all adopt this method and see the result on all hands? Is the gravity of the disease and the saving of life not sufficient to warrant its trial? I think it is. Dr. Wynn of Birmingham says:

"I know nothing in the whole range of medical treatment so dramatic as the rapid defervescence which follows the injection of a suitable dose of vaccine to a patient suffering from pneumonia or influenzal pneumonia within twenty-four hours of its onset. The vaccine I have used is made from primary cultures or at most first subcultures. It should not be detoxicated or sensitized. For acute pneumonia it contains several strains of pneumococci. . . . The important points are that it should be given early and in sufficient amount."

He gives 100 million pneumococci to an adult; to a child aged 12 to 14 he gives 40 to 50 million, and to a child aged 2 to 3 years 10 to 20 million. These doses have been arrived at after many years of experience. When such a dose is used during the first day of the disease, in the majority of cases the temperature falls to normal on the day following and no further treatment is required. By each day's delay defervescence is less likely, and the dose has to be repeated every twenty-four hours until the temperature is normal. His results² show:

Day Treated.	No. of Cases.	Recoveries.	Deaths.	Temp. Normal in —	
				24 hours.	48 hours.
First	28	28	Nil	Per cent. 71.4	Per cent. 85.7
Second	23	22	1	47.85	56.5
Third	22	20	2	50.0	50.0
Fourth	20	15	5	30.0	40.0
Fifth	14	12	2	35.7	63.5
	107	97	10	50.0	65.0

In pneumonia there is no evidence of a negative phase, and so the early large dose is given safely.

Stock vaccines should be used from first cultures and from a highly virulent strain. Even if a case is injected from a stock vaccine and the case does not afterwards develop consolidation, no harm is done. No harm is done by using antitoxin for a suspected case of diphtheria. Sir Almroth Wright, in his work on the use of vaccines in pneumonia, states that inoculation in the form of a single large dose, administered in the incubation period, often arrested the disease and prevented death. I put this method forward with a plea for trial, as it seems to me our best line of action for the future. My results from stock vaccines are striking.

I cannot lay too much stress on the hygiene of the room—free ventilation is essential. Cases have been treated in America in all weathers on the roofs of hospitals, and in the Philadelphia General Hospital, where the cases were of unusual severity, the death rate of 53 per cent. before the adoption of the open-air treatment was reduced after its adoption to 38 per cent. In the Prince Edward Hospital, Sydney, the patients have since 1908 been treated in the open day and night, and have recovered more rapidly and with less complications and less necessity for drugs. I always advise the windows to be well opened, and so long as there is no discomfort from draughts and there is sufficient light covering, no harm will accrue. Overheating of the room should be avoided—the patient is already hot enough; fresh air is the best germicide, and the patient is gasping for a cooler air.

The actual degree of temperature is of little scientific interest, as one can usually tell from the skin and the pulse the existence of a feverish state. Its record is of value to the nurse to avoid too heavy clothing and at a crisis for more. There is a tendency to put on too much covering both by nurses and relatives. It adds to the discomfort of a feverish patient. If the patient is hot it is well he should lose heat. Pneumonia jackets are useful provided they are thin and not too heavy.

Pulse and breathing rates should always be recorded. The respiration-pulse ratio normally is 1:4; but in pneumonia it may be 1:3, 1:2, 1:2.5, 1:1, or even 2:1. It is the index factor of how the patient is going, and helps in prognosis under ordinary lines of treatment. A case is not necessarily hopeless with 1:1. The heart condition decides.

Potassium iodide and creosote have been advocated. With a tuberculous focus it is possible to loosen some fibrous tissue of a semi-healed area. Inunction of 10 minims of pure creosote in half an ounce of water, with or without one drop of oil of peppermint, has been used with success; it causes sweating and, it is claimed, aborts the disease. One of the oldest and best drugs is calomel. Digitalis is recommended from the outset by some, strophanthus by others. Neither of them raises blood pressure, and the cardiac muscle is enabled to act with regular impulse. They are the only cardiac stimulants necessary, and if employed should be used from the outset. Strychnine and alcohol are probably of little avail. Tincture of nuxvomica with digitalis is better than injections of strychnine for a flagging heart. To produce sleep 1/6 grain heroin may be given: 5 to 10 grains of Dover's powder in a saline has been recommended, but I never use it. Paraldehyde in doses of 1 to 2 drachms in very sweet tea is safe. Soap liniment will relieve localized pleuritic pain. For heart failure injection of 10 per cent. glucose is said to be the most valuable measure.

