acquired by training. In painful dyspepsia periods of five to twenty seconds are usually found. In a small proportion of the cases the respiratory symptoms so overshadow the other symptoms that cardiac disease is suspected by patient and physician.

It is well known that the dyspeptic often thinks himself to be suffering from disease of the heart. How often do we find ourselves saying: "That is not your heart, but your stomach"? It is sometimes noted that the patient is still sceptical, especially if he is a physician or has a smattering of medicine derived from the lay manuals. He feels a pain where he knows his heart to be (due to left triangularis or fifth left interchondral), he is short of breath on exertion, he often experiences disordered action of the heart or palpitation, and sometimes has distinct syncopal attacks. Is he to blame for suspecting his heart to be wrong?

On careful consideration the patient is in the right. The cardiologists have thrown the blame of heart disease on every part of the heart and vessels, but have, so far, failed to remember that the heart and vessels—the circulatory system of the present day—are but a half of the vascular pump. The heart and vessels can pump blood onwards efficiently if healthy and if blood is supplied to them, but the heart, by itself, cannot get blood to pump. The auxiliary pump is the respiratory musculature, which derives, or sucks, blood from the great venous cisterns to the right auricle. When the respiratory pump is thrown out of action the heart will stop, unless the body is in the horizontal position, for then respiratory suction is not necessary. The climber who falls on the rope soon succumbs to syncope, as the rope throws the respiratory pump out of action; the laboratory rabbit suspended in a vertical position dies of syncope in a few minutes, for the weight of its abdominal viscera and the poor tone of its abdominal respiratory muscles prevent respiration. It was noted above that the lower animals have little or no thoracic respiration.

We have seen that the dyspeptic frequently shows respiratory disability; he does not use his abdominal muscles because they increase his distress; he cannot use his thoracic muscles because they are painful. He has two causes for shortness of breath—his respiratory movements are inadequate to aerate his blood, and his respiratory pump fails to supply the heart properly with blood.

Another reflection of this referred pain in dyspepsia is seen in the cases which show anginoid pain, or pain which must be regarded as identical with angina pectoris. Such cases are not uncommon. Numerous observers have described the dyspeptic symptoms of angina, but few the angular symptoms of dyspepsia.

The explanation of the syndrome angina has produced as big a literature as dyspepsia, for though not so common it is much more spectacular. Time forbids a long excursion into the various theories of its causation; in brief they are: disease of the proximal part of the aorta with pain radiating into the upper dorsal segments; disease of the coronaries with anoxaemic cramp of the myocardium; Briscoe's conception of fatigue of the respiratory muscles owing to a change over from youthful thoracic to elderly abdominal respiration; vaguer nervous mechanisms. Evidence for and against all these theories is abundant. It is not my object to deny that each or all of these may not be causes of angular pain, but to point out the possibility that these lesions may also result from the cause which produced angular pain.

When we consider the limitation of effort; the pain when effort is not limited; the immobility of the whole of the respiratory musculature, perceived as a sensation of a vice-like grip; the pallor and breathlessness; the absence of evidence of circulatory failure in the early stages; the dyspeptic symptoms—we have enough evidence to constitute a case for the dyspeptic etiology of angina, at least in some cases. In dyspepsia one can select a perfect sequence of cases to show all steps upward from simple pain after food, through the effort syndrome, to true angular pain. The group showing this pain have recovered, up to the present, when the condition has been treated as a failure of the respiratory pump due to dyspepsia. It is admitted that the number showing severe pain of this kind is few, but a large number have shown milder degrees.

The importance of the vascular lesions is not denied, and it may well be found that after a time the vascular lesion may become the chief one; it is contended that the vascular lesion may be produced by the angina. Proof for this contention is not complete, but there is some evidence: Cunliffe Shaw, Manouélian, Stopford, and H. Todd⁶ have shown that prolonged irritation of the nerves of a part is followed by vascular degeneration in the territory supplied by these nerves. Is it not possible that the prolonged irritation of the sympathetic fibres proceeding from the abdominal viscera, and the sensory nerves supplying the hyperalgesic muscles, may cause vascular degeneration in the areas supplied by these nerves? It appears suggestive that the segments postulated to be concerned in gastric pain by Mackenzie are the same as those which are blamed by the upholders of some of the neurogenic theories of angina.⁶

It should be noted that hyperalgesia of the muscles of respiration is not limited to patients who suffer from painful dyspepsia. Similar hyperalgesia is found in subjects suffering from fatigue of respiration from purely respiratory and circulatory causes.

