whether to operate, and when. Dr. A. KAY (London) has looked at this and suggests that, while metacarpophalangeal joint inflammation tended to persist, that of the proximal interphalangeal joints might diminish during the first year but then remains constant.

Assessment of results in rheumatoid disease is notoriously difficult, and Dr. B. M. ANSELL (Taplow, Bucks) put forward some simple tests which might give answers relatively easy. The proformas of Professor Flatt and Dr. Swanson were much more complicated, and needed a computer for assessment, and as yet this has not been able to provide an answer. Observers were left with many fine ideas but little in the way of practical statistics of the relative merits of the various procedures.

Mr. D. L. SAVILLE (Edinburgh) and Mr. Vaughan-Jackson argued very strongly that excisional arthroplasty was a simple, safe, and satisfactory procedure, and that they were not impressed with the various prostheses offered.

Three questions remain: What has a prosthesis to offer? Firstly, it should increase the range of movement—not to normal, but to 40°–50° on average—and the function in other joints may also be improved. Cosmetic improvement is usual, and pain is alleviated. Secondly, which patients are likely to benefit? A single metacarpophalangeal or proximal interphalangeal joint in any finger, but not the thumb, which is fixed or relatively fixed, or conversely is grossly disorganized, can be improved. Appreciable disease of two joints in any one finger makes that digit unsuitable for this type of surgery. Thirdly, which patients are unsuitable? Those with multiple joints affected in any one digit, and those with very active disease where further destruction of other joints of the arm and leg may throw an extra strain on the prosthesis. Finally, evidence of carpal tunnel syndrome and arteritis are definite contraindications to the use of a tourniquet.

To overcome the objection to operating on a finger in which two joints are involved, Mr. N. PAPAVASSILIOU (London) demonstrated a new method of passing a silicone rod through the cavity of the proximal phalanx and into the metacarpal and middle phalanx, with silicone rubber collars at the level of the joints. Early results with this simple technique were reported to be good.

It is obvious that only the early results of this type of work are being put forward, but it is equally obvious that rapid expansion in the field is occurring, and if for that reason alone the proceedings of this meeting should make interesting reading for anyone entering this field.

The proceedings of the workshop will be published in a supplement to the *Annals of the Rheumatic Diseases*.

Synergy of Trimethoprim and Sulphonamides

[FROM A SPECIAL CORRESPONDENT]

A symposium on the synergy of trimethoprim and sulphonamides was held at the Royal College of Physicians, London, on 9 May. It was sponsored by the Wellcome Foundation Ltd. and Roche Products Ltd.

The evolution of trimethoprim as an antibacterial agent was described by G. H. HITCHINGS (New York), whose early work on diamino pyrimidines as antagonists of folic-acid metabolism led to the demonstration of their antimalarial and antibacterial properties. He pointed out that the diamino pyrimidines competitively inhibited the enzyme dihydrofolate reductase, blocking the synthesis of folinic acid, and thus prevented the formation of purines. Trimethoprim was effective as an antibacterial agent in man because of its selectivity for the bacterial rather than the mammalian enzyme. J. J. BURCHALL (New York) accounted for this selectivity on the basis of differences of the molecular structure of dihydrofolate reductase between species.

Sulphonamides blocked the preceding stage of the biosynthesis of folinic acid in bacteria, and synergy between trimethoprim and sulphonamides against bacteria in vitro was demonstrated by S. R. M. BUSHBY (Beckenham). The combination was bactericidal for a variety of common pathogens. He found that maximum potentiation occurred when the two drugs were present in proportions equal to the ratio of their respective minimum inhibitory concentrations.

Synergy in vivo was confirmed by ERIKA BÖHNI (Basle), who had treated infections in mice with the drugs individually and in combination. PAMELA WATERWORTH (London) discussed the problems of assessing sensitivity and synergy in the laboratory, emphasizing the need to use special culture media containing lysed horse blood. She had noted the development of resistance to trimethoprim, but had not found transferable drug resistance.

Biological Half-Life

Using ^{14}C-labelled trimethoprim, D. SCHWARTZ (Basle) had found a biological half-life in plasma of 6·2–12 hours in man. Almost the whole of an oral dose of trimethoprim was excreted in the urine in two days, and more than 80% of this was unchanged. Studies of the renal handling of trimethoprim and sulphamethoxazole were described by P. SHARPSTONE (London). There were striking differences between their methods of excretion by the kidney, and he suggested that for the treatment of patients with renal failure the dose of each drug would have to be modified independently.

The results of chronic toxicological studies in mammals were reported by V. UDALL (Beckenham), who had found that the predominant effect of trimethoprim and sulphonamides in high dosage was depression of bone marrow function which was reversible by folinic acid. No significant toxic effects occurred in human volunteers who received trimethoprim and sulphafurazole in therapeutic dosage for 13 weeks in a trial reported by E. N. WHITMAN (New Jersey). T. HANLEY (Beckenham, Kent) estimated that the incidence of adverse reactions to trimethoprim–sulphamethoxazole in clinical practice was about 1%—rashes, nausea and vomiting, and glossitis being the commonest.

Urinary Infections

Trimethoprim–sulphamethoxazole was shown to be highly effective in the treatment of urinary infections occurring in hospital inpatients by W. BRUMFITT and his colleagues (London). They had found a cure rate of 67% four to five weeks after the completion of a 7-day course of trimethoprim 160 mg. with sulphamethoxazole 800 mg. twice daily, compared with 52% after ampicillin 500 mg. 8-hourly and 15% after sulphadimidine 1 g. 6-hourly.

In the management of chronic infection of the urinary tract F. W. O'GRADY (London) favoured the elimination of the infection by the combination in standard dosage, followed by long-term prophylaxis against reinfection using a lower dose. C. E. COX (North Carolina) presented evidence for the synergy of trimethoprim and sulphonamides in man by the cure of chronic urinary infection by trimethoprim and sulphafurazole in combination in 18 of 23 patients whose infections had previously failed to respond to either drug individually.

Bacteriuria of pregnancy had been eradicated in 31 of 43 patients by a 7-day course of trimethoprim–sulphamethoxazole in a trial reported by J. D. WILLIAMS and his colleagues (Birmingham and London). Ten of their patients were treated during the first 17 weeks of pregnancy and no foetal malformation had occurred in this group. Since bacteriuria of pregnancy was associated with an increased risk of foetal abnormality and since trimethoprim–sulphamethoxazole seemed to be the most effective agent available for its treatment at present, E. H. KASS (Boston) argued that further therapeutic trials should be conducted, despite the absence of proof of freedom from teratogenicity of trimethoprim.

Treatment of Gonorrhoea

Trimethoprim–sulphamethoxazole was shown to be a valuable chemotherapeutic agent for gonorrhoea by G. W. CSONKA (London), who, using trimethoprim 480 mg. with sulphamethoxazole 2,400 mg. daily for four days, had obtained a cure rate of 95% in men and 83% in woman. C. B. S. SCHOFIELD (Glasgow) reported a failure rate of only 1·5% in women with gonorrhoea.

In a trial of treatment of exacerbations of chronic bronchitis D. T. D. HUGHES (London) had found significantly greater improvement in sputum volume and purulence with trimethoprim 160 mg. and sulphamethoxazole 800 mg. twice daily for one week than with ampicillin 500 mg. four times a day; and in a similar trial S. LAL (Bury) had shown that the combination gave better results than with tetracycline 500 mg. twice daily.