CASE III.

The radiograms in this case (see Fig. 6) illustrate excellently how an infected kidney may fail to yield a shadow. The right kidney pelvis, which filled within a quarter of an hour, is dilated, and shows cupping of the calyces, possibly due to an infection. There is no uroselectan shadow of the left kidney, but the faint outline of multiple calculi can easily be seen. At biopsy, after operation, multiple chronic staphylococcal abscesses were found scattered throughout the renal cortex.

FIG. 6.

From the patient's point of view this in itself is the greatest possible advantage.

In cases where cystoscopy and catheterization of the ureters is difficult or impossible its routine use will be a necessity—for example, in children, and patients with ureteral strictures or pelvic tumours which compress the ureters from without. In cases of movable kidney it is easy to estimate the degree of mobility because the patient can stand up, or, in fact, assume any position that circumstances may require.

The disadvantages are two—namely, its expense, which is considerable, and the fact that no shadow is obtained when the renal function is greatly diminished.

It is probable that in the future intravenous pyelography will invariably be carried out before the decision is arrived at that the patient must be submitted to the ordeal of ureteric catheterization.

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- ¹Swick: *Klin. Woch.*, 1929, No. 45, p. 2087. ²Ibid. ³Ibid. ⁴Ibid.
⁵Von Lichtenberg and Swick: *Klin. Woch.*, 1929, No. 45, p. 2089. ⁶Ibid.

SWELLING OF THE FEET AND ANKLES NOT ASSOCIATED WITH ALBUMINURIA OR GROSS ORGANIC DISEASE.

PATHOGENESIS AND TREATMENT OF A COMMON SYMPTOM.*

BY

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OEDEMA without albuminuria occurs in a variety of well-known conditions, such as several of the anaemias, chlorosis, war oedema, starvation oedema, beri-beri, and varicose veins in the legs. It also not infrequently precedes the appearance of albuminuria in the early stages of some cases of nephritis and pregnancy kidney. The type of oedema which is described here, however, is one which is quite commonly met with, especially among patients of the so-called hospital class, though it is by no means confined to them. It cannot be ascribed to any of the conditions already enumerated, and is seen chiefly in adult women, in the form of "puffiness," or swelling of the feet and ankles. It is, however, occasionally met with in debilitated adult males, and even in children. In women,

not always of the poorer classes, it is the cause of much misery and distress, partly for cosmetic reasons, and also because in bad cases walking is difficult or impossible, and so leads to loss of employment. Tennis and dancing also have frequently to be given up because of this symptom. The milder cases do not seek advice for this, but for associated symptoms of that state of subnormal health commonly called "debility," such as headaches, constipation, lassitude, amenorrhoea, etc. Other patients complain chiefly of swelling of the feet, and are diagnosed as cases of anaemia, and iron, tonics, and various glandular extracts are prescribed. Some of the wealthier resort to beauty parlours, where they are given massage and local hypertonic salt compresses. As a rule none of these measures appears to be very effective in affording relief for this exceedingly common symptom.

The Pathogenesis of "Swollen Feet."

There are, of course, several varieties of "puffy," swollen, or "thickened" feet and ankles which are not associated with cardiac, renal, or other gross organic disease. In some cases the swelling is due entirely to an increase in the water content of the tissues of the part, in others to excess of fat, and again in others to a combination of excess of both water and fat. There is also the variety associated with blueness of the extremities, referred to by Parkes Weber¹ under the descriptive title of "erythrocyanosis crurum puellarum." No hard-and-fast line can be drawn between these conditions in many cases, but this paper is concerned only with the enlargement of the extremities, generally the feet and legs, due to true oedema, or excess of water in the tissues.

As will be seen later, there is reason to believe that the relative frequency with which the oedema is complained of in the feet and ankles is probably due entirely to the effects of gravity, as in reality the excess of water, or oedema, is present in all the tissues of the body, though often not in sufficient amount to attract attention. During the course of the day the oedema tends to drain down to the feet, and by the evening has there collected in sufficient amount to be noticed by the patient.

The following case is typical of the disorder which is being considered here.

