar region and labia and very slight in the extremities. The swollen hands and feet are cold and deeply cyanosed. The pulse at the wrist is feeble and in some cases imperceptible. The temperature is sub-normal, not infrequently dropping to 95°F. or even less. Any marked rise of temperature above the normal usually indicates some complication such as broncho-pneumonia. A slight pyrexia is sometimes associated with an increase in frequency and looseness of the stools; sometimes with constipation.

On examination no increase of cardiac dulness or other evidence of heart disease is found. Four of the cases developed signs of broncho-pneumonia before death; in the remainder no abnormal signs were discovered in the lungs. Enlargement of the liver was noticed in two cases. Marked abdominal distension due to flatulence occurred in a few, but in most of my cases the abdominal walls were lax. Ascites was never detected.

A careful examination of the urine led to some interesting /

interesting results. On admission the patients passed a small amount of turbid urine with a normal specific gravity. Under treatment large quantities of pale watery urine were passed and the specific gravity fell to 1005 or less. The reaction was usually acid but in five cases alkaline. My attention was frequently directed to the extremely offensive odour of the urine. In only one case was I able to prove the presence of albumen and even here the cloud on boiling and acidifying was almost imperceptible.

The discovery of a colon bacilluria in Case II. (the details of which are given below) led to a bacteriological examination in the other cases with surprising results to which I shall refer later.

The character of the stools varied enormously but in every case they were extremely offensive. This feature was so noticeable that not only the nurses but the East-end mothers almost invariably called one's attention to it. They might be yellow, brown, green, greenish grey or clay coloured, digested or undigested, formed or unformed, but they were always offensive. Dr. Eustace Smith's[1] description of the stools in cases of chronic diarrhoea in children applies here. "In any case, they have an intolerable stench; and may be dark coloured and watery; or thicker, /

thicker, but still fluid, like thin paste; or may consist of green matter, like chopped spinach, diffused through a dark brown liquid."

One was frequently struck with the curious heavy odour which always hung about the cots of these patients. It in no way resembled the smell peculiar to other infants suffering from diarrhoea, and yet one was inclined to attribute it to soiled napkins. The Ward Sisters were appealed to, and even with the greatest possible attention to the cleanliness of these patients, they were unable to get rid of it, and did not hesitate to declare that the cause was other than the urine and faeces.

Sooner or later the majority of these children begin to desquamate. Over the oedematous areas the skin is glazed but when the swelling subsides the skin becomes dry and harsh and a fine desquamation sets in, commonly beginning on the lower extremities, but sometimes on the body, and continuing for two or more weeks. The skin over the abdomen is usually loose, wrinkled and inelastic.

It is a somewhat remarkable fact that although tetany occurred in one case, convulsions were never observed nor did the mothers give any history of these previous to admission to hospital.

In this series of twenty-five cases there were eight /

eight deaths and seventeen recoveries. One of the first signs of improvement was a change in the stools. These became less frequent, less offensive, and regained their natural colour and consistency. The child became brighter and much more attractive; his pulse improved, his colour returned, the dropsy diminished, and his extremities became warm and pink. The disagreeable odour about the cot was no longer noticeable. The disappearance of the odema however, was not necessarily a sign of improvement for some of the children were dangerously ill after the swelling of the face, hands and feet had gone. Loss of appetite, continued loss of weight, increased feebleness and drowsiness, drawn features and sunken eyes foretold a fatal result. In four of the eight fatal cases the end was hastened by broncho-pneumonia.

LIST OF CASES.

	Name	Age	Sex	Date of admission	History	Result
1.	E.M.	3/12	F	Sept. 16th 1911	D.&V.3 weeks before odema	Death
2.	J.H.	2 5/12	M	" 9th "	D.& V.2weeks	Recovered
3.	A.S.	2 2/12	M	" 25th "	D.& V.3 "	Death
4.	F.N.	1 2/12	M	" 12th "	D. 3 "	Recovered
5.	B.M^{c}C.	2 5/12	M	" 12th "	D. 5 "	"
6.	P.T.	1 8/12	F	" 22nd "	D.& V.6 "	"
7.	J.L.	1 3/12	M	" 26th "	D.& V.7 "	"
8.	E.B.	1 6/12	F	" 26th "	D.& V.3 "	"
9.	G.H.	2	F	" 30th "	D.& V.3 "	"
10.	W.M.	2 6/12	M	" 29th "	D.& V.5 "	"
11.	E.N.	7/12	F	" 26th "	D.& V.2months	Death
12.	B.S.	2 6/12	F	" 30th "	D.& V.7weeks	Death
13.	A.D.	1 2/12	M	Oct. 24th "	D. 5 "	Death
14.	R.L.	1 1/12	M	" 26th "	D.& V.4 "	Recovered
15.	W.J.	1 10/12	M	" 23rd "	D.& V.6 "	"
16.	M.D.	2	F	" 2nd "	D.& V.3 "	"
17.	J.C.	3	M	" 12th "	D.& V.5 "	Death
18.	G.B.	2	M	" 9th "	D.& V.7 "	Recovered
19.	J.S.	3	M	" 11th "	D.& V.5 "	"
20.	H.G.	1 7/12	M	" 27th "	D.& V.3months	"
21.	K.B.	2 6/12	F	Nov. 1st. "	-	"
22.	S.B.	1	F	" 1st. "	D.& V.3months	Death
23.	E.P.	1 8/12	F	" 1st. "	D.& V.5weeks	Death
24.	M.J.	4 6/12	F	July 27th " Sept. 17th " Jan. 22nd 1912	D.& V.2 "	Improved
25.	L.B.	1 8/12	F	Dec. 4th 1911	D.& V.3months	Recovered

CASE II.