The cyanosis depends on anoxaemia of the arterial blood, and if oxygen is administered properly and by a suitable apparatus, such as Haldane's, it has been proved that this anoxaemia will be diminished and so the cyanosis relieved. Otherwise it is probably useless. Too often it is used as a last resource when nothing could be achieved. It is more important to let the fresh air into the room from the very outset.

As regards diet, milk (citrated if there is vomiting), with soda-water or barley water, or a little flavour of tea, or malted milk may be given. All sugars are good for the heart, so from the outset sugar or honey should be given. Water is essential in small quantities, as also is ice. Two pints of water should be given in the day—albumin water or water flavoured with beef-tea; beef-tea alone is not advisable. The mouth should be cleaned every two hours.

PERNICIOUS ANAEMIA WITH FOCI OF INFECTION IN THE ALIMENTARY TRACT.

BY

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It has long been held that foci in the alimentary tract may play an important part in the production of pernicious anaemia; it has not been clearly established exactly how this obtains, and the theory does not reconcile the facts that, whereas pernicious anaemia is comparatively uncommon, septic foci are relatively of frequent occurrence.

Hurst¹ believes that achlorhydria is almost invariably the predisposing cause. He collected 12 cases in which this was known to have preceded the onset of anaemia by periods of from one to twelve years. He considers the absence of HCl, probably in the majority of cases of constitutional origin, to be the important factor, and not the cause of the absence. According to him the achlorhydria not only favours infection but results in the arrival in the intestine of proteins in an unaltered condition. He classifies the possible results which may accrue from achlorhydria thus:

1. Delayed protein digestion, with an undue proportion remaining in the lower part of the ileum, in a form readily prone to bacterial decomposition.
2. Provision of material likely to form toxins, which may be (a) haemolytic, the cause of the anaemia; (b) neuro-toxic, causing subacute combined degeneration of the spinal cord; (c) a toxin stimulating bone marrow to form abnormal types of red blood cells.

The fact that subacute combined degeneration of the cord may appear with little or no evidence of blood changes in no particular detracts from the likelihood of the above theory being practically possible, and this is enhanced in value by the good results Böttner and Werner² obtained by duodenal lavage. Nor does the order in which changes may appear in the blood or in the cord. On the other hand, Biffis³ states that achylia gastrica may be absent, and that it occurs later than the blood changes. Maynard and Sturton⁴ record two cases of pernicious anaemia with foci in the alimentary tract, one with dental sepsis and the other with colitis. The autopsy of the latter showed ulcers in the ileum. They

* *Lancet*, September 2nd, 1922, p. 493.

quote a fatal case of pernicious anaemia following dysentery. Hunter⁶ describes a case of subacute combined degeneration of the cord with patches of croupous enteritis in the jejunum.

It is mainly because of the prominence of the alimentary lesions that the following three cases are described.

CASE I.

W. D., male, aged 39, was admitted to hospital for dysentery on December 13th, 1921, with a history of having had malaria, gastritis, colitis, and dysentery in 1919 while in India and Mesopotamia. In April, 1919, examination of stools, liver, and spleen proved negative. In January, 1920, the spleen was palpable and there was tenderness of the descending colon; some carious teeth were removed. In June, 1921, he was sallow, and there was tenderness of the colon; the liver and spleen showed nothing abnormal.

On examination the patient was sallow and anaemic; the mouth was clean; nothing gross was detected in heart, lungs, or abdomen. Blood pressure 96. There was oedema of feet. The urine was normal; examination of stools repeatedly negative. There was nothing to note in the central nervous system except marked pallor of the optic discs without haemorrhages. A test meal gave no free HCl. The Wassermann reaction was negative. Examination of the blood showed:

Red corpuscles	...	...	...	...	1,370,000
White corpuscles	...	...	...	...	2,700
Haemoglobin	...	...	...	...	37 per cent.
Colour index	...	...	...	...	1.3
Differential count—					
Polymorphonuclears	...	...	...	...	45 per cent.
Lymphocytes	...	...	...	...	48 "
Large mononuclears	...	...	...	...	6 "
Eosinophiles	...	...	...	...	1 "

Microcytes, megalocytes, and poikilocytes were present. There were no normoblasts nor megaloblasts.

Course.—There was occasional slight to moderate rise of temperature. Severe vomiting for one week. The liver became easily palpable. After several courses of arsenic and drachm doses of dilute HCl with his meals, he was discharged, after five months, with a blood count of nearly 5 million red cells and 3,000 white, and a colour index of just over 1, declaring himself well. The spleen could never be felt, and no megaloblasts were ever seen.

CASE II.

