TREATMENT IN GENERAL PRACTICE

This article is one of a series on the management of some of the major medical disorders met with in general practice

SEPTICAEMIA

BY

C. E. LAKIN, M.D., F.R.C.P., F.R.C.S.

In clinical medicine the term "septicaemia" is employed to denote an infection of a high grade of intensity in which organisms make their appearance in large numbers in the circulating blood and are rapidly and widely dispersed through the tissues of the body, the disease being the expression of the interaction between the invading organisms and the tissue elements of the host. The temporary presence of organisms in the blood forms an integral phase of many infections, such as typhoid fever and pneumonia, their transitory appearance being usually spoken of as bacteraemia.

In bacteraemia the organisms generally exist in the blood for a certain period of time, the length of which can be stated more or less accurately. In the later stages of septicaemia the organisms actually multiply in the blood stream, and are likely to persist up to the moment of the fatal termination. Secondary lesions may arise in bacteraemia, and when these happen to affect vital tissues, as, for instance, when meningitis occurs in pneumonia, there may be a fatal issue without widespread generalization throughout the tissues. The generalization or localization of an infection is determined, of course, not only by the character of the invading organism, but also by the resistance of the host. Yet it must be allowed that a bacteraemia may go on to a septicaemia. Instances of rapid and widespread generalization of infection are well exemplified in streptococcal and staphylococcal septicaemias, and it is with this type of case that we are more nearly concerned in the present contribution.

Septicaemia may be further complicated by pyaemia, a condition in which there is suppurative phlebitis at the site of the primary lesion with detachment of particles of the infected thrombus and their impaction in some distant situation, with the formation of secondary abscesses. Pyaemia is more common in cases of staphylococcal than in streptococcal septicaemia.

Treatment of the Primary Focus

In the earlier stages, then, of a septicaemia a rapid and continuous invasion of the blood stream is taking place by organisms from the primary focus or from multiple foci which have developed during the course of the disease, and the actual multiplication in the blood stream would appear to be a rare event till quite late in the process. In the case of suppurative diseases in which the primary and secondary foci are accessible to surgical intervention the results of adequate drainage bear striking witness to the ability of the blood to deal with even a massive grade of infection if continuous reinvasion can be prevented.

This must not be taken to imply that every case in which localized infection has occurred is to be treated by a surgical incision. Incision of many an infected punctured wound has been the means of initiating the fatal septicaemia which it was intended to prevent. The knife, in attempting to liberate pus, has cut through the encircling protective zone successfully built up by the inflammatory reaction of the tissues, and massive infection of the tissues beyond the protective zone has led to a widespread and overwhelming invasion of the blood

stream. Hot fomentations, in order to encourage vascular dilatation and exudation of phagocytes, should therefore be the treatment adopted in dealing with a wound such as a pathologist might sustain while making a post-mortem examination or a surgeon in dealing with some infected condition. When at the centre of such a wound pus begins to show itself beneath the epithelium, great care should be taken not to cut through the surrounding protective zone, but only to liberate the presenting pus with the point of the scalpel. When a wound of this sort has been inflicted, if it can be ascertained that the source of infection was streptococcal in nature, anti-streptococcal serum should be given. Antiscarlatinal serum appears to be the most efficacious, and 10 c.cm. should be injected subcutaneously as early as possible, and a further supply kept in readiness for use the following day if any signs such as a rise of body temperature and quickened pulse indicate the probability of a generalized infection, when, as will be seen later, larger quantities may have to be given by the intravenous route.

Cryptogenic Infections

Apart from cases arising secondarily to an easily recognized primary infected focus, septicaemia may arise in so-called cryptogenic infections, where the site of entry of the infection may be undiscoverable, at any rate at first. In some of these cases the patient is already debilitated, and the clinical picture may be so variable that the condition may not be recognized as one of septicaemia unless an organism has been obtained by culture from the blood. In some pyrexia is continuous, in others remittent or intermittent, with a temperature chart showing spikes of 105° or 106° F. In cases of extreme virulence the temperature may be raised scarcely at all. Rigors are frequent, and often associated with profuse sweating. The pulse is small, soft, and rapid. The tongue may be furred and dry, but in streptococcal cases is often smooth, red, or raw-looking, and diarrhoea is frequent. The urine contains albumin, and red cells and casts are commonly met with. Prostration, with progressive anaemia and wasting, is the rule. While some cases remain preternaturally mentally clear, others may become delirious. Examination of the skin frequently discloses the presence of petechiae or purpuric areas, and erythema. Bronchopneumonic patches are likely to be present in the lungs. The spleen may be enlarged, though often difficult to feel. Blood examination often reveals a leucocytosis, with a relative increase in polymorphonuclear leucocytes, though in some of the most acute forms leucopenia may be encountered. The diagnosis will be established when a positive blood culture is obtained.

