

unusually close contact with their mothers, who were the dominant members of families in which the fathers were ineffectual characters. These are the children who prefer the clothes and companionship of the opposite sex and generally behave like the opposite sex. At a gender identity clinic in Los Angeles, Green and his colleagues are studying four to seven year old boys who have these characteristics, in the hope that they will be able to find the cause of the trouble, perhaps in the family relationships, and cure it before the boys grow up into transsexual men.

There are six gender identity clinics in the United States, dealing with hundreds of patients—a very small but particularly unhappy section of the population. The social problems of transsexuals are considerable, and not made easier by their frequent designation as freaks. The Albany Trust in London and the Erikson Educational Foundation in New York, which together sponsored the symposium, are particularly concerned with the social distress of transsexuals. One of their aims is to set up more gender identity clinics. In London there are some doctors, psychologists and sociologists who form an unofficial group working on these problems, but a properly appointed clinic is clearly a real need.

## DRUGS

### Combating *Pseudomonas*

from our Microbiology Correspondent

ONE of the outstanding problems of medical microbiology is the treatment of pseudomonal infections. The epidemiology of *Pseudomonas aeruginosa* infection is reasonably well known and the occurrence of the organism in persons with impaired resistance, such as that induced by protracted administration of drugs or by severe burning, has been particularly well recognized. Unfortunately, *Pseudomonas aeruginosa* infections have proved to be very intractable as a result of the singular resistance of the bacterium to most chemotherapeutics. Although certain polymyxins and the relatively new drug gentamicin have potent anti-pseudomonal activity *in vitro*, their general adoption for clinical treatment has not been possible because of their toxicity. Two years ago, a new semisynthetic penicillin, carbenicillin (disodium  $\alpha$ -carboxybenzyl penicillin), was introduced and thought to be one answer to the pseudomonas problem. Unhappily again, the use of carbenicillin was found to have its drawbacks—Smith and Finland (*Appl. Microbiol.*, **16**, 1753; 1968) found a necessity for very high doses and a rapid development of carbenicillin resistance by the pathogen. Subsequently, the traditional measures of prescribing combinations of drugs and of designing more effective and specific "bullets" against pseudomonads have been undertaken.

Sonne and Jawetz (*Appl. Microbiol.*, **17**, 893; 1969) recently reported the results of their study of the combined action of carbenicillin and gentamicin on *Pseudomonas aeruginosa*. They hoped that this approach would enable them to use smaller and non-toxic doses of gentamicin and to prevent or delay emergence of carbenicillin resistance. They found that the bacteriostatic effect of carbenicillin was enhanced by additions of non-inhibitory concentra-

tions of gentamicin, but the most impressive effect was the bactericidal activity of combined drug treatments. Sonne and Jawetz indicate that the bactericidal action occurred at low enough concentrations to be attainable both in urine and in tissues. They suggested also that cross-resistance is unlikely to develop because of the different modes of action of carbenicillin (inhibition of cell wall synthesis) and gentamicin (disturbance of protein synthesis) although it is necessary to be wary of multiple resistance transfers.

A group at Bristol Laboratories has been equally concerned with pseudomonal infections. This group has made a systematic study of a new class of semi-synthetic penicillins (Price *et al.*, *Appl. Microbiol.*, **17**, 881; 1969). The most potent of these new sulphoamino penicillins, which have a potency similar to carbenicillin, were about eight to sixteen times more effective against *Pseudomonas aeruginosa* than benzylpenicillin, but the latter had greater potency against Gram-positive bacteria. The effectiveness of the sulphoamino penicillins was to a significant extent a result of their high resistance to degradation by  $\beta$ -lactamase. Neither the sulphoamino penicillins nor the carbenicillin-gentamicin mixtures have been subjected to thorough clinical trials—indeed the former class of drug has not yet been assessed for its toxicological properties. These preliminary findings, however, are encouraging. The bactericidal action of the combined drug treatment is particularly important because persons with reduced host defence are prone to *Pseudomonas* infection; in such circumstances a bactericidal treatment is much preferable to a bacteriostatic treatment. If the interpretation of toxicological properties of the sulphoamino penicillins is correct, their most effective deployment will also be as a component in mixed drug therapy of pseudomonal infection.

## PROTEIN SYNTHESIS

### Chain Terminators

from our Cell Biology Correspondent

THE two nonsense codons, amber (UAG) and ochre (UAA), have now been identified in a eukaryotic cell, the yeast *Saccharomyces cerevisiae*. In the latest issue of the *Journal of Molecular Biology* (**43**, 71; 1969), Hawthorne reports that treatment of mutant strains of yeast which have the properties of nonsense mutants either with ethylmethanesulphonate or with hydroxylamine results in the conversion of one class of nonsense mutants into the other. Because these two mutagens promote the transition of guanine to adenine, he believes the mutagens are increasing the frequency of the conversion of amber UAG to ochre UAA codons. The reverse conversion of ochre to amber is not detected, which is to be expected because neither mutagen is capable of the transition of adenine to guanine. The mutant yeasts contain two classes of suppressor mutants, one class able to suppress both amber and ochre mutations and the second able to suppress only amber or ochre.

The third nonsense codon, UGA, has been investigated in the RNA phage f2 by Model, Webster and Zinder (*J. Mol. Biol.*, **43**, 177; 1969). They have isolated seven mutants of f2 after fluorouracil mutagene-