J.H., aged 2½ years, was admitted to the East London Hospital for Children on September 9th, 1911. He was brought on account of swelling of the face, hands, feet, legs, scrotum and penis; and his mother stated that he could not pass his water.

History :-

The patient was quite well until a fortnight ago when diarrhoea and vomiting set in and lasted three days. When the diarrhoea stopped the legs and feet began to swell; later the swelling appeared in the hands, scrotum and penis. The face became puffy every now and then. During the past week he has passed very little urine. Since the illness began "he has been ravenous for food and drink".

Previous History :-

Scarlet fever, measles and whooping cough. He usually enjoys good health.

Family History :-

Father, mother, two sisters and one brother - alive and well.

State on admission (Sept. 9th 1911) :-

Temperature 99.4 - Pulse 128 - Resp^{s}. 44.

The patient, a well nourished child, was drowsy and /

and very peevish. His face was pale and swollen especially round the eyes. There was very marked oedema of the lumbo-sacral region, legs, feet, scrotum and penis. The same condition was present, in a less marked degree, in the upper limbs. The oedema was firm but pitted well to prolonged pressure. The hands and feet were not only oedematous but icy cold and deeply cyanosed. His general appearance suggested nephritis. The skin was dry and harsh and a fine desquamation was taking place on the back and lower extremities.

On examination the heart and lungs were found to be normal. The pulse at the wrist was feeble but could be counted. The stools were small, loose, clay coloured and very offensive.

Urine :- Specific gravity 1010, faintly alkaline, pale and slightly turbid. Neither albumin nor tube casts were present. It was extremely offensive when passed and became more so on standing.

Greatest circumference of calf (right and left)

= 9 inches.

Diet :- Fluids only (milk, beeftea and veal broth)

Given castor oil - two drachms.

Sept 11th :-

No appreciable change. He was losing weight but /

but oedema did not seem to be any less. Given hypodermic injection of adrenalin chloride (1 - 1000), five minims.

Sept. 13th :-

No marked change. Ordered ten minims adrenalin chloride twice daily, by mouth.

Blood count :-

Red cells	=	4,350,000
White cells	=	21,500
Haemoglobin	=	75%
Colour index	=	0.86

Differential count :-

Polymorphonuclears	=	33.2%
Small mononuclears	=	38.3
Transitional cells	=	8.0
Large mononuclears	=	19.3
Eosinophils	=	1.0

The specific gravity of the blood (estimated by the glycerine method) = 1043.

Sept. 15th :-

Oedema less. Losing weight rapidly. In six days he had lost four pounds, fifteen ounces. The patient's appearance however did not improve. He was more drowsy, had a muddy complexion, the edges of his eyelids were blue and although his hands and feet were less cyanosed, they were still very cold. Temperature subnormal. Pulse fuller with increased pressure.

Abdomen /

Abdomen distended and tympanitic. Stools clay coloured and very offensive. The urine had been examined frequently for albumin with negative results. The amount passed had steadily increased from eight ounces during the first twenty-four hours to seventy ounces on Sept. 14th.

Adrenalin treatment stopped. He had one hypodermic injection (M.V) and four doses (M.X) by the mouth.

Sept. 16th :- Given calomel gr. $\frac{1}{4}$ hourly (4 doses).

Sept. 17th :-

Great improvement. The oedema had gone and the extremities were no longer cold and cyanosed.

Greatest circumference of the calf was now $7\frac{1}{4}$ inches, i.e. a loss of $1\frac{3}{4}$ inches.

From this date patient made a slow but uninterrupted recovery. He began to sit up in bed and play with his toys. The pale drowsy, peevish child became interesting and attractive. That curious heavy odour which was always present about his cot and which was frequently remarked upon by sisters and nurses disappeared. The stools improved and lost their extreme offensiveness. The desquamation which had become general, ceased.

On September 20th, his urine was noticed to have a /

a greenish opalescence. This suggested an examination for B. Coli. and they were found to be present. The urine was drawn off with a sterile catheter and the nature of the organism was not pronounced until it was proved beyond doubt, by means of the differential culture media to be the bacillus coli. There were no symptoms to indicate a bacilluria.

During the week the improvement continued and on September 27th patient was discharged from hospital - recovered.

CASE II.

Date	Fluids taken	Urine	Weight
Sept. 9		8 oz.	2 st. 3 lbs 5oz
" 10		8½	2 2 11
" 11*		9½	2 1 2
" 12		19	2 1 0
" 13	51 ounces	41	2 0 10
" 14	41	70	1 13 10
" 15	37	50	1 12 6
" 16	31	39	1 12 4
" 17	44	30	1 11 8
" 18	47	34	1 11 12
" 19	37	35	1 11 12
" 20	40	35	1 11 6
" 21	33	38	1 11 6
" 22	34	32	1 12 0

* Adrenalin treatment begun.

CASE VI.