G. S. C., male, aged 23, was admitted to hospital for sprue on November 21st, 1922. He had had jaundice and diarrhoea when in China from November, 1919, till May, 1920. In London, in 1921, he was treated for sprue by alkalis, pancreatic extract, *B. coli* autogenous vaccine, and by dieting. He gave a history of frequent copious stools, sore mouth and tongue, and much flatulence.

Examination showed: marked pallor of membranes; much emaciation with dry scaly skin. Teeth excellent; tongue smooth and ulcerated. There was no enlargement of the heart; apex beat fixed; reduplicated basal second sound. Early clubbing of fingers. Blood pressure, 88. Friction over lower half of lung from base to heart's apex. No tubercle bacilli had ever been found in the sputum. The abdomen was doughy and distended; liver dullness decreased. The stools were copious, acid, and frothy, with excess of fat, and yielded a plentiful growth of *B. coli* and streptococci; yeasts also were present, but no protozoa. There was nothing abnormal in the central nervous system except marked pallor of the optic discs without haemorrhages. The patient was too ill for analysis of the gastric contents. Examination of the blood showed:

Red corpuscles	...	...	...	...	1,500,000
White corpuscles	...	...	...	...	2,000
Haemoglobin	...	...	...	...	40 per cent.
Colour index	...	...	...	...	1.4
Differential count—					
Polymorphonuclears	...	...	...	...	45 per cent.
Lymphocytes	...	...	...	...	52 "
Large mononuclears	...	...	...	...	3 "

Polychromatophilia, anisocytosis, and poikilocytosis were present. There were two normoblasts and many megalocytes.

Course.—There was an occasional rise of temperature; petechial haemorrhages; loss of left knee-jerk. Hypostatic pneumonia developed, and death took place on February 8th, 1922, in spite of all forms of treatment, both dietetic and therapeutic. No post-mortem examination was obtained.

CASE III.

W. A., male, aged 34, was admitted to hospital for dysentery on September 16th, 1922. His history showed that he had had bacillary dysentery in August, 1918, and malaria in September, 1919. In January, 1920, however, he suffered from no disability. In April, 1920, he had his teeth attended to. In February, 1921, the spleen was palpable. He complained of loss of appetite, sore tongue, and diarrhoea.

On examination he seemed to be in fair condition, but was very pale. The mouth was clean; tongue atrophied. Liver not palpable; spleen, two fingers. Nothing to note in the central nervous system except pallor of the optic discs without haemorrhages. He passed one to three stools daily with nothing to note. The Wassermann

reaction was negative. A test meal gave no free HCl. Examination of the blood showed:

Red corpuscles	...	...	...	...	2,200,000
White corpuscles	...	...	...	...	4,100
Haemoglobin	...	...	...	...	42 per cent.
Colour index	...	...	...	...	0.95
Differential count—					
Polymorphonuclears	...	...	...	...	35 per cent.
Lymphocytes	...	...	...	...	60 "
Large mononuclears	...	...	...	...	3 "
Eosinophiles	...	...	...	...	2 "

There was some anisocytosis and poikilocytosis; granular basophilic well marked; one normoblast.

Course.—He ran an evening temperature of 100°. His liver became palpable. He developed copious early morning stools, very acid, and containing undigested fat. Yeasts, but no organisms of protozoal nature were found. There was one attack of bright red rectal haemorrhage. One knee-jerk disappeared, to reappear; his red cells became progressively less in number; megaloblasts and high colour index made their appearance, and he died on November 15th, 1922.

It is quite possible that many would place Case I in the category of aplastic anaemia, but this contention need not be disputed, because, however strongly this might be urged, the fact remains that the anaemia was of a primary as opposed to a secondary type. It is not unlikely that the colitis was never of dysenteric origin, since no evidence could be found in his army documents as to the exact cause of the dysentery, but presumably at one time he was diagnosed as suffering from true dysentery by those competent to make the clinical diagnosis.

Case II is of exceptional interest. Manson-Bahr⁶ says that the anaemia of sprue may approach the pernicious type, with alteration in the size and shape of the erythrocytes and with the appearance of normoblasts, and that it is apparently secondary to the intestinal toxæmia. Bassett-Smith⁷ holds that sprue is different from pernicious anaemia in that the colour index is low, and that the anaemia is a true secondary and not a primary one. The anaemia in this instance also would appear to be of the aplastic type.