General Therapeutic Measures

If the condition is well established when the patient is first seen, probably some form of intravenous therapy will be carried out, but it cannot be insisted upon too strongly that general measures directed to maintaining and increasing the patient's natural resistance are of no less, and probably of greater, importance. These will include:

1. *Complete Rest in Bed.*—The more a patient exerts himself the quicker will the heart beat, and more blood will be hurried through the infected focus in unit time, with the result that toxins and organisms will be disseminated in increasing degree throughout the body.

2. *Open Air*.—Whenever practicable cases of septicaemia should be at rest in a protected situation in the open air. This will tend to the greater comfort of the patient in that more rapid evaporation from the skin is encouraged; the greater degree of light and gently moving air will exert a metabolic influence upon the skin, while a more abundant supply of oxygen will lead to increased transpiration of exhaled aqueous vapour from the lungs. Appetite will be increased, and restlessness and tedium diminished.

3. *Diet*.—This should be carefully chosen in relation to fever and diminished digestive secretions, but should be ample in amount. An abundant supply of fluid in order to maintain diuresis and increase the excretion of toxins and organisms should be forthcoming. Drinks containing fruit juice and glucose should be liberally provided.

4. *Judicious Nursing*.—Restless activity on the part of a nurse cannot be too strongly deprecated. An experienced nurse, who is neither too subservient to the fetish of washing a patient twice a day nor bent on making constant needless demands which only serve to weary the patient, is essential if a successful issue is to be obtained. Hydrotherapy may be necessary to control the pyrexia and induce sleep.

5. *Drugs*.—Elimination may be assisted by adding sodium citrate to freshly made lemonade or orangeade. Small doses of hydrarg. c. creta or salol (5 grains thrice daily) may be of service in relieving abdominal distension or diarrhoea. Cardiac tonics, including digitalis, will be of service when heart failure threatens. Alcohol should be allowed if the patient has been in the habit of taking it.

Serum and Vaccine Therapy

In acute streptococcal cases antiscarlatinal serum is likely to yield better results than polyvalent serum. Whichever variety is used 20 to 60 c.cm. may be given intravenously or intramuscularly, and 20 c.cm. or more may be injected every six or eight hours by the same routes till several doses have been administered if benefit, as judged by the temperature, pulse rate, and general condition of the patient, appears to be accruing. Some prefer to prescribe doses of 50 to 100 c.cm. of serum well diluted with normal saline and repeated once in the twenty-four hours. In giving serum the usual precautions as regards the previous administration of horse serum must be observed, and desensitization may have to be carried out as a preliminary measure. For staphylococcal, gonococcal, and pneumococcal cases corresponding sera can be procured, and are usually prescribed in 25 c.cm. doses.

If as a result of treatment on these lines definite improvement results, the question arises as to whether vaccine treatment should be instituted. If the case is one that appears to have originated from some hidden focus of infection as opposed to one in which an infected wound was responsible for the septicaemia, vaccine therapy may be undertaken. It is wise to start with a small dose of vaccine prepared from the organism obtained from the patient's blood. A negative phase is to be avoided at all costs, and in the case of a streptococcal infection a quarter of a million organisms will not be too small for the initial dose. The dose may then gradually be increased every third day, till from two to five millions are being injected. Some prefer to use sensitized vaccines in these cases.

Simple and Immuno-transfusion

Immuno-transfusion, though occasionally attended by brilliant results, is usually disappointing. In carrying out this procedure a donor whose blood is compatible with that of the patient is given a vaccine prepared from the sufferer's organism, or, failing that, a stock homologous vaccine. At the same time the donor may receive an injection of nucleinate of soda, in order to bring about an increase of leucocytes. If the vaccine is injected subcutaneously the immunizing response is generally well established by the end of five hours, after which time

the donor's blood is transfused into the patient. It is best not to employ citrated blood. Wright, Stoner, and Colebrook have shown that not only a specific but a general immunity to most pathogenic organisms is developed by the injection of a stock staphylococcal or typhoid vaccine, so that the method can still be utilized in cases in which the infecting organism is unknown.

It has long been recognized that in cases of septicaemia the blood becomes deficient in complement, and simple transfusion of 150 to 300 c.cm. of compatible fresh human serum or whole blood is often successfully employed. In highly febrile cases about the second week of the illness dilatation of the right side of the heart is not infrequent, and as at this stage the transfusion of any large quantity of blood may be attended with danger, it is preferable to administer the donor's serum in small repeated doses.