P.T., girl, aged twenty months, was admitted to the East London Hospital for Children on September 22nd 1911. The mother sought advice because the child had had swollen legs for one week.

History :-

Patient had an attack of diarrhoea and sickness six weeks ago. The vomiting ceased three weeks ago but the diarrhoea still occurred at night. The motions were yellow, watery and very offensive. Swelling of the legs began one week ago; swelling round the eyes appeared two days later. For the last fifteen days patient had been given nothing but albumin water. The swelling of the face and legs seemed to disappear at night when the child was warm in bed.

Previous History :-

During the past fourteen months patient had had measles, whooping cough and chicken-pox.

State on admission (Sept. 22nd 1911) :-

Temperature 96°F. Pulse ? almost imperceptible at the wrist. Respirations 28.

The child appeared to be well nourished but the oedema, owing to its very general distribution was apt to deceive one. She was listless and peevish. The face was pale and puffy round the eyes; the lower limbs /

limbs were swollen as high as the groin, and the upper as high as the elbow. The lumbar region was also oedematous and pitted well to pressure.

Her hands and feet were cold, glossy and had a bluish purple colour.

On examination I failed to detect any abnormality in the heart or lungs and there was no enlargement of the liver or spleen. The stools were loose, brown and offensive but did not contain excess of mucus.

In this case, a female child, I was unable to measure the daily amount of urine. It was pale, turbid and faintly alkaline with a specific gravity of 1010. Neither albumin nor blood was present.

Treatment and Progress :-

The patient was kept warm in bed surrounded by hot bottles and the extremities were wrapped in cotton wool.

Diet :- Milk and water, equal parts with two grains of sodium citrate added to each ounce.

Sept. 24th :- Patient had gained fourteen ounces in weight since admission but there was no obvious increase of the oedema. The amount of urine secreted was small - about 14 ounces. The hands were still cold and blue but the feet were warm.

Treatment with hypodermic injections of adrenaline chloride /

chloride commenced. Ordered five minim doses twice daily.

Sept. 26th :-

The oedema had suddenly diminished and she had lost 28 ounces in two days. Adrenalin treatment stopped. She had six injections of five minims each.

Sept. 27th :-

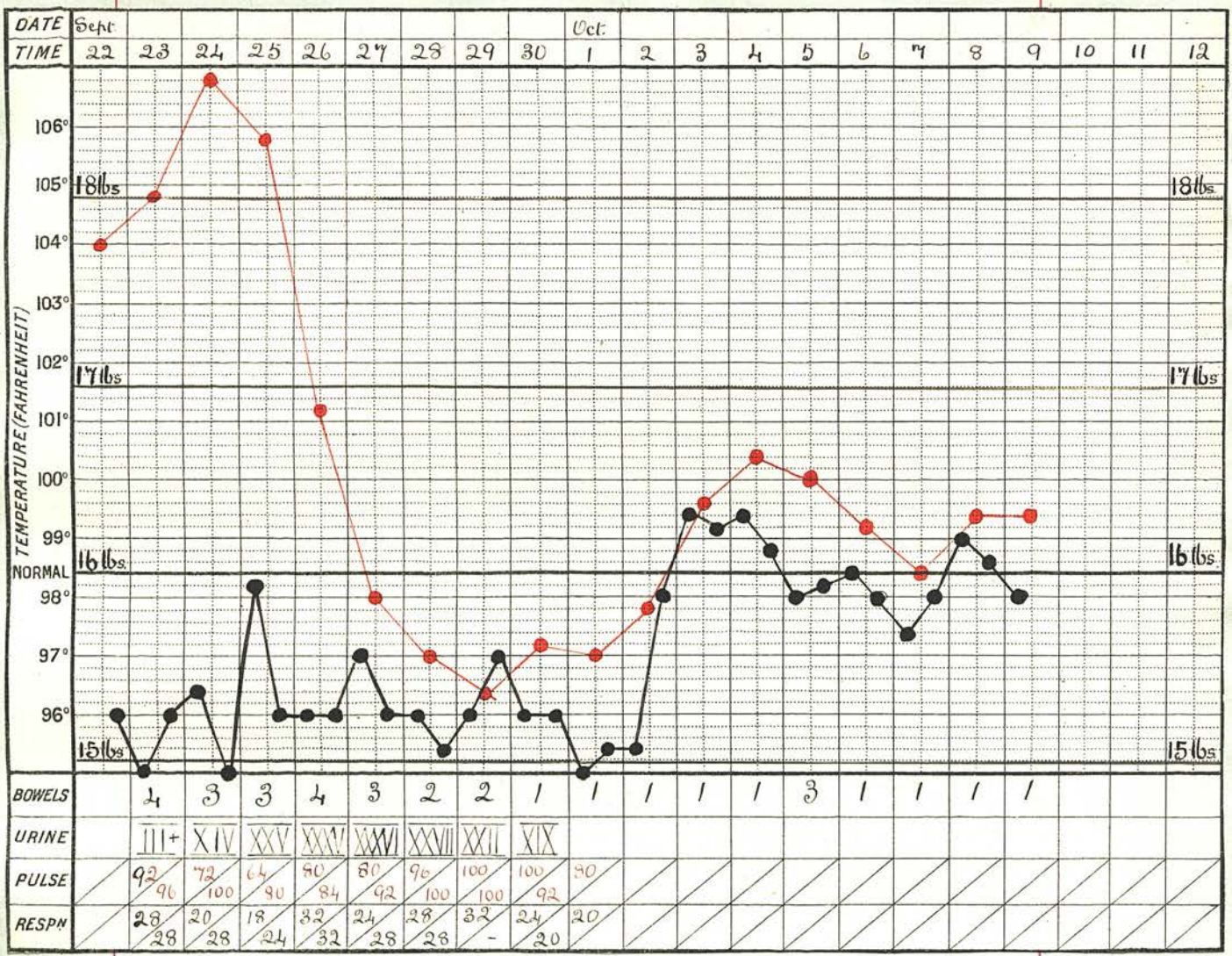
The child was much better. There was now no evidence of oedema but she was still losing weight. During the last twenty-four hours she had passed more than 35 ounces of urine which was pale, watery and had a specific gravity of 1010. No albuminuria.