The autopsy of Case III showed not only the changes usually found in pernicious anaemia but definite ulcers in the large gut, which was in part entirely denuded of mucous membrane, so as to be quite transparent. An enlarged ileocolic gland was seen draining the area of an ulcerated patch in the intestine. This was especially looked for, since these enlarged glands can be felt through the abdominal wall in many cases of chronic dysentery. The gastric mucous membrane was much atrophied, and $1\frac{1}{2}$ inches from the pylorus there was a thickened encapsulated mass in the duodenal wall, projecting into the lumen of the bowel, giving the appearance of an adenoma.

Until some organism or virus can be identified as the specific cause of pernicious anaemia it would not appear unscientific to suggest that the disease may be caused by a combination of circumstances. The importance of achlorhydria can be gauged by the emphasis rightly laid upon this by all authorities. Hunter has placed stress on the co-existent secondary anaemia from oral sepsis and the improvement obtained by dental toilet. The fact that toxins can more easily get into the circulation through an abraded or ulcerated surface than through a normal one lends colour to the part played by the ulceration in two of the cases quoted above, and there is every reason to think that secondary infection can be imposed upon an ulcer in the large bowel, originally dysenteric. The following case illustrates this contention.

S., aged 25, admitted to hospital for dysentery. He gave a history of having had dysentery, caused by Flexner's bacillus, in France in 1917. Had had colitis and attacks of diarrhoea with frequent stools containing blood and mucus since that time—the last attack incapacitating him for ten weeks.

Examination showed thickening of gut in both iliac fossae, and large tender glands in these regions, more marked on the left. The stools were semi-formed, and contained much bright blood and glairy mucus, and small patches of necrotic tissue lying on the outside of the faeces, and not intimately mixed with them as in the enteritis of malignant malaria. Amoebic cysts were recovered from the mucus. Sigmoidoscopy revealed congested bowel surface covered with yellowish-white mucus, and 12 cm. from the anus a small superficial ulcer. A direct swabbing from this was effected, and the stained smear showed six acid fast bacilli morphologically bovine in type.

These cases are published in the hope that any additional factor, however apparently trivial, brought to light in the investigation of pernicious anaemia may help towards establishing the cause of this disease, be it specific, or consequent

upon a chain of circumstances, the sum-total of which leads to the ultimate production of such an intractable malady.

Either Colonel Cowan or Dr. P. O. Ellison kindly carried out the bacteriological and biochemical investigations referred to in this paper.

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THE ACTION OF HISTAMINE ON THE VEINS:

A METHOD OF DIFFERENTIAL PERFUSION: NITRITES IN THE PREVENTION OF HISTAMINE SHOCK.

(Preliminary Communication.)

BY

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DALE and LAIDLAW¹ have shown that in histamine shock there is capillary dilatation, with fall in blood pressure and respiratory failure within a very short time of the injection of the drug. They conclude that histamine produces an active dilatation of capillaries, and dismiss the possibility of active constriction of veins. I have devised a method of perfusion which differentiates between the action of a drug on arteries and on veins respectively.

Method.

Cannulae are inserted into the artery and vein of the organ; bleeding points are ligatured, and the organ after excision is perfused for a short time in the ordinary way with warm oxygenated Ringer's fluid under hydrostatic pressure, in order to wash out the blood and to determine there is no leakage. An incision is made in the organ, avoiding large vessels, or the surface may be scarified. For perfusion of the veins the Ringer's fluid is led to the cannula in the vein and the artery is occluded. The perfusion fluid now passes backwards through the veins and escapes by the incision, and the rate of flow is measured. For arterial perfusion the reverse process is adopted—the vein is occluded and the fluid from the arteries escapes as before. A fresh preparation must be used for arteries and for veins, because after the tissues have been perfused with the drug by the one channel they are so affected that only a small effect may be obtained if perfused afterwards by the other channel.

Certain details of procedure may be briefly indicated for particular organs. For the small intestine cannulae are inserted distally in the portal vein and superior mesenteric artery. The incision in the isolated loop of gut is made longitudinally on the opposite side to the attachment of the mesentery. In the liver a cannula is inserted in the portal vein directed towards the liver; another cannula is placed in the inferior vena cava in the thorax, directed tailwards, and the diaphragmatic veins are ligatured. The liver is then removed after a ligature has occluded the inferior vena cava and hepatic artery in the abdomen. After scarification of the liver separate perfusions of the portal ramifications in the liver and of the hepatic vein may thus be obtained.

For the hind limbs the usual preparation is made, and after skinning the limbs the fascia lata is removed and the superficial fibres of the thigh muscles cut away with scissors. The perfusion fluid exudes from the raw surface thus exposed.