Summary.

1. Pain of some of the upper abdominal viscera is shown to be referred to some of the muscles of respiration.
2. This respiratory muscular hyperalgesia may interfere with the respiratory pump and the supply of blood to the right auricle.
3. It is considered possible that some cases of pain resembling angina pectoris are due to this factor, and that properly directed treatment may result in cure in the early stages.

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CHRONIC HYPOGLYCAEMIA.

BY

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CHRONIC HYPOGLYCAEMIA is regarded by most clinicians as a rare phenomenon of scientific rather than of practical importance, but, as I have met with a fasting blood sugar of 70 mg. per cent., or less, in more than 200 patients during the past five years, it cannot be so uncommon as is generally assumed. Unfortunately there is no characteristic sign to draw attention to hypoglycaemia, as glycosuria does to hyperglycaemia, but in most cases the history and symptoms are sufficient to suggest a diagnosis if the possibility of its presence is borne in mind. It will, I hope, help others to recognize chronic hypoglycaemia more frequently if I classify and discuss my cases, most of which had been treated for a variety of symptoms without success until the abnormal condition of their blood was discovered.

TABLE I.

Age.	No.	Sex.		Heredity.	Chronic Infection.	Faeces.				Urine.				Blood.	
		Male.	Female.			Enterocolitis.	Enteritis.	Colitis.	Normal.	Sugar.	Acetone.	Albumin.	Calcium Excess.	Calcium Low.	Calcium Normal.
0-10	44	27	17	31	27	31	4	4	5	20	28	3	3	3	3
11-20	19	10	9	12	8	9	4	5	1	12	7	2	5	5	4
21-30	32	18	14	12	7	11	11	5	5	20	10	5	8	10	11
31-40	32	15	17	7	6	13	7	9	3	17	6	7	4	11	9
41-50	35	27	9	5	15	16	13	1	6	18	4	5	12	13	7
51-60	19	11	8	1	2	6	6	5	2	7	2	3	4	4	7
61-	18	14	4	1	6	9	4	4	1	10	1	3	7	6	6
	200	122	78	69	71	95	49	33	23	107	58	28	43	52	57

AGE AND SEX.

The age of my patients ranged from under 1 year to over 70. Classified in decades (Table I), the highest proportion falls within the first ten years; in the next ten years there is a striking diminution, but in the following period the incidence increases again and is maintained at a fairly constant level up to the age of 50. Every age period, excepting 31 to 40, shows an excess of males, and the whole series gives a ratio between the sexes of about two to one. It is therefore clear that chronic hypoglycaemia is not limited to any particular age or sex, and that, although a low blood sugar figure appears to be most commonly associated with symptoms calling for treatment in children, no period of life is exempt.

HEREDITY.

Breeding experiments with mice, which Mr. Howard and I have been engaged upon for some years, have indicated that a naturally occurring hypoglycaemia is a hereditary character transmitted in accordance with Mendel's theory. It is interesting, therefore, to find that in my series of cases a history of symptoms suggesting a hypoglycaemic complex was obtained among blood relations in 35 per cent. The proportion of cases giving such a history was highest in the first ten years and steadily diminished with advancing age, falling from 70 per cent. in the first decade to 5 per cent. in the seventh. Such a distribution suggests either that the family history of parents is more reliable than adults give of themselves, or that heredity plays a greater part in the hypoglycaemia of early life than of later years.

Evidence of the transmission of a chemical abnormality is naturally more difficult to obtain in human beings than in animals, but in 48 of my cases of chronic hypoglycaemia, distributed in nineteen families, experimental proof has been possible. A low blood sugar figure was found in one of the parents of affected children in 36 instances, two patients were uncle and nephew, cousins were similarly affected in two families, and a daughter, mother, and grandmother in another. The last is particularly interesting, as it indicates that, given suitable conditions, the abnormality may appear in at least three successive generations.