A lady, aged 36 years, was sent to the out-patient department complaining of pains and swelling in the feet and legs, most marked in the right ankle, which she had noticed for several months. The swelling was most prominent in the evening, and had usually almost disappeared on rising in the morning. The periods were regular, but rather scanty. The swelling was always much worse at the time of the menstrual periods. She had frequent severe headaches and a tendency to constipation. Six months ago she had lumbago, the only definite illness she remembered having had in her life. She was pale, and the complexion was "greasy" and spotty. The hands were not swollen or blue, but were clammy and sweaty. Examination of the heart revealed nothing abnormal, and there was no albuminuria. There was no obvious focus of sepsis. She was unmarried. The blood pressure, blood urea, and urea concentration were all normal. A blood examination, for which I am indebted to Dr. L. Hewlett, showed: red blood cells 5,936,000 per c.mm., haemoglobin 90 per cent., colour index 0.8. The plasma bicarbonate was 0.0278 M. (normal=0.0300 M.). The urine contained no albumin. It is clear, then, that in this case neither heart disease, kidney disease, nor anaemia provides an adequate explanation of the oedema. The latter was not sufficient to prevent walking, but it was of that degree which would have attracted the attention of lay persons.

Elsewhere² it has been shown that "debility," whether occurring in children or adults, is a state which is generally associated with some degree of "acidosis," which, in turn, is frequently accompanied by an increase in the water content of the body as a whole. The term acidosis was defined as a reduction of the concentration of bicarbonate in the plasma, and therefore does not necessarily imply any change in reaction (pH) of the blood.

It is suggested here that it is this underlying "acidosis," the exact cause of which is not known, which leads to excess of water in the tissues, and that in minor degrees of the disorder the accumulation of fluid is only sufficiently great to attract attention under the influence of gravity, and hence the frequency with which it apparently occurs in the feet and ankles alone. Taking the group as a whole, there is a considerable diminution in the plasma bicarbonate values in these waterlogged subjects, compared

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with the normal, which is probably not due to hydraemia or wateriness of the blood, as then the haemoglobin percentage would also be reduced.

It may be mentioned that a normal plasma bicarbonate may be present at the same time as a true "acidaemia," or change in reaction (pH) of the blood to the acid side of normal; and, further, that a normal reaction in the blood does not necessarily preclude an abnormal reaction in the tissues. The results of treatment in some of the cases described below, where the plasma bicarbonate was normal at the time treatment was commenced, suggests that "tissue acidosis" may have been present all the time. In the paper referred to above² it has been shown that the plasma bicarbonate is highest in normal adult males, and that it decreases slightly in the following groups in the order given: normal adult females (intermenstrual values), normal adult females (menstrual values), debilitated adult females, and normal pregnancy. It was pointed out, too, that the plasma chlorides, and the water content of the body, as measured chiefly by the frequency with which clinically apparent oedema occurred in each group, tended to increase in inverse relation to the plasma bicarbonate—that is, oedema, unaccompanied by albuminuria, was most often encountered in pregnancy, then in debilitated females, in normal women during the menstrual periods, in normal women in between the menstrual periods, in debilitated adult males, and least often in normal adult males. This is certainly in accordance with clinical experience, and to some extent has been confirmed by more accurate methods.² These points are well brought out in Table I.

TABLE I.

Group.	No. Cases.	Average NaHCO ₃	Average NaCl.	Water Content.
		M.	Gram %	
Normal adult males	86	0.0320	0.587	Least.
Normal adult females (intermenstrual)	31	0.0301	0.0585	+
Normal adult females (menstrual)	31	0.0291	0.591	++
Normal children	38	0.0299	0.606	+++
Debilitated children	68	0.0276	0.608	+++
Debilitated adult females	72	0.0271	0.594	++++
Normal pregnancy	68	0.0247	0.596	+++++

The type of oedema described in this paper occurs mainly in the feet, ankles, and legs, is at its maximum in the evenings, is worse after exertion and in hot weather. It may be constantly present, waxing and waning with the factors just mentioned, or may only occur under some of these conditions, disappearing apparently spontaneously for weeks or months at a time, and then perhaps recurring. It should be noted that those conditions—menstruation, exercise, etc.—which are associated with an increase in the oedema are also those usually accompanied by a decrease in the plasma bicarbonate.

