solid organs. Thorough survey of the patient, almost daily, for these metastases must be made. Effusions are to be dealt with by aspiration for preference, but if this is unsuccessful, then incision and drainage become necessary. Great exercise of judgement is required at both these stages of the disease. Surgery is indicated more often, and more early, in staphylococcal than in streptococcal infections. The favourite sites for staphylococcal metastases should be passed in review again and again.

GENERAL REMARKS

The individual case is to be treated on its merits, due consideration being given meanwhile to any general specific remedy offered by the immunologist, and applicable to the particular infection concerned. The physician should work hand in hand with the bacteriologist, but should not take the cue entirely from him in matters of treatment. Close liaison with the surgeon is a *sine qua non* for success. Expectant measures should be mobilized promptly and thoroughly. All the therapeutic "eggs" should never be put into one basket. A plan of campaign appropriate to the case in point should be decided upon and steadily continued, and the patient should not be disturbed by too many treatments. Panic on the part of the friends is a frequent deterrent, but is pardonable; panic on the part of the medical adviser is sometimes fatal and is unforgivable.

SURGICAL ASPECTS OF SEPTICAEMIA *

BY

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The question under discussion to-day, whilst of vital importance and wide interest, is, at the same time, one on which fruitful debate is difficult. Many of us have had considerable experience, of an occasional and isolated nature, of cases of septicaemia; few have had the opportunity of treating a series on truly scientific lines. The features peculiar to the individual case, the intermittent and irregular incidence of cases, our own changing ideas of the value of certain lines of treatment, all tend to render judgement difficult. Further, we are so apt to enthroned in the sunshine of our memory the apparently striking success, and to allow the many failures to slip into the quiet shadows of forgetfulness.

The surgeon may be called on to deal with septicaemia under three sets of circumstances:

- (1) Following an infected accidental wound;
- (2) Accompanying an idiopathic infection, such as acute osteomyelitis, cellulitis, or phlebitis;
- (3) Following operation on an infected area.

In (1) and (2) active surgical intervention may be called for, but nicety of judgement is necessary in determining how much must be done, and when. In many cases it will be found that active surgery must be held in restraint until such time as the indications for intervention have become abundantly clear—in other words, the knife may be a lethal weapon if prematurely or incautiously applied (for example, in the infected puncture wound too hasty incision may induce septicaemia by bursting imperfectly formed natural barriers and throwing open to micro-organisms a pathway into the blood stream). Respect for, and aid to, the formation of such barriers are essential criteria of the successful treatment of such infected wounds.

* Introductory remarks in a joint discussion in the Sections of Medicine and Surgery at the Annual Meeting of the British Medical Association, Eastbourne, 1931.

In the common streptococcal infected wound of the finger or hand, with rapidly developing lymphangitis, the judicious use of passive congestion and administration of antiserum should always precede any treatment by incision. The value of Bier's passive congestion is not sufficiently recognized. Rightly used, I believe that it is a very real help in preventing and limiting blood infection. Bier laid no claim to be the originator of the idea of passive venous congestion as a therapeutic measure. He has, however, fully earned lasting credit for demonstrating how by this means a local infection, which was tending to invade the blood stream, might be hemmed in and held up until such time as local defences had been mobilized, and the general protective mechanism had been stirred to action. Rightly applied, a Bier's bandage will always relieve pain. If the pain persists or is increased, the bandage should be removed and reapplied more lightly. It should be worn for twenty-two hours out of the twenty-four.

Many deaths have resulted from a precipitate use of the bistoury, no time having been allowed for a leucocytic encirclement to develop and a natural localization of the contest to occur. Only when dangerous tension has arisen, or dead or moribund cells have accumulated in the shape of pus, can incision be helpful.

In certain tissues, such as bone and deep cellular planes, where rigid walls prevent the deployment of natural resistant forces, early incision may be of the utmost value in permitting expansion and the entrance of protective elements. Total excision of the focus—for example, in anthrax pustule, in carbuncle, and in the very earliest stages of an infected punctured wound—may sometimes be justified; as a general rule, however, surgery must exercise a watching brief, prepared to step in when, and only when, nature cries for help.

When we consider the various means by which the patient's resistance to the invading germ may be supplemented we turn first to antiserums. Varied opinions will doubtless be expressed as to the value of anti-streptococcal serum. As with anti-tetanic serum, large doses (60 c.cm.) must be given early and repeated daily. My experience has been that it is in the *very earliest stages* of the general infection, before cellular damage to the organs has occurred, that the help from passive immunity is great and real. I have no hesitation in placing it first in importance, just as I believe it should take precedence in time of all other measures.

Copious quantities of fluid must be given, usually by mouth. In exceptional cases where vomiting occurs fluid must be given rectally or subcutaneously. If an abscess develops at the site of subcutaneous injection, it will be a matter for rejoicing. With the fluid, alkalis and glucose must be freely given. As a rule they are both welcomed by the patient, which is significant.

Immuno-transfusion should certainly be considered in the weakly patient, and I have seen it followed by remarkable betterment in a case in which blood infection had supervened in a feeble and anaemic patient. How much of the benefit was due to the introduction of specific antibodies and how much simply to the supply of healthy blood was impossible to determine.

The production of a really efficient anti-staphylococcal serum is a real need, and I trust that the antitoxic serum now on trial may prove to have for the human subject as true and specific a protective action as it has been proved to possess for animals.

The use of vaccines in a fulminating blood infection I have always regarded with scepticism and, along with protein shock therapy, I have left to those who can visualize their action and believe in their efficacy. Sensitized vaccines have given favourable results in some hands, and they undoubtedly deserve an extended trial.