CHRONIC INFECTION AS A CAUSE.

Although animal experiments and human histories both suggest that heredity is a predisposing cause of chronic hypoglycaemia, it is probable that an exciting agent is necessary for the development of the condition as a rule, and maybe is the sole cause in some cases. In my experience the most common exciting cause is a chronic infection, which, in the early years of life, is often located in the tonsils, antrum, or middle ear, and later in life is often met with in the mouth, but at all ages is most frequently found in the intestine. Comparatively few patients with chronic hypoglycaemia are free from gastrointestinal disorders; long-standing constipation is common, but frequent and offensive stools are not unusual, especially in children, and some patients have distension, flatulency, and heartburn. Even when no complaint is made, examination of the faeces very commonly reveals abnormalities of digestion and absorption. The analyses in my cases have pointed to a chronic intestinal catarrh involving both the large and small intestine in over 47 per cent.; in another 24 per cent. the upper intestinal tract was mainly affected, and in 16 per cent. the large bowel was chiefly concerned. Experiments upon animals have demonstrated that the injection of a poison having a specific action on the liver, such as hydrazine phosphate, is followed by a fall in the blood sugar level,¹ and it is possible that chronic infection may act similarly as an exciting cause of hypoglycaemia by interfering with the functions of a liver already more or less inefficient congenitally. Further, since a chronic catarrh of the upper intestine is generally associated with an infection of the bile and pancreatic ducts, the consequent disturbances of the functions of the liver and pancreas may contribute to the production of a low blood sugar in that type of case. Whatever the explanation may be, I find that patients with chronic hypoglycaemia and intestinal disturbances do not improve satisfactorily unless the bowel condition is successfully treated.

THE URINE.

At first sight it is rather strange that sugar should have been found in the urine of 53 per cent. of my cases, in spite of the fact that the blood sugar level was invariably subnormal and never attained a percentage at which glycosuria might be expected. In 19 cases the sugar proved to be pentose, laevulose, pseudo-laevulose, or lactose, but in the majority it was found to be entirely, or almost entirely, dextrose, thus indicating abnormal permeability of the kidneys for that sugar. The low renal threshold for glucose was possibly accounted for in some instances by a low calcium content of the blood² produced by an excessive loss of lime through the walls of the large intestine,³ or by way of the kidneys; but as dextrose was discovered in the urine of 18 patients whose blood calcium proved to be within the normal range, a deficiency of lime salts was evidently not the only explanation. In 46 cases where the urine was found free from sugar, the presence of an excess of dextrins pointed to there being defects of carbohydrate metabolism due to faults in the functions of the liver or pancreas.

Albumin was rarely encountered in the urine, only 13 per cent. showing traces; these traces could usually be accounted for by an associated oxaluria, probably produced by abnormal fermentative changes in the contents of the upper intestine.⁴ When I first drew attention to the chemical abnormalities occurring in children suffering from cyclical vomiting, in 1923,⁵ I pointed out that the alkali reserve is apt to be reduced and that acetone is very frequently present in the urine. Subsequent experience has confirmed these observations, and also shown that acetonuria is not uncommon in other conditions where chronic hypoglycaemia is a feature. Acetone was discovered in the urine of 29 per cent. of the cases in the present series, and it is worthy of note that it occurred with diminishing frequency as the ages of the patients increased, falling from 65 per cent. in the first decade to 6 per cent. in the seventh. Sugar was found in the urine with the acetone in 74 per cent. of the cases, and when acetone was present alone the patients were usually children. The cause of the acetonuria is no doubt essentially the same as in chronic hyperglycaemia, although the mechanism of its production is different. In both the acetone arises from defective oxidation of fat owing to a deficiency of available sugar, but in hyperglycaemia the deficiency is due to inability of the tissues to use the abundance of sugar present in the circulation, whereas in hypoglycaemia the supply in the blood is insufficient, the power of the tissues to store and utilize sugar being normal.

SYMPTOMS.

