Bismuth Skiagraphy.—Not much information could be obtained by this means. The stomach was viewed with the fluorescent screen, and behaved normally. After four hours a small trace of the bismuth meal remained in the stomach, but most of it was in the pelvic coils of the ileum. On one occasion an attempt was made to determine whether irritation of the caecal wall had any reflex effect in delaying the emptying of the stomach. A clip was applied to the caecal mucosa near the valve, and left on; at the same time a bismuth meal was given. It was found impossible to keep the clip applied; the peristaltic movements of the ileum underneath repeatedly threw it off. The stomach emptied in the normal time.

Influence of Local Stimulation on the Activity of the Ileo-caecal Sphincter.—It was not possible by stimulation of the mucous membrane of the caecum to start efflux. On the other hand, I repeatedly found that pinching up a fold of caecum near the orifice, when it was in full activity after a meal, delayed the outflow and made the jets less frequent, though it did not check them altogether. This is of considerable importance, as bearing on the question whether chronic inflammation in the ileo-caecal region, as for instance chronic appendicitis, can delay the passage of bowel contents through the sphincter.

Influence of Enemata.—In Rutherford's case, enemata given per rectum stirred up more activity in the ileum than in the colon. In the present observation, enemata and colon wash-outs did not provoke activity of the ileum or discharge of ileal contents.

Plugging the Orifice.—In Rutherford's case inserting a finger into the sphincter caused pain and spasm. My patient, on the other hand, wore a plug in the hole for some time before he came to me, without inconvenience. It was used, so he said, to control the efflux, but needless to say, it failed to do so.

REFERENCE.
[1] A. H. Rutherford, *The Ileo-caecal Valve*, 1914.

RENAL EFFICIENCY TESTS IN NEPHRITIS AND THE REACTION OF THE URINE.*

BY

J. B. LEATHES, M.B., F.R.S.,

PROFESSOR OF PHYSIOLOGY, UNIVERSITY OF SHEFFIELD.

THE functions of the kidney include three that are equally important—the excretion of the nitrogenous end-products of metabolism, the regulation of the osmotic tension of the blood by the removal of a fluid of higher or lower tension as the case may be, and lastly, the regulation of the reaction of the blood. The efficiency of the kidney in nephritis in regard to the first two of these functions has been studied by many; in regard to the last, only, so far as I know, by Henderson and Palmer. They collected the daily urine of large numbers of nephritic subjects, and found that it tended to be more acid than that of other subjects.

I started some years ago in Toronto the investigation of the nephritic kidney in the performance of this function, but the work was interrupted before much more had been done than to employ for taking the reaction a double titration method, using methyl orange and phenolphthalein. In a solution of sodium phosphate, if all the phosphate is acid phosphate, methyl orange turns pink; if any of it is dibasic this indicator is yellow; when it is all dibasic, and not before, phenolphthalein turns pink. In a solution of mixed phosphates, therefore, by titrating on the one hand with methyl orange and N/10 acid the amount of the dibasic phosphate present is determined, and on the other with phenolphthalein and N/10 soda, the amount of acid phosphate present is determined, and the ratio of the amounts used in the two titrations gives the ratio in which the two phosphates are present. This ratio varies with the reaction, and the reaction of the phosphate mixture may be given as so much per cent. acid or so much per cent. alkali, according to the results of the titration. The reaction of the urine practically always lies between these two points, the turning points of methyl orange and phenolphthalein respectively. And since the principal constituents of the urine that determine its reaction are the phosphates, the reaction of the urine may be expressed in the same way as that of a pure phosphate solution, in acidity or alkalinity per cent.

In 1916 an exceptional opportunity for prosecuting inquiry into this subject occurred when the nephritis cases of the 3rd Northern General Hospital were collected together in a branch hospital and entrusted to me. The method of testing the condition of the kidney, which I used during two and a half years at this hospital, was what is well known as a water test. The patients, kept in bed, received at 8 a.m. 500 c.cm. of water to drink, but had no food or drink otherwise from supper the night before till noon. Urine was collected, measured in six fractions, from 11 to 7 and then at 8, 9, 10, 11 a.m. and 12 noon; in each the reaction was determined by the method described. It soon became apparent, from the study of perfectly normal subjects under the same conditions, that a large number of the cases still undergoing treatment for nephritis reacted to this test exactly as the normal organism, while others did not. The normal subject produces during the night a urine that is acid, as does also the nephritic subject, but in the morning the reaction in the normal subject swings strongly over to the alkaline side. This more alkaline reaction persists generally to the last specimen collected.

