SURGICAL PROCEDURES IN GENERAL PRACTICE

This is one of a series of articles contributed by invitation

SULPHONAMIDE CHEMOTHERAPY IN SURGICAL INFECTIONS—II

BY

A. J. COKKINIS, M.B., B.S., F.R.C.S.

Gonococcal Infection

The gonococcus has always been a difficult organism to eradicate, and although it can be got rid of by sulphonamide therapy in a small fraction of the time taken by other treatments, this is by no means easy. Nevertheless, in a series of more than 600 cases, Dr. McElligott and I have shown that a male patient with gonorrhoea (whether simple or complicated) treated with sulphanilamide can be given a 90 per cent. chance of complete cure in a few weeks if the following principles are faithfully observed: (a) Chemotherapy must not be started until the discharge is at least eight to ten days old (it takes that much time for immunity to develop). (b) It should be preceded and combined with vaccine treatment (with the object of increasing this immunity). (c) It should be continued for three weeks, and the dosage must be adequate (for example, 4 grammes of sulphanilamide daily for an adult male of 11 or 12 stone). (d) Administration must be properly spaced (preferably four doses each day) and absolutely uninterrupted. (e) Relapses should be treated with a second course after an interval of some weeks. (f) The most rigorous tests and three months' observation must be passed before a patient is pronounced cured. Treatment with small doses (such as one tablet three times a day) over short periods is worse than useless; this and other errors of technique may lead to obstinate resistance to subsequent chemotherapy. Owing to the large total dosage required special care must be observed against the more serious toxic properties of the drugs. Minor toxic effects are naturally very common with this dosage, and may constitute an obstacle to effective administration, particularly in female patients.

The above summary applies to sulphanilamide only. In its place we are now using T 693, which promises to produce at least equally good results, but unfortunately without any diminution of the incidence of toxic effects. The only other sulphonamide with a definite action on gonococcal infections is uleron, which we have tried in some 150 cases. The immediate results are often excellent; but whatever method of administration is employed most cases relapse, and continue to do so until a more powerful sulphonamide compound is used.

Coliform Infections

Sulphonamide chemotherapy produces its best results in cases of "primary" urinary infections with *B. coli* and certain other organisms of the coliform group. These are cases of pyelitis, cystitis, or genital infections without an obvious gross cause (for example, a senile prostatic enlargement). Quite small doses and a short period (such as 2 grammes of sulphanilamide daily for six to eight days) suffice to clear up, both clinically and bacteriologically, most cases of "primary" pyelitis or pyelitis of pregnancy. I have noted, however, a tendency to relapse, and in consequence it is now my practice in non-urgent cases to give an autogenous vaccine (three or four times

weekly) for one to four weeks before starting sulphonamide treatment, and to increase the period of chemotherapy to ten to fourteen days; also to give further courses if the pyuria recurs.

Cases of "secondary" urinary infection (such as those complicating an enlarged prostate or a calculus) are much more difficult to cure permanently, but a "cure" is less important than in the former group. The principal treatment here must be directed to the primary cause, whatever this may be, and the chief object of the chemotherapy is a temporary clearing up of the urinary infection as an adjunct to operation. This is most effectively obtained with sulphanilamide or T 693, but patients with this type of urinary infection may be too debilitated to tolerate these toxic drugs easily, and I have often preferred the less complete urinary disinfection obtained with a short four-day or five-day course of uleron (3 grammes daily) or prontosil soluble (10 to 20 c.cm. of 5 per cent. daily). This course should be given during the pre-operative stage of a prostate case, and may be repeated after prostatectomy to deal with the common post-operative exacerbation of the urinary sepsis.

Acute Appendicitis

The repeated discovery of coliform bacilli and non-haemolytic streptococci in acute appendices and in the peritoneal exudate induced me to explore the possibilities of sulphonamide chemotherapy in this disease, and there is now no doubt in my own mind that an indiscriminate use of these compounds in acute appendicitis—and in other urgent abdominal conditions—can be dangerous. An experience of more than forty cases treated in the past nine months, many of them bacteriologically controlled, has led to the following conclusions: (a) Sulphonamide therapy should not be used in the first forty-eight hours of an acute attack of appendicitis, either as an alternative to operation or as an adjunct to it. The only rational treatment for such cases is, and I think always will be, removal of the appendix. Chemotherapy at this stage is definitely unwise, as it may mask a dangerous complication or perhaps interfere with the first stages of the immunity response. (b) On the other hand, I have found sulphonamide compounds to be of real value as an adjunct to operation in the more advanced stage, when the appendix is perforated or necrosed, there is a purulent effusion in the peritoneal cavity, and the immunity response is presumably awakened. In such cases post-operative chemotherapy often rapidly clears up the peritoneal infection, and thus may prevent a prolonged illness, with wound sepsis and more dangerous complications. (c) The most striking results, however, have been obtained in late acute appendicitis with localized lump formation (plastic peritonitis without obvious abscess development). For some years it has been customary to treat these cases by expectant methods, which aim at complete resolution of the inflammatory process before appendicectomy is performed. Unfortunately, this expectant treatment may take several weeks before its object is attained, and sometimes it fails to prevent the development of an abscess, ileus, or other complications. This is the type of case in which sulphonamide chemotherapy seems most successful. Not only does the lump completely resolve and the patient become well often in a few days (without starvation), but abscess

formation and other complications are obviated, and appendectomy may be safely performed after only a small fraction of the time one had to wait in pre-sulphonamide days.