Treatment.

The rationale of the method of treatment adopted in many of these cases is an outcome of the theory of the pathogenesis of the symptom outlined above. It consists in giving sufficient alkali, in the form of equal parts of potassium citrate and sodium bicarbonate, by the mouth, to raise to, and to maintain the plasma bicarbonate at, a normal level, and possibly to increase the alkalinity of the tissues—at all events, to give enough alkali to promote a diuresis sufficient in amount to remove the excess water from the tissues. The method, in fact, is the same as that described in detail elsewhere³ for the treatment of certain cases of nephritis accompanied by oedema, without the dangers incident to the giving of large doses of alkalis in the presence of grossly damaged kidneys. For reasons of space it is not possible to give details of all the cases here, but it may be said that of the 16 treated up to date, the oedema cleared up entirely in 13, though 6 subsequently relapsed, and the oedema returned on discontinuing the treatment. Of these 6, 4 were again cured on resuming their former dose, and in 2 all further treatment com-

pletely failed to remove the oedema, though it was slightly improved in 1 of them.

It must be noted that, with two exceptions (Cases vi and vii), all the patients were attending the out-patient department for treatment, and most of them were meanwhile pursuing their usual avocations. There were therefore no control over the intake of fluid, the diet, or the amount of exercise taken. In many cases, too, the dose of medicine prescribed was not taken regularly. It is possible that the explanation for the lack of response to treatment in some of the cases may lie in one or more of the above factors; in any event it is not claimed that the treatment is always effective, but that it is so in a sufficient number of the cases to lend strong support to the correctness of the views put forward concerning the causation of the disorder.

From the practical point of view it is admitted that the treatment is tedious, clumsy, and not always effective; but, though it requires a good deal of supervision to get good results, it appears to be practically free from danger if confined strictly to the type of case under consideration. Further, estimations of the plasma bicarbonate are not necessary before or during treatment, provided there is no associated renal defect or accompanying dyspnoea or vomiting. Incidentally, it should be noted that, as in cases of nephritis with oedema treated by this method, there often occurs a preliminary increase in the oedema before final subsidence takes place.³ Treatment, therefore, should be continued until this preliminary stage has been passed.

In detail, the treatment consists simply in giving by the mouth a mixture of 30 grains each of potassium citrate and sodium bicarbonate with 30 minims of syr. aurantii, in an ounce and a half of water, increasing the number of doses in the day according to need. It may often be necessary to give as much as 600 or 700 grains a day or more. With large doses, the strength of each individual dose may be increased to 50 grains of each ingredient per dose, thus allowing fewer doses in the day. It is probably wise to limit the intake of fluid roughly to a known amount in the twenty-four hours—say three or four pints, but no serious restrictions of fluids need be imposed. No other dietetic modifications appear to be necessary.

No unoward symptoms of any kind have been encountered in treating these cases in the manner described, except in one instance, where, for some reason unknown, the bladder became accidentally infected, and a cystitis resulted. The alkalinity of the urine appeared to favour the growth of the organism concerned, and treatment was therefore abandoned. The plasma NaHCO₃ was measured in these cases by the method of Van Slyke, Stillman, and Cullen,⁴ the results being expressed as molar concentration.

TABLE II.