Ordered the following mixture three times daily :-

Tinct. Strophanthi	Minims	II.
Spirit. Aeth. Nit.	"	XV.
Spirit. Chloroform.	"	V.
Aq. ad.	Drachms	II.

October 4th :-

The child improved steadily and began to put on weight. There was no return of the oedema. The extremities were now warm and pink. She sat up in bed and took an interest in her surroundings. The stools were normal. A fine desquamation had begun on the /



Weight = red.

Temperature = black.

This chart shows the sudden fall in weight after the adrenalin treatment was begun on the 24th September.

The characteristic subnormal temperature is also well shown.

the lower limbs. Catheter specimens of her urine were examined for organisms on two occasions with the same result. A bacillus belonging to the B. Proteus group was found.

October 6th :- Allowed to get up.

October 9th :- Discharged - "recovered".

CASE NO. XXIV.

M.J., girl, aged 4½ years, was admitted to the East London Hospital for Children on July 27th 1911, suffering from diarrhoea and vomiting. The diarrhoea had lasted one week and the vomiting three days. On admission the child had a very bad colour and was evidently suffering from an intense toxaemia. She was drowsy, had a bluish-white complexion and round the sunken eyes were dark rings.

During the first twenty-four hours in hospital she passed eight yellow watery offensive stools. The urine did not contain albumin. Treatment consisted in washing out the rectum and lower portion of the colon; in the administration of calomel gr. $\frac{1}{6}$ hourly for /

for eight doses, and twenty minims of brandy every two hours. Eight ounces of normal saline were infused subcutaneously from a vacuum flask.

During the next three days patient showed no signs of improvement. On July 30th the rectal lavage was repeated and she was ordered a tablespoonful of the following mixture every six hours.

Ol. Ricini	Minims	V.
Vin. Ipecac.	Minim	I.
Glycerini	Minims	V.
Mucil. Tragacanth	Minims	XV.
Aq. ad.	drachm	I.

Patient had been getting whey and albulactin by the mouth. This was now stopped and water only was allowed for two days. On Aug. 2nd she had oedema of the face especially on the side on which she was lying.

The next day the swelling of the face was more marked and the feet and ankles were slightly oedematous. She now had the appearance of a case of acute nephritis.

On Aug. 3rd a severe attack of tetany began and lasted five days. The typical position of the hands was present but the feet were not affected. There was facial irritability (Chvostek's sign) on both sides.

Ammonium /

Ammonium bromide was administered after the stomach had been washed out. On Aug. 8th patient began to improve. The tetany and oedema had disappeared but the stools were still large, loose, frequent and offensive. On Aug. 28th she was well enough to be sent to a convalescent home.

During her stay in hospital the temperature was usually subnormal and never rose above 99.6°F.

Patient was readmitted on September 17th. She had lost 4½ pounds in weight. The medical officer at the Convalescent Home reported that vomiting had occurred from time to time and that the stools had been loose and frequent.

When readmitted the temperature was 96.2, pulse 120, and respirations 26. She was apathetic but quite conscious, and lay on her back with legs drawn up, and hands held to the head making continual restless stroking movements over the temples and occiput. The face was flushed and the tongue dirty. Examination of the chest revealed nothing abnormal. The abdomen was slightly distended. The liver and spleen not enlarged. The limbs were wasted, there was no loss of power, and the reflexes, superficial and deep, were normal. The eye movements were apparently normal but at times there was a suspicion of a squint. The pupils /

pupils reacted to light and the fundi were normal. A diagnosis of tuberculous meningitis was made by all who saw her. Lumbar puncture was performed and the fluid escaped under increased pressure. It was clear and contained the normal number of cells and amount of albumin.

On September 23rd she seemed brighter and did not keep her hands to the head. Hard faecal masses could now be felt in the ascending and transverse colon. An injection of olive oil followed by a simple enema brought away a very large pale grey constipated stool. During the course of the day she developed tetany. Again the hands assumed the typical "obstetric" position but the feet were not affected. Slight facial irritability was present. There was no oedema. The tetany continued for three days and then she began to improve. By October 23rd although her stools were still pale and offensive, she was considered well enough to be treated as an out-patient.