The compounds mostly used in such cases have been prontosil soluble (10 to 30 c.cm. of 5 per cent. solution daily) and sulphanilamide (2 to 4 grammes daily). The former is particularly suitable for the first few days after an operation, when sulphanilamide often causes very troublesome toxic effects, such as vomiting, prostration, and cyanosis. Best results have been obtained when the chemotherapy is continued for about ten days.

Appendix and Other Abdominal Abscesses

Cases of definite appendix abscess have responded to sulphanilamide at least as well as those with a lump but without evidence of suppuration. Of eight such abscesses treated, every one resolved completely in five to fourteen days, while constitutional symptoms cleared up in twenty-four to seventy-two hours. None had to be drained, and only one developed a relapse (after two months), which was treated by early appendectomy. The dosage of sulphanilamide has been between 2 and 4 grammes daily, and the period of administration has varied between six and fifteen days.

I have also obtained complete resolution of a large and increasing subphrenic abscess (of appendicular origin) in a desperately ill patient, with ten days' sulphanilamide treatment. The clinical improvement was immediate, while the rapid diminution of the abscess was easily followed by radiography.

Acute Cholecystitis and Cholangitis

The usual causative organisms are again coliform bacilli and streptococci, and the lesions might therefore be expected to respond to chemotherapy. A trial of sulphonamide compounds in six cases of acute cholecystitis and two of acute cholangitis has indeed shown that recovery from the acute illness is very materially hastened by the chemotherapy (Fig. 1). Unfortunately, four of the cholecystitis cases, all with gall-stones, afterwards relapsed and were treated by cholecystectomy. One may conclude that in such cases the chemotherapy is likely to be of only secondary or palliative value.

Acute General Peritonitis

My experience with sulphonamide compounds in acute peritonitis suggests that, when used correctly, chemotherapy may prove of life-saving value, but also that when used indiscriminately it may prove the reverse. The deciding factor again appears to be the immunity response of the patient. Although the cases treated have been comparatively few, they show quite decisively that sulphonamide compounds should not be used as a prophylactic measure against peritonitis in such lesions as perforated ulcer and intestinal strangulation, or after such operations as colectomy. They also suggest that it is unsafe to employ chemotherapy in the very early stage of actual peritonitis—that is, while the effusion is still serous and the immunity presumably unawakened. On the other hand, when the more powerful sulphonamide compounds have been administered to cases of fully developed coliform or streptococcal peritonitis, with either a profuse purulent effusion or an extensive peritoneal oedema, the result has usually been a dramatic and lasting improvement (Fig. 2). Once started, the chemotherapy should be continued in adequate dosage for at least ten days, but it should never be begun until after any removable and unlocalized source of infection has been dealt with by operation.

Infections of the Hand

No condition gives more striking evidence of the bacterial selectivity of sulphonamide compounds. In a fairly large number of septic hands treated no case of pure staphylococcal whitlow has responded. On the other hand, infections from which streptococci had been isolated on the whole responded very well. It is therefore necessary to make a bacterial diagnosis—for example, by aspiration—before chemotherapy is commenced. Streptococcal infections tend to spread along the superficial and deep

FIG. 1.—Temperature chart of case of acute cholangitis, treated with sulphanilamide and prontosil soluble.

FIG. 2.—Temperature chart of case of streptococcal peritonitis treated with sulphanilamide.

lymphatics, and nearly all the successful cases have been infections of the great spaces of the hand or examples of acute lymphangitis. Tendon sheath infections are mostly staphylococcal, and of six such cases treated with sulphanilamide the only one which showed any improvement was a mixed infection of staphylococci, streptococci, and, strangely enough, *Cl. welchii*. The staphylococcal cases proved equally resistant to uleron.

Owing to the speed with which streptococcal infections of the hand spread, it is unwise in these cases to wait for immunity, and chemotherapy should be started as soon

as bacterial diagnosis is made. Whenever possible, however, this should be combined with some form of rapid immunotherapy, such as by anti-streptococcal serum. The dosage of sulphanilamide used has been 2 to 4 grammes daily for five to twelve days. In no case should the chemotherapy be employed as an alternative to surgical drainage if there is the least indication for the latter. The only exceptions to this rule are cases of streptococcal lymphangitis, where the primary focus of infection is often insignificant (for example, a puncture of the finger at a septic operation) and where the real danger is a septicaemia. I have seen two such cases, both caused by a haemolytic streptococcus and both already with evidence of blood infection, respond with dramatic suddenness to sulphanilamide. This experience justifies the hope that the new chemotherapy may afford some protection against a danger to which our work exposes us, and by which many a brilliant career has in the past been brought to an abrupt end.