Case.	Sex.	Age.	Duration of Oedema.	Initial Plasma NaHCO ₃ .	Maximum Daily Dose.	Result.
				M.	Grains.	
1	F.	32	18 yrs.	0.0270	400	Cured, relapsed, cured again.
2	F.	28	11 yrs.	0.0250	600	Cured, relapsed, failed to cure.
3	F.	26	2 yrs.	0.0284	500	Failed.
4	F.	24	1 yr.	0.0267	480	Cured.
5	F.	51	1 yr.	—	360	Cured.
6	M.	16	? 14 days	—	780	Cured.
7	M.	51	3 mths.	0.0297	360	Cured.
8	F.	19	3 yrs.	0.0205	1,000	Failed.
9	M.	48	4 mths.	0.0300	940	Cured, relapsed, cured.
10	F.	25	13 yrs.	0.0270	540	Cured, relapsed, cured.
11	M.	55	1 yr.	0.032	1,000	Cured, relapsed, cured.
12	F.	19	4 yrs.	0.0268	420	Cured.
13	F.	33	"Some yrs."	0.0228	400	Cured.
14	F.	28	"Some yrs."	0.0302	400	Cured, relapsed, improved.
15	F.	26	2 yrs.	—	360	Failed.
16	M.	44	10 wks.	0.0281	600	Cured.

Conclusions.

1. Analbuminuric oedema of the type described is most common in debilitated females.
2. It is generally associated with, and is probably due to, an underlying acidosis, with consequent increase in the water content of the body as a whole.
3. In many cases the symptom can be abolished by the giving of alkalis by the mouth in amounts sufficient to overcome the acidosis and promote diuresis.
4. The results of treatment confirm the thesis presented as to the pathogenesis of the disorder.

In conclusion, I should like to thank the many colleagues and friends who have helped me with the investigation of these cases, especially Dr. H. G. Close. I am indebted also to the physicians at Queen Mary's and Guy's Hospitals for sending me cases for investigation and treatment, especially to Dr. A. F. Hurst and Dr. H. French for access to Cases vi and vii respectively, and to Dr. J. A. Ryle for Case ii. My thanks are also due to Professor R. Donaldson and Dr. Arthur Davies, directors of the pathological laboratories of Guy's Hospital and Queen Mary's Hospital respectively; and, finally, to the Medical Research Council, for a grant enabling this work, which forms part of a larger investigation, to be carried out.

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Memoranda:**MEDICAL, SURGICAL, OBSTETRICAL.****AFTER-HISTORY OF CASE OF GALL-STONES IN A YOUNG SUBJECT.**

I. C., aged 24, was operated on at the age of 15 years for gall-stones, in May, 1920, by cholecystotomy (vide *British Medical Journal*, 1925, vol. i, p. 1126).

Following the operation she remained well till a year or two ago, when she began to experience spasmodic pain in the right hypochondrium. On August 13th, 1929, the scar became swollen and tender, and one week later the swelling burst, giving vent to green discharge containing numerous small stones. The pain subsided, but discharge of stones continued, sometimes as many as twenty at a time. She was readmitted to hospital on August 27th with a biliary fistula in the old operation scar, and with stones in the discharge.

Paramedian laparotomy showed gall-bladder adherent by fundus to site of the fistula. Cholecystectomy was performed, the subhepatic space being drained by a tube inserted through the fistula, and healing was uneventful.

Pathological Report.—Greatly thickened gall-bladder wall showed muscle hypertrophy and much inflammatory fibrosis, with cellular infiltration of subacute and chronic type. Mucosa showed abundant new formation of mucous glands.

Glasgow.

G. H. EDINGTON.

MENINGITIS FOLLOWING OPERATION ON THE ANTRUM IN A PATIENT WITH COMPLETE TRANSPOSITION OF VISCERA.

THE case here recorded is of much interest, and seems worthy of publication.

A man, aged 24, seen during September, 1929, complained that he had been suffering from nasal obstruction for years, but that it had been very severe for the last two years. Examination revealed large multiple polypi on the left side. He was x-rayed. The films show an absent frontal sinus, but sphenoids, ethmoids, and both antra dull, especially the left.

He was admitted to hospital on October 13th, and examination confirmed the findings in the out-patient department, but also revealed the heart on the right side of the body. No other abnormality was detected.