From this date until she was admitted for the third time on Jan. 22nd 1912 patient steadily became worse. Her stools again became loose frequent and offensive. The mother said that she was always drowsy and had no appetite. When readmitted to hospital /

CASE NO. XXIV. showing oedema of the face, and tetany affecting both hands and the right foot. The photograph was taken after the oedema had partially subsided.

hospital there was general oedema but it was particularly well marked on the face. The urine was very pale, almost watery, with a specific gravity of 1002. Neither albumin nor tube casts were present. On Jan. 23rd the oedema had increased and the eyes were completely closed. Again she developed tetany and this time the right foot was affected as well as the hands. Examination of the chest and abdomen revealed nothing abnormal. Her stools were loose, frequent, pale, putty-like, undigested and very offensive.

Blood examination :-

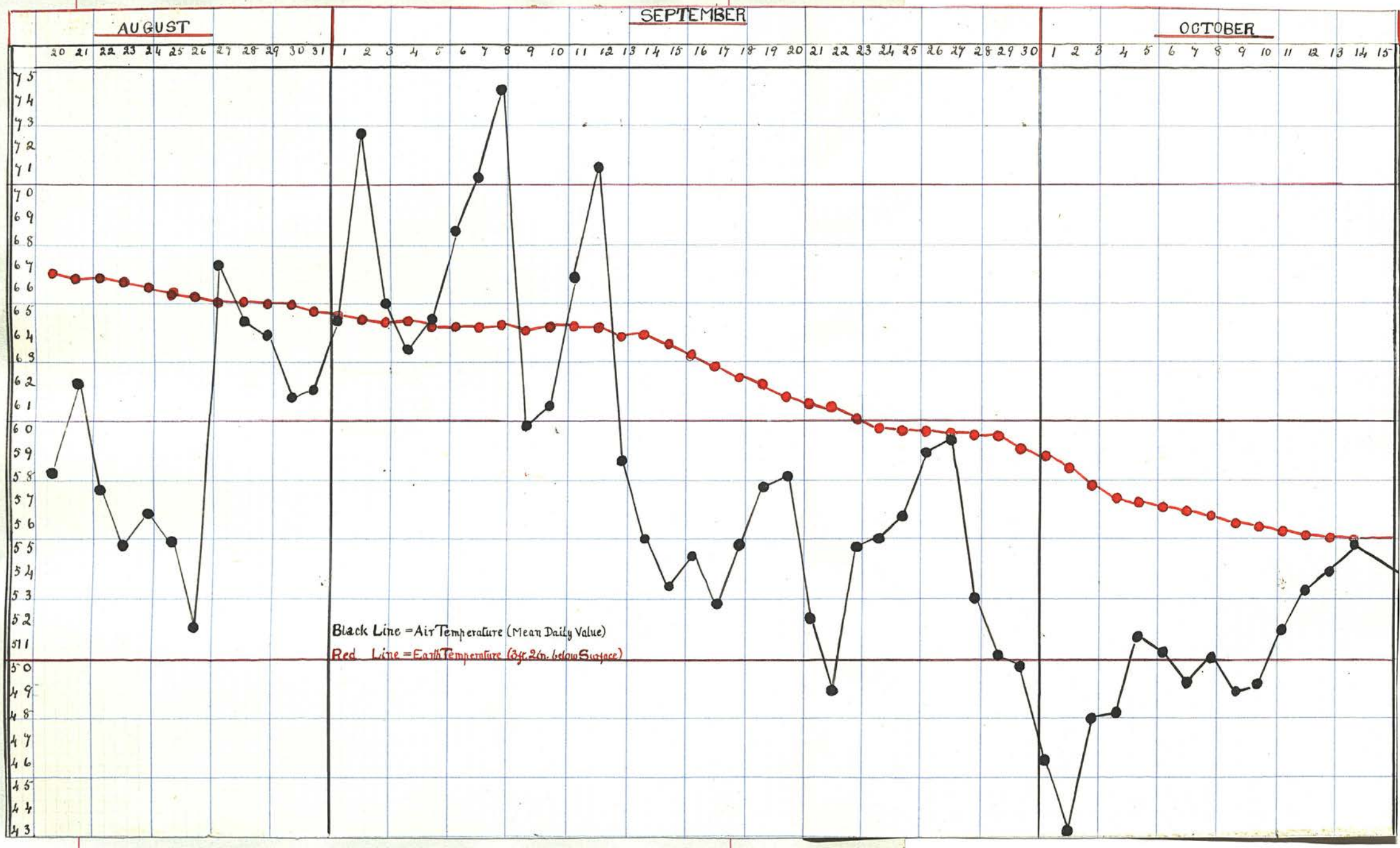
Red cells	=	5,300,000
White cells	=	11,800
Haemoglobin	=	85%
Colour Index	=	0.8

Differential Count :-

Polymorphs	=	58%
Small lymphocytes	=	13
Large lymphocytes	=	20
Transitional cells	=	9

A catheter specimen of her urine was examined on Jan. 26th and bacilli were found. On the differential culture they proved to be B. Coli.

This examination was repeated a week later with the /



This chart was constructed from figures supplied by the Registrar General. The observations were taken at the Greenwich Observatory, which is less than a mile distant from the East London Hospital.

the same result. On Feb. 3rd patient was ordered urotropin Grs. IV three times daily. On Feb. 9th no bacilli were found after centrifuging at 3000 revolutions per minute, for half an hour, and staining films from the deposit.