The cases with a low blood sugar coming under my care fall into two main groups: (1) those where the hypoglycaemia was definitely part of a symptom complex of which complaint was made (128 patients); and (2) those where the condition of the blood was discovered incidentally in the course of examinations for some other purpose (72 patients). The character of the symptoms in the first group varied considerably, and, while some apparently resulted directly from the low sugar content of the blood, others were more probably attributable to the effect of fundamental pathological changes, of which the hypoglycaemia itself was an expression. The distinction is, however, of theoretical rather than of practical importance, for treatment bringing about a permanent rise in the blood sugar has been found to ameliorate the symptoms in either case. This group can be best considered in subdivisions corresponding to the prevailing clinical features.

Cyclical Vomiting of Children.—The more important results obtained in the investigation of 32 cases of this type are summarized in Table II. These confirm the conclusions I reached nearly seven years ago, but I may draw attention to a few points of particular interest. The most important is the evidence these figures furnish of the hereditary nature of the condition, there being in 73 per cent. of the cases a history of similar symptoms occurring in a blood relation, but not necessarily in an immediate relative. The percentage of cases (53) with evidence of a chronic infection is also striking, but even more remarkable is the very high percentage (84) which, on analysis of

TABLE II.

Symptom.	No.	Age Incidence.	Sex.		Heredit.	Chronic Infection.	Faeces.				Urine.				Blood.	
			Male.	Female.			Enterocolitis.	Enteritis.	Colitis.	Normal.	Sugar.	Acetone.	Albumin.	Calcium Excess.	Calcium Low.	Calcium Normal.
Cyclical vomiting	32	0-9	17	15	23	17	21	2	4	5	15	30	2	2	0	0
Bilious attacks	13	14-61	4	9	6	1	6	5	2	0	9	5	1	2	2	2
Pregnancy, vomiting	6	23-35	0	6	3	0	1	3	2	0	4	6	3	3	2	1
Recurrent headache	23	12-50	8	15	8	10	9	6	5	3	13	5	5	6	4	8
Neurasthenia	11	21-35	5	6	3	0	7	2	2	0	2	1	0	2	4	2
Convulsive attacks	7	40-72	5	2	0	1	3	3	1	0	2	0	0	1	1	4
Lack of energy	35	9-75	30	6	10	13	19	8	7	2	24	7	1	7	15	8
Life insurance	24	20-38	23	1	9	4	8	6	4	6	22	3	2	6	9	10
Routine examination	48	9-57	30	18	7	25	21	14	6	7	16	1	14	14	15	22
	200		122	78	69	71	95	49	33	23	107	53	28	43	52	57

the stools, were found to be suffering from chronic catarrh of the intestinal tract. Early prophylactic treatment for the children of hypoglycaemic parents and recognition of the part chronic infection and toxic absorption play in the production of cyclical vomiting are, I believe, the essentials for success in dealing with a very troublesome complaint.

Recurrent Bilious Attacks.—Sporadic "bilious attacks," usually precipitated by indiscretions of diet, are too well known to call for comment, but the severe recurrent attacks, coming on at short intervals and incapacitating the subject for a day or two, of which the 13 patients comprising this group complained, are a very different matter. All the patients were beyond the age when cyclical vomiting occurs, but in several instances there was a history of attacks in childhood, and a family history of vomiting or of bilious attacks in 46 per cent. Evidence of chronic infection, apart from the intestine, was much less common than in the preceding group, but analysis of the faeces revealed a possible source of toxæmia in the alimentary tract in every case. Nine of the 13 patients passed sugar in their urine, but further examination showed that this consisted mainly of laevulose, pseudo-laevulose, or pentose in 7. Acetone was discovered in the urine of 5 cases (38 per cent.), a much smaller proportion than was found in the children suffering from cyclical vomiting (94 per cent.).

Pernicious Vomiting of Pregnancy.—Four of the 6 patients in this group were sent to me after labour had been induced, as the persistent presence of sugar and acetone suggested they were suffering from diabetes, but the discovery of a subnormal blood sugar disproved the diagnosis. In 2 the glycosuria was probably accounted for by a low percentage of calcium in the blood, and in the other 2 the sugar proved to be a mixture of laevulose and lactose, with a very slight excess of glucose. The remaining patients came with intractable vomiting, both had low blood sugars, and both were excreting acetone in their urine, but neither was passing any sugar. Three patients gave a family history of a hypoglycaemic complex; 4 had children who suffered from cyclical vomiting and were proved to have low blood sugar figures. Evidence of an abnormal condition of the intestinal tract was found in all the cases.