On October 14th a Caldwell-Luc operation was carried out on the left side, and the polypi were removed through the antrum. A simple antrotomy was performed on the right side. He had an uneventful convalescence until October 21st, when he complained of headache and his temperature went to 102° F. A complete general and neurological examination was carried out, with negative findings. On October 22nd the condition was the same, except that his temperature was 106.2°, and again no other abnor-

mality could be discovered. On the 23rd his temperature had fallen to 104° F., and he looked very ill. He was seen by the physician, who also found no other abnormality, but on account of his general condition ordered him three doses of 20 c.cm. polyvalent antistreptococcus serum at eight-hourly intervals. On October 24th he was given 50 c.cm. intravenous saline. The following day he had lung signs. The whole of the left lung, although normal to percussion, had an almost complete cutting off of breath sounds. Late that afternoon he had an epileptiform convulsion of the whole body. A blood culture was taken, and 10 c.cm. of 1/2 per cent. mercurochrome was given intravenously. By midnight he was having almost continuous epileptiform attacks, but they were gradually settling down to the left side of his face. These persisted in spite of 1/3 grain of morphine and a little chloroform inhalation. Lumbar puncture was performed. The fluid was under intense pressure, and 20 c.cm. were withdrawn. This had a few cells with intracellular bacilli resembling the influenza bacillus. He slowly sank, and died at 6 o'clock the following morning.

A post-mortem examination was carried out, with the following findings. The heart was lying on the right side. The spleen also was on the right side. The liver and appendix were on the left side. Both lungs were rigidly bound to the pleura throughout, and the large branch of the left pulmonary artery had an ante-mortem thrombus about three inches long. The brain had an area of pus over the whole of the upper part of the parietal lobe on the right side. The remainder of the brain, including the left side, was slightly congested but otherwise normal. A culture was made of the blood within the heart by Dr. Ponder, and was negative. The pus on the surface of the brain contained *Streptococcus longus*, and the thrombus was organized and infiltrated with leucocytes. We thank Dr. Ponder for the many bacteriological and microscopical examinations.

I wish to thank my honorary surgeon, Mr. J. Aldington Gibb, for permission to publish this case, and also for the following note.

"The operation performed by me was so usual and uncomplicated that the possibility of traumatic involvement never entered my head. The occurrence of two consecutive cases of erysipelas in the ward at the time may have been the source of infection. Moreover, the heating apparatus failed at the time, which inclines me to the view that this may have been an exciting cause of the onset. Mr. Mitchell, the house-surgeon, was unremitting in his care of the patient, and the post-mortem findings are his entirely, for which he deserves any credit. The case is interesting and well worthy of publication."

It was interesting to note that there was no macroscopic evidence of the disease having tracked up from the nose by a direct path, but it was completely isolated high up on the right side of the brain; also that the man was passed for the police force as perfectly fit in spite of his complete dextrocardia, and that he had done hard manual work all his life without any ill effects.

Maidstone.

HUGH G. MITCHELL, M.B., B.S., D.L.O.

HERPES OPHTHALMICUS FOLLOWING CHOREA AND ASSOCIATED WITH VARICELLA.

THE following histories are rather difficult of interpretation.

A healthy-looking girl, aged 7, was admitted on December 9th, 1929, with a history of "jumpiness" for six days. Her well-marked chorea was treated with large initial doses of liquor arsenicalis, which were gradually decreased. By December 28th she had taken 424 minims, and her movements had almost stopped. On January 4th, twenty-six days after admission, she developed herpes in the distribution of the upper division of the left fifth cranial nerve, the cornea escaping. The herpes was confidently diagnosed as being due to arsenical poisoning of the fifth ganglion, a well-known arsenical symptom, though uncommon in the treatment of chorea, and also rare as the site of shingles in the child. However, in the same ward, three days later, a girl, aged 5, with acute suppurative pneumococcal arthritis of the left hip, developed chicken-pox, thirty days after admission.

Ought this second event to throw any doubt on the diagnosis of the cause of the fifth nerve herpes? There have been no further cases of herpes or chicken-pox. The patient with chicken-pox was isolated at once; twelve other patients had not had chicken-pox, and three patients had had chicken-pox. The bias of the writer's view is betrayed, for the girl with herpes ophthalmicus was not isolated.

I must thank the medical superintendent of the West Middlesex Hospital for permission to publish these cases.

Isleworth.

THOS. VIBERT PEARCE, F.R.C.S.