On the sixth day after admission the tetany and oedema had completely disappeared. The treatment adopted on this occasion was thorough evacuation of the bowels with castor oil and the administration of ten grain doses of calcium chloride every four hours. The patient soon lost her drowsiness and regained her appetite but the stools remained pale, though less frequent and offensive. She was discharged - improved - on Feb. 12th. Patient is still being kept under observation in the out-patient department.

In this case there were some unusual features. Firstly, it is the only one of my series which developed tetany. Secondly, the symptoms recurred, a fact which I attribute to the enteritis never having been completely cured. The stools were still pale and offensive when the child left the ward. Thirdly, very curious and restricted sites were chosen by the oedema. On one occasion the face and labia only, were oedematous. I believe the head symptoms (spurious hydrocephalus) which so closely simulated meningitis may have been due to an oedema of the brain.

There can be little doubt that a subacute or chronic enteritis is the primary factor in the causation of these oedemas. One usually gets a history of diarrhoea commencing four or more weeks, and sometimes three months, before the oedema appears. In many cases the diarrhoea has stopped when the swelling begins, but in all some abnormality is still noticeable in the faeces. Is there any other factor? The long hot Summer of 1911 came to an end on September 12th, when there was a sudden fall in atmospheric temperature. Previous to that date no less than 2313 children were treated at the East London Hospital for various forms of diarrhoea, but only two of them had developed oedema. From September 12th to November 1st 805 cases of diarrhoea were treated at the hospital, and no less than 22 cases of oedema came under my observation. A study of these figures, and a glance at Chart II, which shows the variations in atmospheric temperature during this period, at once suggest that the atmospheric conditions play some part in the etiology of oedema associated with enteritis. From 12th to 30th September twelve cases were admitted to the hospital. Surely this is suggestive when we remember the sudden change in the weather on the former date. It is true that/

that cases of chronic diarrhoea are more common towards the end of a summer, but it is a remarkable fact that 2313 cases of all varieties of diarrhoea came under observation before September 12th, and only two had developed oedema. Quite recently W. E. Hume described 13 cases of "General oedema following gastro-enteritis in children", and it is interesting to note that all his cases were seen between the months of September and March. I succeeded in finding records of two other cases among the notes of the East London Hospital for 1910-11. One was admitted in November 1910 and the other in January 1911. Therefore, as far as we can judge from the study of a limited number of cases, this complication of enteritis in children appears to be very much more common during the colder months of the year . In Ashby's (3) experience it is most common during the Autumn. Dr. Eustace Smith has repeatedly emphasised the injurious effects of cold damp weather in cases of chronic diarrhoea in children. " .... indeed the sensitiveness to barometric changes is so extreme that on damp days the patient is always less well than on days which are bright and dry."(4)

I do not propose to discuss the various theories as to the causation of this or other forms of oedema, for that seems useless as long as the physiology of normal/

normal lymph formation and absorption is only partially understood. Suffice it to say that, in these cases of oedema associated with enteritis in children, we have a toxaemia, which in some way acts on the endothelium of the capillaries and leads to increased lymph transudation. Rolleston (5) classes these cases with the toxic oedemas. Hume has proved that retention of chlorides plays no part in their production. The anasarca is accompanied by a general lowering of the blood pressure and loss of vascular tone, as evidenced by the feeble pulse and the coldness and blueness of the extremities. Still (6) says "Oedema, especially of the extremities, is not an uncommon complication of infantile diarrhoea; ..... and it is no doubt similar in its pathology to the oedema which is often seen with severe marasmus in infancy; what this pathology may be is uncertain; but it is probable that some altered state of the blood and perhaps of the walls of the blood-vessels together with some feebleness of the circulation is sufficient cause for the oedema."

In my experience it is uncommon to find any albumin in the urine and I was able to prove there was no nephritis in six of the cases which ended fatally. Still believes the slight albuminuria met with/

with in cases of infantile diarrhoea may be due to uric acid granules in the pelvis of the kidney resulting from concentration of the urine.

Examination of the blood was carried out in several cases but no constant changes were discovered. The majority of the cases examined had a slight increase in the number of leucocytes. The red cells were sometimes over 5,000,000 per c. mm. Hume found some degree of secondary anaemia in his cases while Ashby believes that the blood is concentrated and diminished in volume. In a typical case he finds 80 per cent. of haemoglobin and 5,500,000 red blood corpuscles per cub. mm. It is, of course, important to obtain the blood from a non-oedematous part.

I was able to make a thorough bacteriological examination of the urine from 19 of my patients. Of the others, two had such extreme phimosis that it was impossible to be sure of obtaining non-infected specimens and three died before the examination could be carried out. In the 19 specimens the bacillus coli was isolated in pure culture from 9, a bacillus belonging to the B. Proteus group from 8, a bacillus of the Gaertner group from one, while the 19th was sterile. The examination was repeated in several cases and similar results were invariably obtained.

It/

It is interesting to note that there were no symptoms to indicate a bacilluria in any of my patients. The findings in these cases made it advisable to have the urine from other children in the wards thoroughly investigated. Catheter specimens were obtained from three infants suffering from diarrhoea without oedema. Two contained bacilli of the Proteus group and the third contained B. Coli. It was then thought advisable to examine the urine of some children in the surgical wards, and for this purpose I selected patients suffering from inguinal herniae, cleft palate, glands in the neck etc. Eight catheter specimens were tested and found to be entirely free from bacilli.