In spite of differences, possibly attributable to the ages of the patients and the character of the diet, the recurrent bilious attacks of adults, the pernicious vomiting of pregnant women, and the cyclical vomiting of children, have so many points in common that it would seem probable their etiology and pathology are similar, if not identical. The fundamental defect is almost certainly in the liver, and, in most cases at least, is inherited. Occasionally it is so severe as to cause symptoms at an early age, but, as a rule, it is only brought into prominence at a later stage by the cumulative effects of an acquired infection, unsuitable diet, or a growing foetus which overstrains

the defective hepatic functions. Hypoglycaemia, although a constant feature and undoubtedly the cause of the acetonuria in some instances, is mainly important as an index of the severity of the liver deficiency to which it is related.

Recurrent Headaches.—The cases falling in this category are of two types—one where the attack recurred at intervals measured by days or weeks, the other where the headache, which was of a less severe character, was of daily occurrence and was particularly prominent in the morning or after an unusual strain. The former is probably akin in origin to a recurrent bilious attack, the latter appears to be a direct effect of the low sugar content of the blood, and can be prevented by a light meal or a dose of glucose, in the morning before rising. Both varieties were met with at all ages between 12 and 50, but a morning headache was more common in middle life. A hereditary basis appeared to be present in 35 per cent. of the cases; a chronic infection was discovered in 46 per cent., and 87 per cent. were shown by analysis to have affections of the intestinal tract. Thirteen patients excreted sugar in their urine, and 5 acetone as well. The urine of 6 contained an excess of calcium, and all but one of these were found to have oxaluria and to be passing traces of albumin.

Neurasthenia was the diagnosis with which 11 patients, subsequently found to have a low blood sugar, came to me, but as they rapidly improved when the hypoglycaemia was treated, and the intestinal disturbances from which they all suffered were corrected, it appears probable that their symptoms were connected with the deficiency of sugar in their blood. A family history suggesting a hypoglycaemic complex was obtained in only 27 per cent. of the cases in this group, and no exciting cause in the form of a chronic infection was discovered in any. On the other hand, the proportion (64 per cent.) suffering from chronic catarrh of the whole intestinal tract was remarkably high.

Convulsive Attacks.—Four of the cases coming under this heading were believed to be suffering from mild epilepsy; 2 had been diagnosed as having Ménière's disease, and one was reported to be a victim of secret alcoholic excess, although he was actually a total abstainer. The attacks of inco-ordination of movement from which they suffered were proved to be associated in every instance with a pronounced hypoglycaemia, and were prevented by raising the sugar content of the blood artificially. There can be little doubt, consequently, that there was a direct connexion between the symptoms and the low blood sugar level. The attacks developed rather late in life in all the cases, the youngest being 40 and the oldest 72 years of age. No family history bearing on the condition could be obtained from any of the patients, but all were found to be suffering from abnormalities of digestion and absorption, which may have been the exciting cause of the hypoglycaemia.

Lack of Energy.—Mild hypoglycaemia does not give rise to noteworthy symptoms unless there is some complication; if the patient complains at all, he usually says he lacks energy and is very easily tired. On inquiry, it is often discovered that consecutive thought is difficult, and work requiring concentration can only be performed with great effort. As a rule, the symptoms are most pronounced in the morning and diminish as the day advances, especially if small frequent meals are taken, as many patients have learnt from experience. Most of the 33 patients with hypoglycaemia of this type seen during the past five years were sent to me as diabetics, owing to their lack of energy and the discovery of sugar in their urine. A smaller number came on account of digestive troubles, which were held responsible for their lassitude, but, although that may have been a partial explanation in some instances, the history of many, and the response of all to symptomatic treatment for hypoglycaemia, indicated the low blood sugar as the more important factor. As a whole the group contained a high proportion (75 per cent.) of cases exhibiting evidence of affections of the upper intestine, and comparatively few (6 per cent.) were found to have normal faeces. A hereditary factor in the production of the hypoglycaemia was suggested by the histories of 28 per cent.