In nephritic patients often the acid reaction persists throughout the test. Normally, of course, too, the urine, scanty during the night, becomes very abundant after drinking water. It is well known that in nephritis diuresis often cannot be produced by drinking water. When there is no diuresis there is frequently not any change in the reaction either, and cases of this kind occurring early in the series studied, suggested naturally that the change in reaction constant in the normal subject undergoing the water test was merely that which, as was shown by Rüdel in 1892, accompanies any diuresis. But tests done on the normal subject and similar in all respects except that the amount of water taken was reduced to 250 or to 100 c.cm. and that consequently the diuresis was proportionately reduced, showed that nevertheless the change in reaction persisted in the same degree as when diuresis was well marked; results are given in Table I that were obtained in this way.

TABLE I.—*Normal Subjects.*

(Three tests done on the same normal subject.)

	Diuresis, c.cm. per hr.		Alkalinity per cent.	
	Before.	Maximum After.	At Night.	Maximum (at 10 or 11 a.m.).
I. 500 c.cm. ...	40	285	20	91
II. 250 c.cm. ...	27	116	23	85
III. 100 c.cm. ...	37	88	20	89

Precisely similar results were obtained from three tests done on another normal subject, the conditions observed being in all respects the same as in the water tests done on nephritic patients, except as to the amount of water taken in the experiments numbered II and III in Table I.

With more experience of the reaction to the test in nephritic patients it soon became apparent that in them, too, the phenomena occurred separately and were independent of one another. For, in the first place, the matutinal alkaline tide was undiminished in many cases in which the drinking of 500 c.cm. of water produced little or no diuresis, and, secondly, a considerable number of cases were observed in which the diuretic response was normal or but little impaired, while the alkaline tide was missed altogether.

The study of nephritic patients in this way, therefore, brought to light three abnormal types of response—one in which there was little or no diuresis but a normal alkaline tide (Groups III and IV, Table II), one in which there was a diuretic reaction but no alkaline tide (Group V in Table II), and a third in which neither the one nor the other of these phenomena was present in a normal degree (Group VI in Table II).

*Communicated to the Association of Physicians at the annual meeting, July 11th, 1919.

TABLE II.—*Nephritic Subjects.*

Mean figures for response to 500 c.cm. water in nephritis:
Groups I and II practically normal.
Groups III and IV showing tendency of diuresis to be weakened, but normal alkaline tide.
Group V showing fair diuresis but little alkaline tide.
Group VI showing little diuresis and little alkaline tide.

	No. of Cases or Tests from which Mean Figures are Calculated.	Diuresis, c.cm. per hour.		Alkalinity per cent.	
		Before.	Maximum After.	At Night.	Maximum (at 10 or 11 a.m.).
I. Normal...	49	55	336	27	84
II. Normal...	65	55	256	26	73
III. Weak ..	51	61	182	23	74
IV. Weaker...	16	56	96	30	74
V.	56	63	221	22	42
VI.	53	75	115	22	36

Of these abnormalities in the water test of cases of nephritis, the failure of the diuretic response has long been known and discussed; the absence of the alkaline tide is new. In order to understand its significance, the significance of the matutinal alkaline tide in the normal subject must be defined. It is a striking phenomenon which can be observed also under the ordinary conditions of life when the subject is up and takes the usual meals. It is, indeed, then sometimes even enhanced by the diuretic action of the drugs, tea, and coffee, but sometimes partially obscured by other complicating activities, the intercurrent influence of which is eliminated under the standard conditions of the water test. And incidentally, it should be observed, the traditional ascription of the alkaline tide to the secretion of hydrochloric acid in the stomach appears to be erroneous. An intense alkaline tide is normal in the morning when no food is taken; alkaline tides after other meals than the first in the day are certainly not the rule, and in the experience of the writer do not occur. It is not even *a priori* probable that they should, since the passage of acid from the stomach is the signal for the secretion of alkaline digestive juices into the small intestine, and for absorption into the blood from the intestine to begin.*