The technique in all cases was as follows. The urine was drawn off with a sterile catheter under complete aseptic precautions. In each case some of the urine was centrifuged, and from the deposit films were prepared and stained. In most instances bacilli were found together with a variable number of polynuclear lencocytes, which were not however sufficiently numerous to justify the diagnosis of pyuria. Very often phagocytosis could be demonstrated, a fact which negatives the supposition that any accidental contamination could have occurred. With the/

Case.	Age.	Sex.	Organism in urine.
No.2.	$2\frac{5}{12}$	M	B. Coli
3	$2\frac{2}{12}$	M	B. Coli
4	$1\frac{2}{12}$	M	B. Proteus
5	$2\frac{5}{12}$	M	B. Proteus
6	$1\frac{8}{12}$	F	B. Proteus
7	$1\frac{3}{12}$	M	B. Proteus
8	$1\frac{6}{12}$	F	B. Coli
9	2	F	B. Proteus
10	$2\frac{6}{12}$	M	B. Coli
12	$2\frac{6}{12}$	F	B. Proteus
15	$1\frac{10}{12}$	M	B. Proteus
16	2	F	B. Coli
18	2	M	B. Proteus
19	3	M	Sterile
20	$1\frac{7}{12}$	M	B. Coli
21	$2\frac{6}{12}$	F	B. Gaertner
22	1	F	B. Coli
24	$4\frac{6}{12}$	F	B. Coli
25	$1\frac{8}{12}$	F	B. Coli

the remaining portion of each of the urines I inoculated tubes of peptone broth and McConkey's bile salt broth. Cultures were obtained in 18 of my cases. From the the peptone broth I inoculated tubes of agar-agar, while from McConkey's medium I inoculated tubes of neutral red agar. Subcultures were obtained in all instances. From these, films were prepared and stained by Gram's method, and Gram negative bacilli were invariably found. The reactions of these bacilli were then investigated in litmus milk, litmus lactose, litmus maltose and litmus mannite. It was not infrequently found that the proteus organism could only be differentiated with certainty from B. Coli by the nature of the colony (colour reaction) on neutral red agar and by the liquefaction of the gelatine slope. In every case the true coli organism produced acid and gas in the McConkey, mannite, maltose and lactose media. These findings may help to throw some light on the etiology of the infection of the urinary tract in children by coliform organisms.

I had the opportunity of studying the post-mortem appearances in six cases and the findings were very similar. The mucus membranes of the large and small intestines showed patches of swelling and congestion with numerous petechial haemorrhages. The Peyer's patches, especially in the lower part of the ileum, were swollen, congested, and in two cases showed /

showed slight superficial ulceration. In case III. there were multitudes of small ulcers, about the size of pin's heads, affecting the mucus membrane only, in the caecum and ascending colon. As a rule the congestion and swelling of the mucous membrane were more marked in the colon than in the small gut. The liver was invariably large and fatty and in two cases the degeneration was extreme. No abnormal changes were noticed in the heart. Broncho-pneumonia was discovered in two cases. Neither with the naked eye nor on examination of stained paraffin sections was I able to detect definite evidence of nephritis. Cloudy swelling of the tubules was present, but I believe it to have been a post-mortem change. Hume thus describes pathological changes in the suprarenal glands of the two cases he had the opportunity of examining. "In the medulla the most noteworthy pathological changes are present. There are large masses of fibrous tissue, apparently beginning in and spreading out from the cells of the blood capillaries. Many of the localised masses are linked by strands of tissue, so that a core of fibrous tissue appears to run through the gland. There seems to be an absence of cells of the medulla." After a careful study of the suprarenals in six cases I am unable to confirm these changes. The absence of /

of medullary cells might easily be explained. Post-mortem changes take place rapidly in the medulla of the suprarenal, and it is impossible to prepare satisfactory microscopical preparations unless the gland is removed, and placed in a suitable fixing agent a few hours after death. Unless this is done within 24 hours and sections are cut there is an almost entire absence of medullary cells, but the fibrous reticulum remains, giving the appearance of an increase of fibrous tissue. I have examined over 100 sections of the suprarenal gland taken from infants who have died from diarrhoea, marasmus, general tuberculosis, congenital syphilis, pneumonia, and other acute diseases. Some of these were cut in paraffin, others with a freezing microtome. In some of them, as well as in the suprarenals from one of my cases of oedema, interesting developemental changes were met with, which at first sight appeared to be pathological. These changes have recently been described for the first time by Elliot and Armour(7). These authors point out that the large size of the glands at birth is due to an hypertrophied foetal cortex. This cortex rapidly degenerates and is replaced by cells which grow in from the periphery to form the adult cortex. The cells of the foetal cortex/

cortex undergo a fatty degeneration, are in part replaced by fibrous tissue which in its turn disappears, until at the end of the twelfth month the true cortex and medulla meet and the development of the gland is complete.

The general appearance of these cases at the time when the oedema is most marked, closely resembles that of a case of acute nephritis. The diagnosis, however, is readily made after an examination of the urine. It is necessary to go into the history carefully because the children are brought to hospital on account of the swelling of the face, legs and feet and the mother sometimes forgets to mention the diarrhoea, which may have commenced three months before . If the desquamation has begun and the oedema is still present another difficulty arises. When case II. came under my observation, he had already been notified as a case of scarlet fever in the desquamating stage with nephritis. The doctor had been unable to obtain a specimen of the urine. I have already mentioned the similarity between the oedema which occurs in cases of severe marasmus and the oedema of these cases. The former is never so marked and is usually confined to the hands and feet.