Life Insurance.—A previous application for life insurance is usually presumptive evidence that the applicant considers his health is normal, and this was so with the 24 patients we are now considering who had been rejected on medical grounds. Careful inquiry disclosed, however, that most of them had experienced symptoms which could be reasonably attributed to a deficiency of sugar in the blood, and in some instances these symptoms dated back to early childhood. Twenty-two of the cases had been rejected by the insurance examiners for glycosuria and two for albuminuria. Blood examinations showed no evidence of renal disease in either of the latter, and the albuminuria was probably of the "cyclical" type. The glycosuria in the other cases was evidently dependent upon a low renal threshold for glucose, which was associated with a sub-normal percentage of calcium in the blood in 9. The presence of traces of acetone in the urine of 3 patients indicated defects of fat and carbohydrate metabolism. Evidence of heredity was obtained in 37 per cent. of the cases. Analysis of the stools gave normal results in slightly over 25 per cent.—a higher proportion than in any other group.

Routine Examination.—Routine examination of the blood revealed 48 cases of chronic hypoglycaemia; the majority were sent to me for the elucidation of obscure disturbances of digestion or metabolism, but 6 came for treatment for obesity, 4 had gall-bladder affections, 2 were suffering from pernicious anaemia, one was found to have cancer of the pancreas, and a child was examined on account of delayed development. Evidence of heredity as a causative factor of the hypoglycaemia was found in only 15 per cent. of this group, and the positive cases were nearly all children. Chronic infection as a possible exciting cause was present in 52 per cent., and affections of the intestinal tract in 86 per cent. One-third of the patients passed sugar in their urine, but this was associated with acetone in only one instance. Albumin was found in the urine in 29 per cent.—a higher proportion than in any other group, which is possibly accounted for by the relatively large proportion discovered to be excreting an excess of calcium in the form of oxalate crystals.

The case of cancer of the pancreas mentioned in the last group is of interest since it is one of the few in which conclusive evidence was obtained that the hypoglycaemia was entirely dependent upon an abnormality of the pancreas. Theoretically hypoglycaemia may arise in two ways: either from an inadequate supply of sugar to the blood by the liver, or from an abnormal removal of sugar from the circulation consequent upon excessive formation of the pancreatic internal secretion, but it is not easy to distinguish in practice. A differential diagnosis is sometimes possible from the clinical characters of the case, for hyperinsulism is usually characterized by a comparatively rapid onset and progressively increasing faintness or severe hunger between meals; it is promptly relieved by food, and occurs in a previously healthy person, who is practically

always an adult. Hypoglycaemia due to hepatic defects is, however, common in children as well as in adults; it is generally associated with a more gradual onset, less definitely related to meals, and of a milder and more chronic character, which may be connected with an infection or other exciting cause, and may be hereditary. As a rule, a reliable diagnosis can only be made if the results of analyses of the blood and excreta are taken into account. The character of the symptoms, and the analyses made in my cases, have suggested a hepatic origin for the hypoglycaemia in the majority; hyperinsulism appeared to be an additional factor in some where there was an infection of the upper intestine, and in only a small proportion could the low blood sugar be attributed entirely to an excessive formation of insulin by the pancreas.

Whether a chronic hypoglycaemia gives rise to symptoms demanding treatment or not depends largely upon the manner of its production and the conditions associated with it. I have met with patients whose blood sugar frequently dropped as low as 40 mg. per cent., yet they appeared to be healthy; on the other hand, patients with appreciably higher blood sugar figures suffered from symptoms which seriously interfered with their comfort or occupations. The explanation of the difference seems to be that in the latter the hypoglycaemia had developed comparatively suddenly, possibly as the result of some intercurrent infection which, besides depriving the tissues of their accustomed supply of sugar, affected them in other ways; whereas the former had been used to a low blood sugar all their lives, since their history pointed to the existence of the disability from early childhood, and there was in most cases a family history as well. A congenitally low blood sugar figure usually causes no serious inconvenience so long as the patient's defective metabolism is not subjected to any extraordinary strain, but severe physical or mental exertion rapidly causes collapse, while ketosis, sickness, and other symptoms due to an insufficient supply of available carbohydrate develop from causes which would have little or no effect upon a normal individual.