In the lung a cannula is inserted into the pulmonary artery through the right ventricle; another cannula is inserted into the left auricle through the mitral orifice. The remains of the heart are cut away and the lungs with the trachea removed from the body. Into the trachea a small quantity of warm liquid paraffin is introduced, and the lungs are inflated to about their normal volume in the chest and the trachea ligatured. In this way air-locks are made in the bronchi. The surface of the lungs is then scarified to provide exit for the perfusion fluid. The air-locks prevent the lungs from collapsing, and the scarification allows the pulmonary artery and veins to be perfused separately.

By this method of perfusion it was found that after histamine both venules and arterioles were constricted in the isolated limbs and lungs of both cats and rabbits, and constriction of both portal and hepatic veins occurred in the liver of these animals. In the isolated intestine of the cat a similar constriction of venules and arterioles was observed. The rabbit's intestine, however, showed no constriction of mesenteric venules but only the arterial constriction. Ring preparations of the portal vein and mesenteric artery of the pig (from the slaughterhouse) also showed tonic constriction by histamine. It would appear that constriction of venules is an important action of histamine, leading to capillary engorgement and consequent oedema. In view of the above observations the shock induced in the cat, and its absence in the rabbit, would appear to be largely due to the difference in the reaction of the splanchnic veins to histamine in these animals.

These experiments suggested that a preliminary treatment by nitrites in order to dilate the veins, followed by the infusion of a sufficient quantity of Ringer's solution into the veins to fill the dilated vessels, might prevent death in the cat after a toxic dose of histamine.

A cat of 1.9 kilos anaesthetized with urethane received an intravenous injection of 16 mg. of sodium nitrite in 1 per cent. solution; Ringer's solution was then intrafused under 20 cm. water pressure into the vein; 6 mg. of ergamine (B. W. and Co.), containing approximately 2 mg. histamine base, were injected intravenously. The animal did not require artificial respiration, and was alive one and a half hours after the injection of the histamine; the blood pressure and respiration improved considerably within half an hour.

Further experiments on these lines are in progress; a method of treatment after the induction of histamine shock is being attempted.

These experiments suggest that the wheal described by Dale and Laidlaw which arises at the point of local application of histamine may be due to intense local constriction of venules leading to local congestion and consequent oedema. This may be a protective response on the part of the organism to prevent the admission of histamine into the general circulation. If histamine shock be regarded as a generalized extension of such a response it is clear that for treatment the venules must be dilated sufficiently to provide an adequate circulation in the organism, but the oedema must be encouraged in order to assist the elimination of the histamine from the blood.

The regulation of the flow of blood through the veins would appear to be important. Gunn² has shown already that veins are constricted by adrenaline.

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A SIMPLE DIET TABLE.

BY

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THE following table has been in use in both hospital and private practice for nearly twelve months; the results obtained have been so satisfactory that I venture to think that it may prove of value to others who have to undertake the dietetic management of various metabolic disorders.

Most food analyses are expressed in percentage values of carbohydrates, fats, proteins, water, and salts, the quantity of food itself being given a unitary or workable value. In clinical work, on the other hand, it is obvious that what is required is a unitary value for the specific carbohydrate, fat, or protein content, and with this end in view I was led to devise this simple table. The factors which determine the success and accuracy of any particular diet would appear to be the ease of original construction, an elasticity which allows, if necessary, of a daily change, and a small demand only on the time and intelligence of helpers and patients. This table has been found to meet these requirements, the only other essential being a small pair of scales. The specific contents have been worked out from the excellent tables given by Joslin¹ and Cammidge² and from other sources; the quantities are not strictly accurate, as the unit idea was kept mainly in mind, in view of the ordinary conditions under which patients arrange their own dietary. The scheme has been principally used in the dietetic management of chronic nephritis, diabetes mellitus, hyperchlohydria, and achylia gastrica. In these conditions, where specific intolerance of carbohydrates, fats, proteins, or their derivatives is often manifested, a simple control of intake has been obtained by the use of this table; determinations of output or utilization have been made in the case of carbohydrates by glucose estimations in blood and urine, in the case of proteins by determination of urea in the blood and of total nitrogen and urea in the urine, and in the case of fats by the ordinary methods of detecting the onset or degree of acidosis. By these means it has been found that growth or loss of tolerance for carbohydrates and proteins is readily observed and that the onset of acidosis is easily controlled.

The following chart may serve to illustrate the simple method of prescribing food, quantities of which are shown daily; growth of tolerance for carbohydrate (without fasting or the use of "ladder" schemes) and maintenance of nitrogenous equilibrium are also clear. The case is one of a woman of 26 suffering from diabetes mellitus. Blood sugar