When a general oedema supervenes on a chronic enteritis/

enteritis the prognosis must always be serious for I believe it indicates an intense intestinal toxaemia. Hume reports two deaths in thirteen cases; in this series there were eight deaths in twenty five cases. The younger the child, the graver the outlook.

The treatment is largely symptomatic. The temperature is usually subnormal, so the child is put in bed surrounded by hot bottles and the extremities are swathed in cotton wool. The daily bath is carried out with as little delay as possible in a warm room. These children have come through a long illness and are, in many cases, extremely wasted. It is, therefore, very necessary to nourish them as much as possible and at the same time to treat the enteritis. It is advisable to begin by washing out the stomach and rectum. The "rectal lavage" may be repeated daily for we have seen that the enteritis chiefly affects the colon.

The question of feeding is a most difficult one. Milk, if given at all must be well diluted, and in the case of infants, must be citrated. In severe cases it may be necessary to resort temporarily to albumin water, whey or albulacten. Most of the children over two years did well on a diet consisting of diluted milk, veal broth, beef tea and Benger.

In/

In my opinion there is no drug more valuable than calomel. At the outset a single dose of one to three grains is given to ensure thorough evacuation of the bowels; later the drug may be given in small doses ($\frac{1}{4}$ - $\frac{1}{12}$ gr) at frequent intervals. Naphthalene tetrachloride, $\frac{1}{4}$ - 3 grains according to the age, three times a day, was also useful as an intestinal antiseptic. The majority of these patients need some stimulant, and brandy, in ten to thirty minim doses every four hours, is the most suitable.

Although I cannot confirm Hume's findings in the suprarenals in these cases, the treatment by injections of adrenalin chloride which he suggested, often produced the most striking results. It is commonly stated in text books that small doses of adrenalin chloride injected subcutaneously have a local effect only. I gave 5 minims hypodermically or 5 - 10 minims by the mouth in several of my cases and the results were often astonishing. The pulse improved, the amount of urine increased; there was a sudden fall in weight and a disappearance of the oedema. The results were more rapid when the drug was administered hypodermically. Although the patient generally improved under the adrenalin treatment, this did not always occur. In Case II. particularly it was noted that/

that the patient seemed worse for a time under its influence, although there had been a sudden disappearance of the oedema with loss of weight and improvement in the pulse. In such cases I believe the injection of adrenalin chloride by raising the blood pressure hastens the absorption of the dropsical fluid and increases the circulation of the toxins ; the increase of blood pressure, however, is accompanied by a more free secretion from the kidneys, the toxins are eliminated, and in the course of a day or two the child begins to improve. In case VII. very similar results were obtained by administering small doses of digitalis .

From these observations I conclude that adrenalin, when injected hypodermically, has more than a local effect; that it raises the blood pressure and increases the amount of urine secreted. The transient effect of intravenous injections on the blood pressure are well known and Fleisher and Loeb (8) have proved that they increase the flow of urine. It would appear that subcutaneous injections have a more lasting effect. Adrenalin chloride has been used with success in the treatment of cardiac cases with dropsy and other signs of failing compensation. Voigt (9) has recently published/

published some striking examples, in which he gave 5 - 15 minims subcutaneously, or a 5 grain tablet of the gland substance by the mouth. In his cases the dyspnoea was relieved, the quantity of urine increased, and the dropsy diminished. These results are very similar to my own in cases of oedema after diarrhoea in children and I believe that adrenalin chloride is a drug which has a greater sphere of usefulness than is at present supposed.

It has been pointed out that the suprarenal glands become exhausted of their adrenalin content in acute fevers and other toxic conditions. Is the marked loss of vascular tone in these cases due to exhaustion of the medulla? Further, it is supposed by some that the cortex of the gland supplies an internal secretion which neutralises toxins. Does the exhaustion of this portion of the gland account for the excessive toxaemia and oedema? In Addison's disease, which we know is due to pathological changes in the adrenalin bodies, persistent diarrhoea is not uncommon and a low blood pressure is to be expected. Elliot and Tuckett (10) have experimented on kittens and found that if one gland is removed the animal soon developes diarrhoea. These facts together with the/

the notable results obtained by injecting small doses of adrenalin chloride in cases of oedema after diarrhoea in children have suggested to me some possible but as yet unknown part which the suprarenals play in their pathology.

REFERENCES.

(1) Eustace Smith - Disease in Children p. 673

(2) W. E. Hume - B.M.J. Sept. 2nd 1911 p.478

(3) Hugh T. Ashby - Practitioner, May 1911 p.686

(4) Eustace Smith - Allbutt & Rolleston Vol. III.

(5) Rolleston - B.M.J. Aug. 28th 1909.

(6) Still - Common disorders and diseases of Childhood p. 614.

(7) Elliot & Armour - Journ. of Path. & Bact. Vol. XV. 1911.

(8) Fleisher & Loeb - Jour. Exper. Med. Vol. II. 1909.

(9) Voigt - B.M.J. Mar. 9th 1912 p. 536

(10) Elliot & Tuckett - Jour. of Phys. Vol. XXXIV. p. 350.