The intramuscular injection of nuclein preparations to induce a leucocytosis, and of various colloidal preparations, I have found to be successful only when an abscess has formed at the site of injection. This development of a "fixation abscess," an old-time method of treatment, is often the signal of improvement, and is a welcome complication in a critical case.

The search for a therapia sterilisans magna—some chemical substance with an affinity for the germ, yet relatively harmless to the host—cannot yet be said to be successful. Intravenous injections of eusol, of mercuriochrome, of collosol argentum, and of certain dyes have each given apparently favourable results in isolated cases. Personally I cannot claim to have seen a cure by the injection of any of these chemical substances in a case where other factors could be ruled out.

A constant watch must be kept for abscess formation, be it in deep cellular planes, in joints, or in the pleural cavity. In the later stages of a septicaemia purulent collections may develop most insidiously, and their timely evacuation may turn the scale. They may very readily be missed if a systematic examination for them be not made repeatedly.

In a few cases the question of amputation of a limb may have to be considered. I believe that amputation is rarely justified except in protracted cases where the infection involves a bone or joint, where adequate drainage cannot be effected, and where the patient's strength is ebbing.

Whilst vaccines, in my experience, have a very doubtful place in the treatment of established septicaemia, they

have a real value when used for preliminary and prophylactic immunization in cases where operation for the removal of a large ulcerating growth may permit of a blood infection. It has been our practice for over twenty years to give a preliminary course of *B. coli* and streptococcus vaccine in operations for removal of growths of the lower bowel, and in particular the rectum. In such operations many infected lymph channels must of necessity be divided, large raw areas are usually left, and the risk of generalized infection is obvious. Preliminary vaccine treatment, particularly if followed by a pre-operative injection of nuclein to stimulate a leucocytosis, was shown experimentally to increase resistance, and in practice it has proved effective.

My practice is to give *B. coli*, 50 millions, and streptococcus, 10 millions, ten days, and again three days, before operation, and on the night preceding operation to give 5 c.cm. of 5 per cent. sodium nucleinate intramuscularly. The patient thus comes on the table with defensive forces warned, and with a slight leucocytosis (10,000–14,000). Since using this preliminary treatment I have lost no case from general sepsis, although local infection of a gross nature has supervened in a number of cases.

With a feeling of security against a general infection, local sepsis after an operation for cancer may be regarded almost as a blessing.

In the treatment of septicaemia the future lies largely in the hands of the bacteriologist. In the clinical field I should sum up the position by saying that the physician must think surgically, and the surgeon must cultivate the restraint of the physician.

DIET AS A PROPHYLACTIC AGENT AGAINST PUERPERAL SEPSIS

WITH SPECIAL REFERENCE TO VITAMIN A AS AN
ANTI-INFECTIVE AGENT

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In a previous paper (1929) on the treatment of puerperal septicaemia with preparations containing vitamin A we stated that an investigation was also being made into the possible prophylactic effect of such preparations against puerperal sepsis. We argued that if vitamin A had even a slight therapeutic effect in such a virulent infection as septicaemia it should be of much greater value as a prophylactic agent. It seemed possible that in the administration of vitamin A prior to labour we might have a valuable auxiliary method which would supply a missing factor so apparent in some cases even where every precaution against sepsis has been taken.

Experimental work on young animals suggested that vitamin A and carotene might well be described as "anti-infective" in their action, because when absent from or deficient in the diet, multiple infective foci develop, resulting in death unless the deficiency is made good (Green and Mellanby, 1928, 1930). The preventive and curative actions of vitamin A and carotene in the autogenous sepsis of the animals were equally great. It was obviously desirable to see whether these substances played any similar part in controlling the resistance of the human body to sepsis. This seemed possible, for the septic lesions which develop autogenously in animals on a vitamin A deficient diet are also commonly found in human beings. These

include septic nasal sinuses, a catarrhal condition of nose and throat and respiratory passages, middle-ear disease, broncho-pneumonia, pyelitis, and a septic condition of the genito-urinary tract. There is also reason to believe that the diet of many individuals in this country is deficient in vitamin A, the main sources of which are found in the more expensive foods—for example, milk, butter, eggs, and certain vegetables, while it is almost completely absent from cereals and cereal products and many other extensively eaten foods.

A study of the prophylactic action of vitamin A against puerperal sepsis in women suggested itself as a promising method of testing the clinical significance of the animal experiments. The duty of the maternal organism during pregnancy is to supply all the substances necessary for the growth of the embryo. These substances she either gets directly from her food, synthesizes them from the ingested foodstuffs, or, when these sources are insufficient, she supplies them from her own body stores as long as they are available. Many substances cannot be synthesized by the body, and must therefore come directly from her food or from her depots replenished by food. Now the body has a great capacity for storing vitamin A, especially in the liver. This store has its origin in the vitamin A, and most probably also in the carotene, of the food eaten (Moore). If the diet is deficient in these factors, as is probably the case in many individuals, the liver stores of vitamin A may be small, even at the beginning of pregnancy. The demands of the growing foetus will make these reserves still smaller, for, in addition to the supplies necessary for actual growth and metabolism, the foetus demands a reserve of vitamin A for its own liver. (H. N. Green examined eight foetal livers and found that six of them contained vitamin A in varying quantities.) These facts indicate that many women at childbirth will be deprived of most of their reserves of vitamin A and, if the animal experiments have any meaning in terms of the human subject, they will have less resistance to the invasion of pathogenic organisms at the time of parturition.