CADHAM'S METHOD

Professor Cadham of the University of Manitoba has introduced recently a method of treating cases of septicaemia which has yielded striking results. Rabbits six months old are given vaccines of streptococci and staphylococci obtained from cases of septicaemia at certain intervals of time till the age of two years is attained. When such a rabbit is to be made use of in the treatment of a case of septicaemia it receives a vaccine made from the patient's organism. After a short interval 10 c.cm. of blood is taken from the heart of the rabbit by a special procedure which does not entail the death of the animal, and the serum is injected into the patient, who also receives human serum from a compatible donor. A hundred cubic centimetres of blood are taken from the donor, and from four to ten portions of serum from this quantity are injected on alternate days. In Cadham's series of ninety-five cases a mortality of only 10.5 per cent. occurred. As the risk of a fatal termination in septicaemia is usually held to be round about 70 per cent. it is to be hoped that an extensive trial of Cadham's method will be carried out in this country.

AN UNUSUAL CASE

Mention must also be made of an article by Dr. Ronald L. Hamilton in the January (1935) number of the *Guthrie Clinic Bulletin* on the treatment of subacute bacterial endocarditis. He reports two cases of apparent cure following the use of bacteriophage. Space will only permit of a short reference to one of these cases—that of a lady in whom a very virulent subacute bacterial endocarditis developed during pregnancy.

Streptococcus viridans was obtained on blood culture, and petechiae and Osler's nodes were present on the fingers and toes. During the course of the illness sudden and almost complete blindness and left hemiparesis supervened. The Cadham treatment was started, but the reactions were so severe that it was discontinued. Daily injections of from 30 to 50 c.cm. of a 5 per cent. solution of acriflavine for a time led to temporary improvement. Showers of petechiae were of almost daily occurrence, and infarction of the spleen and lungs ensued. On three occasions severe convulsions took place.

In desperation treatment by bacteriophage was decided upon. Following the first treatment the patient developed a temperature round about 104° F., and experienced a severe chill, lasting one and a half hours, but from this time onwards she never manifested any further vascular phenomena. Daily intravenous injections of bacteriophage were continued, each one being followed by febrile reactions and chills of decreasing severity. Blood cultures taken since this time have always proved negative, and at the time the article was written the patient was reported to be attending to her household duties, playing golf, and dancing. Twelve intravenous injections in approximately 2 c.cm. doses were given in all. At first the bacteriophage was diluted with 50 c.cm. of normal saline, and with each successive dose the amount of saline was reduced until the bacteriophage was administered alone.

Treatment with Bactericidal Drugs

Finally, reference must be made to the intravenous use of various bactericidal drugs. It is difficult to believe that a degree of concentration sufficient to destroy bacteria without killing somatic cells can be attained, yet in practice a certain measure of success has followed their use. In a case of the writer's, in which the presence of *Staphylococcus aureus* in the blood stream was attended by a pyrexial illness of many weeks' duration, fever abruptly abated and blood culture became negative after three or four intravenous injections of 10 c.cm. of a 0.8 per cent. solution of collosol iodine given at twenty-four-hourly intervals. Eusol is, as a rule, employed in 0.05 per cent. solution in normal saline, from 200 to 500 c.cm. being injected by the intravenous route. If gentian violet is chosen, from 20 to 40 c.cm. of a 0.25 per cent. solution in sterile tap-water may be prescribed every second or third day for three or four doses. Collosol silver has been administered in streptococcal septicaemia, 5 to 20 c.cm. of a 0.05 per cent. solution being given intravenously on alternate days for a fortnight. Where intramuscular injection is preferred, 1 to 2 c.cm. of a 1 in 2,000 solution of collosol argentum may be substituted. Some cases of staphylococcal septicaemia respond to collosol manganese, in doses of 0.5 c.cm. of collosol manganese (Crookes) by the intramuscular route every third day.

Of the stronger poisons, preparations of mercury and arsenic hold the field. Thus mercuric chloride may be injected intravenously, 3 to 6 c.cm. of a 0.05 per cent. solution being used on alternate days, or even daily, till salivation or some more serious indication of mercurial poisoning arise. Should these occur the drug must be discontinued straightway. Mercurochrome, a compound of mercury and fluorescein, appears to be somewhat less toxic, and 5 to 10 c.cm. of a 0.5 per cent. solution may be administered intravenously to an adult. Some physicians recommend that the drug should be employed in a more exact dosage, stating that the correct dose is 1 to 3 milligrams per kilogram of body weight. An initial dose of 1 mg. per kilo body weight in 0.5 per cent. solution is injected intravenously, and the remedy repeated at intervals of four or five days, the amount being gradually increased till 3 mg. per kilo body weight is reached. Neosalvarsan, of the arsenical compounds, is the one most frequently put into requisition. It is prescribed at weekly intervals, provided there is no renal lesion present, in doses starting with 0.3 gram, but it is disappointing in bacterial infections. Slight improvement sometimes follows administration of sodium cacodylate, 1/2 to 1 grain being injected into the muscles daily for twelve days. Its favourable effect is due most probably to its tonic action rather than to any bactericidal efficacy.