The morning alkaline tide suggests correlated variations in the activity of the other function concerned, in addition to that of the kidney, with the regulation of the reaction of the blood—namely, respiration. That respiratory activity can effect the reaction of the urine in a very marked degree is shown by experiments in which the subject voluntarily increased the depth of his breathing for an hour or even half an hour at times when the reaction of the urine is otherwise certainly acid—for instance, in the late afternoon, or still more in the middle of the night. This experiment has been done many times in the afternoon on different subjects. The following figures are typical of the result obtained:

TABLE III.—*Effects of Forced Breathing.*
(J. B. C., July 7th, 1919.)

Time.	C.cm. per hour.	Alkalinity per cent.	Remarks.
1 to 2.45 p.m. ...	84	28	—
to 4.10 ,, ...	56	36	Voluntary hyperpnoea from 4.30 to 4.50
to 4.55 ,, ...	123	91	—
to 5.35 ,, ...	54	82	—
to 6.22 ,, ...	32	44	—

At night the tendency to apnoea that the hyperpnoea induces does not make it easier to lie awake and carry on deep breathing; but in all experiments in which this difficulty certainly was overcome results such as that which follows were obtained.

TABLE IV.—*Effects of Forced Breathing.*
(J. B. L., March 17th, 1919.)

Time.	C.cm. per hour.	Alkalinity per cent.	Remarks.
11.10 p.m. to 2.10 a.m.	92	31	Sleeping in bed.
to 3.10 ,,	100	71	Hyperpnoea in bed for one hour.
to 4 50 ,,	59	61	Sleeping.
to 6.5 ,,	59	51	Sleeping.
to 7.40 ,,	49	46	Sleeping.
to 8.50 ,,	58	53	Up; 400 c.cm. tea at 7.45.

In some experiments not yet concluded the amount of carbonic acid washed out of the system by the voluntary hyperpnoea has been measured. In that from which the following figures were obtained the attempt was made to keep the depth of hyperpnoea uniform throughout a period of twenty-five minutes and the air expired in each fifth minute was collected, and it appeared that 27.4 litres of air containing 1.8 per cent. of CO_2 had been expired per minute.

TABLE V.—*Effects of Forced Breathing.*
(W. R. C., June 13th, 1919.)

Time.	C.cm. per hour.	Alkalinity per cent.	Remarks.
3.50 to 5.10 p.m. ...	92	36	—
to 5.35 ,, ...	50	41	—
to 6.30 ,, ...	67	93	Hyperpnoea from 5.50 to 6.15.
to 7.20 ,, ...	26	39	—

It is easy, therefore, to show that the reaction of the urine can be made alkaline by increased respiratory activity. But in order to show that the morning alkaline tide is accounted for by depression of the respiratory centre during sleep and increased activity on waking, it is necessary to determine the percentage of CO_2 in the alveolar air immediately on waking and some time later. For this purpose the apparatus for collecting alveolar air was fixed up overnight (close to the subject's bed), so that within two or three seconds of waking a sample could be obtained. The following results have been so far obtained:

TABLE VI.—*CO_2 in Alveolar Air.*

Date.	Subject.	Time.	CO_2 per cent. of Alveolar Air.	Remarks.
1919. June 27...	W. R. C.	3.55 a.m.	7.40	In bed immediately on waking.
		7.10	6.63	After rising.
July 5 ...	J. B. L.	1.45 a.m.	6.13	In bed immediately on waking.
		7.30	5.38	After rising.
July 7 ...	J. B. L.	6.40 a.m.	6.13	In bed immediately on waking.
		6.49	5.74	After rising.
		8.30	5.46	After rising.
July 8 ...	S. L.	7.15 p.m.	6.46	—
		2.45 a.m.	6.76	Immediately on waking
		8.0 a.m.	5.07	Up, and 1½ hours after waking.
July 9 ...	S. L.	4.20 a.m.	6.50	Immediately on waking
		7.40 a.m.	5 52	Up; 1 hr. after waking.
		8.15 a.m.	5.07	—

The figures given are corrected for aqueous vapour except in the experiment of June 27th, done by Dr. Campbell; with that exception the analyses were done by Dr. F. A. Duffield.