TREATMENT.

The treatment employed in this series of cases has been the same in principle as I have described in previous papers.⁶ Increasing experience of chronic hypoglycaemia has emphasized the etiological importance of acquired infections and intestinal disorders; and as greater attention has been paid to their detection, and more efficient measures for dealing with them have been adopted, there has been a corresponding improvement in the results. Where dietetic treatment alone has been possible owing to the absence of any discoverable cause, the immediate effects have been satisfactory, but, since it has usually been found that a recurrence of the symptoms followed when the treatment was discontinued, it is evident that an artificial increase in the blood sugar brought about by feeding with glucose, or a diet rich in carbohydrate, has only a palliative effect, as our experience with hypoglycaemic mice has also demonstrated. Observations on these animals have shown that they do not interbreed readily, but that they can be induced to do so by mixing a daily dose of glucose with their food. At first all the progeny were either born dead or only survived a few days; then, as the glucose feeding was continued, some lived for a week or two; later, the death rate diminished, and successive families lived for progressively longer periods, until eventually the mortality was no greater than in the families of normal mice. No matter how long the parental feeding with glucose was continued, however, all the offspring had a low blood sugar and were sterile, and when the administration of glucose to the parents was discontinued they ceased to produce living families. These experiments also demonstrated that, although glucose feeding did not eliminate the cause or influence the transmission of the hereditary defects from which the parents suffered, it prevented the premature death of the offspring and increased their expectation of life. Clinical experience and other experiments with animals have likewise shown that early prophylactic treatment of the descendants of hypoglycaemic parents prevents the development of serious symptoms, and has a beneficial effect on their general health.

There is still much to be learnt about all abnormalities of carbohydrate metabolism, and particularly about those associated with an unusually low blood sugar level, but opportunities for investigation are by no means rare, as the number of cases I have met with in a comparatively short period indicates. I hope this paper may be the means of directing the attention of others to what is, I believe, a matter of considerable clinical importance.

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FLAVINE IN PERINEAL DRESSINGS.*

BY

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THE success of plastic operations on the vagina depends largely on the nursing and after-care received by the patient. Though it is comparatively easy to adopt an adequate operative technique it is sometimes difficult to ensure the healing of the wound by first intention.

The circumstances which may interfere with healing are obvious. The suture line is never dry, being made wet by discharge from the cervix, by menstrual flow, by micturition, and by perspiration. The part is not only constantly wet, but it is bathed in organisms; cervical discharge is never sterile. The skin is always liable to contamination during defaecation, while the urine of many patients subjected to this operation is infected with the *Bacillus coli*. This last circumstance I have found most troublesome of all. The repeated wetting of the wound by infected urine (of which some drops always ascend to the vagina if the patient be recumbent) is, I believe, the most common cause of sepsis following vaginal operations. The infected discharges cause catgut to separate early and silkworm-gut to cut out. Taking these circumstances into consideration it would appear extraordinary that such a wound ever heals by first intention.

I have used a variety of treatments and dressings, pre-operative and post-operative, the common object being to disinfect the vagina before operation, and afterwards to cleanse the wound after each micturition by swabbing with a mild antiseptic and then to apply a dry dressing. I have tried mercury biniodide, eusol, milton, saline, picric acid, iodine, and flavine in water, and I have come to the conclusion that to wash a clean wound with a watery solution of any antiseptic is bad surgery, and that a perineal wound must above all else be protected from urine.

In one of the hospitals to which I am attached patients who have had vaginal operations are allowed to pass water twice only in twenty-four hours, and then in a kneeling position. The woman kneels over a small chamber, her forearms resting on a pillow laid across her thighs. It is difficult to persuade a private patient to adopt this procedure. I have even tried keeping the perineum dry by allowing micturition only through a small funnel held directly below the urethra, but with varying results. The straightforward cases did very well; others gave trouble, one or more stitches giving way too soon, and healing was completed by granulation, the result being more or less imperfect.