Fixation Abscess

Last of all, another procedure, more often practised in France than in this country, must be mentioned—namely, the production of a "fixation abscess." In a case of puerperal septicaemia which had resisted various forms of treatment, I injected 1 c.cm. of turpentine in the interscapular region; the red, brawny swelling which resulted was incised forty-eight hours later, and hot fomentations were applied. The following day, as no discharge had occurred, a slough which lay between the lips of the incision was gently removed by forceps; its removal was followed by an immediate escape of two or three ounces of pus. Hot fomentations were continued, and the pyrexia, which had lasted four weeks, came to an abrupt termination that same evening. In France a slightly different procedure is sometimes employed—namely, to inject a drop or two only of turpentine in ten or twenty different spots over the abdomen or other part of the body. Turpentine should be avoided if there is reason to believe that the kidneys are diseased.

THE INTERPRETATION OF PAIN IN THE ABDOMEN*

BY

HAROLD C. EDWARDS, M.S., F.R.C.S.

SURGEON TO KING'S COLLEGE HOSPITAL AND THE EVELINA HOSPITAL
FOR CHILDREN

Pain is the predominating symptom of all acute and many chronic abdominal diseases. In John Hilton's *On Rest and Pain* is found the following paragraph (quoted by Morley): "I conceive that pain situated upon the surface of the body, and associated with some abnormal state of an internal viscus, must be looked upon as a beneficent provision, enabling us by external pain to appreciate slight organic changes or derangements of function of the internal viscera." This conception appears to have met with acceptance without, at that time, arousing any extended scientific inquiry as to the origin and nature of pain. Indeed, the incentive to such an inquiry was lacking, and it was not until Lister had made abdominal surgery possible that the need for an accurate estimation of the meaning of pain became more clearly realized. Lack of time forbids a detailed description of how the present view of the significance of abdominal pain has evolved, but we owe much to Ross and Sir Henry Head, to that great general practitioner Sir James Mackenzie, and, more lately, to Arthur Hurst and to John Morley of Manchester, whose excellent book is a magnificent contribution to the literature of this subject.†

One of the chance discoveries which upset previous views of the meaning of abdominal pain was that the bowel brought out of the abdomen for the purposes of colostomy could be incised without causing pain. A later and more complex observation was that if the abdomen were opened under a local anaesthetic with the patient fully conscious, the abdominal viscera might be freely handled, incised, or pinched without hurting the patient, but that the slightest mechanical stimulation of the parietal peritoneum gave rise to acute localized pain. The viscera themselves are not, therefore, sensitive to the ordinary stimuli which provoke painful sensations elsewhere in the body, including the parietal peritoneum. Pain in the former can only be caused by distension from within their lumen.

Thus we know there to be two types of abdominal pain: (1) that due to distension of a viscus (visceral pain); and (2) that due to irritation of the parietal peritoneum. These two types present marked differences in their mechanism and clinical manifestations. The viscera are supplied by the splanchnic nerves, part of the sympathetic or autonomic nervous system. There is no clear connexion between the splanchnic nerves and the body or somatic nerves, so that pain arising from distension of an abdominal viscus is not accompanied by the physical signs of tenderness of the abdominal wall or muscular rigidity. Moreover, it is not localized, but invariably diffuse and widespread.

Peritoneal pain is something entirely different, and it is this type which led to Hilton's description of "a beneficent provision." Unlike the abdominal viscera, which have a splanchnic nerve supply, the peritoneum is innervated by the body or somatic nerves. The nerve supply is segmental, corresponding with that to the skin and muscles of the abdominal wall. Take, for example, the tenth dorsal nerve. This nerve passes obliquely downwards and forwards from its segment in the spinal cord, first supplying the parietal pleura, and terminates in the abdominal wall in the neighbourhood of the umbilicus. As it passes through the abdominal wall it supplies, over a narrow segment, the skin, muscles, and peritoneum. There is a reflex arc between the peritoneum and parietes, so that if the peritoneum is stimulated in this segment the muscles supplied by the tenth nerve become rigidly contracted, there is superficial tenderness and hyperaesthesia of the skin, and, finally, and of great importance, the pain is accurately and unerringly localizable by the patient to this area.

* A paper read to the Monmouthshire Division of the British Medical Association, February 15th, 1935.

† Morley, John: *Abdominal Pain*, Edinburgh, 1931.