On every occasion in this short series of experiments the results indicate a higher percentage of CO_2 in the lungs during sleep, and therefore give support to the hypothesis that the morning alkaline tide is related to variation in the activity of the respiratory centre—the experiments are being continued.

* I was reminded by Dr. Poulton that Hasselbalch (*Biochem. Zeitsch.*, 46, p. 416, 1912) found the urine to become less acid after meals; but his results were more exactly these: "After each meal the urine was, without exception, more acid than before, but showed the lowest acidity about three hours later." This applies to breakfast at 8.30 and lunch at noon; the urine after the evening meal was not examined. No attention was paid to the volume of the urine, and no data are given as to the amount of fluid taken or the hours at which it was taken, so that it is impossible to say whether the tendency for the urine to become more alkaline between 2 p.m. and 3.30 p.m. was or was not accompanied by diuresis. I do not think his figures give support to the traditional alkaline tide ascribed to gastric secretion.

Whether or no this proves to be the true explanation, the interpretation of the failure of the kidney in certain stages and cases of nephritis to show any morning alkaline tide still requires investigation; this is being prosecuted. But in the cases available for the work of which this is a preliminary report it is not a failure of the kidney in its power to turn out acid that is indicated; the abnormality is that the kidney gives an acid urine in conditions in which a normal kidney gives an alkaline urine. The question arises, therefore, whether this abnormality may not be an expression of an effect of the disease of the kidney on the function of some other organ. The gradual return to the normal type of response shown in tests done on the same patient at intervals of two or three weeks during recovery is striking, and in a fuller account of the work to appear later will be illustrated by protocols.

NOTES ON THE INFLUENZA EPIDEMIC IN THE EGYPTIAN EXPEDITIONARY FORCE.

BY

J. D. BENJAFIELD, M.D., B.S.LOND., M.R.C.S., L.R.C.P.LOND.;

LATE TEMP. CAPTAIN R.A.M.C.; LATE O.C. 37 MOBILE BACTERIOLOGICAL LABORATORY (WELLCOME PRESENTATION LABORATORY.)

Epidemiology.

THE epidemic in this force commenced in May, 1918, but the maximum incidence was not reached till September and October. The cases during the earlier period of the epidemic were on the whole mild in type and of short duration, only a very small proportion being complicated by bronchopneumonia.

In patients already debilitated by malignant tertian malaria influenza proved much more serious, many developed bronchopneumonia, and considerably over 50 per cent. of such cases ended fatally.

The epidemic continued throughout November, December, 1918, January and February, 1919, but the number of cases showed a marked decrease during the last two months. In the latter part of the epidemic few of the cases were complicated by malaria, and one had a better opportunity of studying the disease in otherwise healthy individuals. The type of the disease also changed somewhat towards the end of December, and showed on the whole a tendency to become less virulent; this feature has been maintained up to the present time.

As regards the incubation period, but little evidence is available, for the sources of infection were so general that it was rarely possible to determine the original focus in any given case. There are many features with regard to the infectivity of this epidemic which call for comment; for, while in the early influenzal stage the disease seems to be markedly infectious, yet directly bronchopneumonia supervenes its infectivity appears to be much diminished or lost altogether. This point is supported by the fact that hardly any of the sisters, medical officers, or orderlies in close contact with bronchopneumonic cases have contracted the disease.

Clinical Types.

The cases can be divided into three more or less well defined groups:

1. Catarrhal type.
2. Bronchopneumonic type.
3. Toxaemic type.

A large proportion give a history of a severe cold preceding the acute febrile period by a few days. Otherwise the onset of the disease proper is sudden, being marked notably by fever, headache, pains in the back and limbs, and lassitude. The more severe attacks were often ushered in by vomiting. The headache is generally frontal, and associated with pain in the eyes. I shall now describe the types of cases more in detail.

TYPE I: *Catarrhal.*—The febrile period usually extended from five to seven days, the maximum temperature being reached on the second day. It rarely exceeded 103° F., though in a few cases temperatures of 104° F. and over were met with. The temperature usually fell by lysis, though in a few cases, more especially in those treated with vaccine, the fall was more rapid. The pulse rate was increased, but rarely exceeded 116 to 120, whilst the respiration rate showed but little change. Tracheitis and pharyngitis were common, and associated with these was a dry and troublesome cough, with little or no secretion. No gastro-intestinal symptoms were present, except those usually associated with febrile disturbance—that is, furred tongue, loss of appetite, and constipation. After the subsidence of the fever the patients rapidly regained their normal strength, and post-influenzal debility was not a marked feature.