Infections of the Skin and Subcutaneous Tissues

Here again the results of chemotherapy depend entirely on the nature of the infecting organism. Thus, in several cases of carbuncle (staphylococcal) treated with sulphanilamide or uleron there has been no response. On the other hand, very marked improvement has been observed in cases of streptococcal cellulitis, and, of course, in erysipelas.

Infection of Bones and Joints

Osteomyelitis is predominantly a staphylococcal disease, and, as might be expected, sulphonamide chemotherapy produces little or no results in it. Actually, some slight benefit was noted in three cases, one of acute and two of chronic osteomyelitis, but it proved very transient.

Infective Arthritis, on the other hand, is often caused by sulphonamide-susceptible bacteria, and I have obtained striking results with sulphanilamide in both gonococcal and streptococcal cases. Now, with the introduction of T 693, one may reasonably expect to be able to influence pneumococcal arthritis also.

Toxic Arthritis (for example, rheumatoid) belongs to a very different category, and is a condition in which useful research could be done in general practice. I know of several cases treated with repeated courses of sulphanilamide, preceded by and combined with vaccine, in which improvement has been obtained. If possible, autogenous vaccine should be used, but a stock anti-rheumatic vaccine may be employed when there is no obvious focus of infection. Improvement is most likely in the relatively acute cases of rheumatoid arthritis seen mostly in youngish people, and I recommend small doses of sulphanilamide (1.5 to 3 grammes daily) in three or more 14 to 21-day courses, with three to four weeks' intervals, a full course of vaccine being given as well.

Traumatic Surgery

In this branch of surgery my experience with sulphonamide chemotherapy has been rather disappointing. For some time it was hoped that it might be of service in the prevention of wound sepsis (for example, in traffic accidents), but I am now very doubtful if such prophylactic use is of any value. On the contrary, there is reason to believe that it may do harm. It is quite rational, however, to treat an infected compound injury with sulphonamide, if the infection is already established, and provided at least one of the organisms present is known to be susceptible. Striking improvement has been seen in several such cases, particularly when the suppuration has been mostly in the

superficial tissues, and also in one case of clinical gas-gangrene, in which the diagnosis was unfortunately not confirmed bacteriologically.

Conclusion

The more one learns of the new chemotherapy the more one feels that it should be employed only when an infection has become fully established, and, as a general rule, the longer the infection has been in existence the better the results are likely to be. Occasional exceptions are bound to occur, such as when a fulminating infection threatens to overwhelm the patient, and when an attempt to arrest bacterial growth must be made without waiting for the immunity response, which may or may not develop. There is one application of sulphonamide chemotherapy, however, which in my experience has proved quite valueless (and even dangerous), and that is its preventive use against the threat of an impending infection.

PROPHYLAXIS OF THE COMMON COLD

BY

J. B. SHERMAN, M.B., B.S.

Medical Officer, Bournville Works

There are few, if any, medical conditions which cause such severe economic losses to employer and employee as the common cold. The great number of so-called treatments and prophylactics bears testimony to our failure to cope with the problem. One of the difficulties facing the general practitioner is that of being able to treat under strict control large numbers of patients, this being the best method of estimating the value of any form of treatment. In the present state of our knowledge it would seem that methods of prophylaxis offer more hope of success than those of treatment.

In view of the opportunity afforded at these works it was decided to try the effects of some of the better-known prophylactics upon a rather larger scale than usual, and by keeping strict records to obtain some idea as to their comparative values.

The Methods Used

Four methods were chosen as all holding out reasonable prospects of success.

1. *Ultra-violet Irradiation*.—The good effects of this as a preventive of respiratory infections have often been quoted. The apparatus used here was a pair of Watson carbon arc lamps. Exposures were given at a distance of three feet twice a week, working up to a total exposure of fourteen minutes. This was carried on throughout the winter months. No ill effects were noticed.

2. *Vitamins A and D*.—Vitamin A, 6,000 units, and vitamin D, 1,000 units, were given in the form of one capsule (adexolin) a day after a meal. A course lasted throughout the winter. A certain number of patients suffered from nausea and other gastric discomfort, but otherwise no ill effects were noticed.

3. *Dissolved Vaccine*.—As supplied by Glaxo Laboratories this consists of a mixed vaccine of organisms found in the upper respiratory passages. The cell walls of the organisms are dissolved by sodium lauryl sulphate. Four injections were given subcutaneously at five-day intervals, starting with $\frac{1}{4}$ c.cm. and increasing to 1 c.cm. for the three subsequent doses. The immunity conferred was intended to last the whole winter. In patients who already had colds it was found to make them worse. The injections often caused stiffness and pain in the arm, but in only one case was real disability noted.