My troubles culminated in a case in which I had done a Fothergill's repair, and on the twelfth day I returned from a Sunday's excursion to find that the lady had had a severe secondary haemorrhage; the city had been searched for help, and after some delay a colleague had kindly come to the rescue and packed the vagina. The haemorrhage was due, of course, to sepsis. On removing the pack the bleeding recommenced, and, finding nothing to tie, both colporrhaphy wounds being laid bare in their upper parts and the raw surfaces oozing, I cast about in my mind for some antiseptic lubricant which would clean up the infection and would not dislodge clots in the vessels when with-

drawn. I thought of an emulsion of flavine in paraffin, which I had seen used in prophylactic disinfection of the abdominal wall after laparotomies. I irrigated the vagina to get rid of the offensive clot, then packed with gauze soaked in the emulsion. I was amazed at the speed and completeness with which the sepsis cleared up and the wounds healed.

Since that time, two and a half years ago, I have used this emulsion of flavine in paraffin as a routine dressing in all perineorrhaphies, to my great comfort and success. I use it as a protective dressing. As a rule I wait for twenty-four or forty-eight hours, so as to allow the natural sealing of the wound by serum, then at latest on the third day, the day on which aperient is given and before the bowels are opened, I start dressing with a narrow strip of gauze about three inches long, soaked in the emulsion, applying it by means of a forceps laid upon the colpoperineorrhaphy wound. A little of the emulsion enters the vagina and protects the colporrhaphy wounds higher up. The dressing is renewed after each micturition. The results have been most happy. When operating now for the cure of prolapse I know that with reasonable nursing the wound will heal by first intention, and that the ultimate result will approximate very nearly to the immediate result obtained when the patient leaves the table.

I have also used this emulsion to my satisfaction as a perineal dressing after craniotomy in cases where previous futile attempts to deliver by forceps had caused great bruising of the vulva. It is made up at a strength of 1 in 1,000, though probably in greater dilution it would be equally effective.

FLAVINE IN GENERAL SURGERY.

BY

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THE three following cases illustrate the value of flavine as a bactericide and as an antiseptic in general surgery.

Traumatic Moist Gangrene of Arm.

On October 25th, 1929, a native woman, aged about 24 years, was brought by canoe to Mongu from Libonda, on the upper Zambesi River about three days away, suffering from moist gangrene of the right arm. The history of this case was that, about two months previously, the woman ran into her finger a piece of wood, which she removed with a needle. The hand swelled up and, as she described it, became rotten. When I saw her there was massive necrosis of the limb, extending up to the junction of the lower and middle thirds of the right arm, where a line of ulceration had formed, revealing necrosed bone. Above the area of ulceration the gangrenous process was extending through the tissues of the arm, which were oedematous and greenish-black in colour, from which very fetid yellow pus was oozing copiously. The skin on the inner side of the arm was involved right up to the axilla. The patient was greatly debilitated, and looked very toxic.

Amputation through the shoulder-joint was impracticable owing to the high involvement of the skin on the inner side of the arm, and the patient's condition would not have tolerated such a formidable procedure as an interscapulo-thoracic amputation. I did a guillotine amputation of the arm a handbreadth below the joint, cutting through living tissue as much as possible, ligated the vessels, and treated the stump as an open wound, using flavine (1 in 1,000) dressings only. The result was dramatic, the foul sloughing tissue becoming bright red, and clean within four or five days. The patient is making an excellent recovery, the temperature since the operation having been absolutely normal.

Traumatic Moist Gangrene of Leg.

On May 17th, 1928, a male native, aged about 35 years, was brought to Mongu for treatment, suffering from spreading moist gangrene of the right leg and thigh. The history of the case was that three months previously, when proceeding to seek work, the patient developed a small sore on the dorsum of the right foot, on the Lui River, three or four days from Mongu; he could not say if the sore was due to an injury or not. The foot became swollen, rotted, and dropped off at the ankle-joint; the disease spread up the leg, which fell off at the knee-joint.

When I saw him about 3 or 4 inches of the lower end of the femur were protruding; the bone was black and necrosed, and a necrosed patella was adherent to the muscles, which were a greenish-yellow pultaceous mass, from which a horribly offensive yellowish pus was freely exuding. The gangrenous process was

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