TYPE II: *Bronchopneumonic.*—During the early stages of the disease there was no means of distinguishing between Types I and II, except on the whole the onset in the latter type was liable to be more severe and the fever during the initial stages to be at a higher level. Usually it was not till the third or fourth day of the disease that one could classify any given case, when the temperature, instead of falling, would remain at the same or at a higher level, and the patient would be much more distressed. At the same time the pulse and respiration rates would show a greater deviation from the normal. Pain in the chest was a prominent feature, though physical signs at this stage would be absent, and they rarely appeared before the fourth or fifth day of the disease. The earliest signs usually detected were some fine sticky crepitations heard at the end of inspiration over one or both bases. A peculiar characteristic of these crepitations was that often they could only be heard once or twice during a single examination and would then disappear altogether. Once physical signs had appeared they became rapidly intensified with obvious crepitations, râles, and accentuation of vocal resonance. As compared with the slight physical signs during life, the striking feature *post mortem* was the wide extent of the pulmonary lesions. The sputum was at first very scanty, glutinous, and streaked with blood. "Rusty sputum" was rare. In the later stages, especially in those recovering, the sputum became abundant and purulent. After the development of bronchopneumonia the course varied, all grades of severity being met with. On the whole the course of cases with a severe onset, associated with vomiting, and those with high fever during the initial stages, was more severe and the prognosis correspondingly graver. There was a marked tendency for the bronchopneumonic process to spread throughout the lung, and perhaps affect the opposite side in similar fashion, so that during the course of the disease practically the whole lung tissue would become involved in the morbid process. Fortunately, in cases of this type, the portion of the lung first affected would rapidly resolve and be functional when other portions were being attacked. Many cases of this type recovered. Pleurisy occurred in a fair proportion of cases, but usually after the temperature had begun to subside. Its intervention did not appear to render the outlook more grave. Cases were seen in which during the early stages tracheitis was absent, but who, at a later date, developed bronchopneumonia, so that tracheitis does not appear to be an essential forerunner of the bronchopneumonic type.

TYPE III: *Toxaemic.*—This type is characterized by acute and severe onset, nearly always accompanied by vomiting, high fever, rapid pulse and respiration. The patient is flushed and anxious-looking, and obviously acutely ill from the commencement. The duration of this type is from two to five days, and they die usually exhibiting more a clinical picture of acute toxaemia than that of bronchopneumonia. In one case death supervened eight hours after the onset. During the later stages the flushing is replaced by a peculiar lilac coloured cyanosis[1] affecting the face and neck, but most marked over the lips and ears. This feature is frequently seen in severe cases of the second type, and once it has set in the prognosis is practically hopeless. Death usually supervenes within forty-eight hours. Apart from a general erythema and herpes, no rashes have been seen. Cerebral symptoms have not been commonly met with, and consciousness is retained almost to the end. Subsultus tendinum, with twitching movements of the hands and arms, have frequently been observed. Delirium was common during the earlier phases of the epidemic, but practically disappeared towards the end. It will be seen that the line of demarcation between the first and second types is by no means well defined.

I have detailed the clinical features of this epidemic in order to establish its identity with that encountered elsewhere as forming part of the pandemic, for when we come to study the bacteriology several points are found at marked variance with those of other observers.

Bacteriology and Vaccine Treatment.

Owing to the prevalence of other diseases requiring laboratory assistance for their diagnosis, but little bacteriological work could be done on influenza during the early phases of the epidemic, and consequently one could not concentrate on it until it had assumed a much more serious aspect. The primary work consisted solely of the examination of sputa from all types of the disease, and the preparation of autogenous vaccines for some few of the serious cases which showed a tendency to become chronic. During the course of these examinations it was observed that a Gram-positive strepto-diplococcus was almost constantly present—thus out of 300 sputa examined it was present in 95 per cent., and very commonly it was the predominant organism, so much so that cultures on suitable media would yield an almost pure growth.