THE INFLUENCE OF ANTIBIOTICS ON EXPERIMENTAL MONILIASIS.

I. Penicillin, streptomycin, chloramphenicol and viomycin.

by

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INTRODUCTION

Candida albicans, a frequent inhabitant of the human gastrointestinal tract, is generally regarded as a commensal. Following the widespread use of antibiotics, hormones and other chemotherapeutic agents, however, clinical moniliasis has become increasingly prevalent (ZIMMERMAN, 1950, 1955; NICKERSON, 1953; BRATLUND & HOLTEN, 1954; CANNON, 1955). The commonest infections are glossitis, pharyngitis and pruritus ani and vulvi, implying a fungal overgrowth on mucous membranes (MOUNTAIN & KRUMENACHER, 1953; SELETZ, 1954, et al.). In a number of cases, haematogenous dissemination from such primary foci of infection results in the formation of metastatic lesions which exhibit no evolutive tendency and are often regressive (MACKINNON & ARTAGAVEYTIA-ALLENDE, 1956).

The causes of primary fungal overgrowth and of haematogenous dissemination are imperfectly understood. It is generally accepted that a partial sterilisation of the surface and contents of the gastrointestinal tract follows administration of antibiotics. As a result, organisms unaffected by the therapeutic agent increase in quantity. Amongst these is C. albicans (TOMASZEWSKI, 1951). The causes of such increase in population may be regarded as lack of competition and removal of the products of bacterial antagonists (HUPPERT, MACPHERSON & CAZIN, 1953). The increase denotes the establishment of a high density of fungal inoculum at the surface of the host. LIENTHAL, HARRIS & ARNOTT, 1957, have suggested that subsequent colonisation of the underlying host tissue is the outcome of decreased resistance in the host owing to hormonal imbalance. Necrosis of the gastro-intestinal tract may be a sequel of avitaminosis B due to elimination of vitamin-synthesising bacteria. It has been suggested that sensitivity of the host to the fungus and/or antibiotic is a factor in genito-crural infections (REICHES, 1951). Although the stimulation of fungal growth rate and power of cellular division in vivo has been advanced as contributory, this has proved difficult to substantiate.
Antibiotic substances such as the tetracyclines, chloramphenicol, streptomycin, penicillin and others, whether used singly or in various combinations, have been implicated in focal and disseminated human, monilial infections. HUPPERT, CAZIN & SMITH, 1955, have recorded the establishment of *C. albicans* in the intestinal flora of mice following the oral administration of such antibiotics.

Using rodents as experimental models, enhancement of Candida infection by chlortetracycline was first described by SELIGMAN, 1952, and confirmed subsequently by others, notably BROWN, HAZEN & MASON, 1953, and WINTER & FOLEY, 1956. WINTER & FOLEY also recorded enhancement with oxytetracycline and tetracycline. Enhancement of fungal infection following the administration of hormones is well known (KASS & FINLAND, 1953). The work reported below deals with variations in the host/parasite relationships of experimental moniliasis of the mouse after treatment with penicillin, streptomycin, chloramphenicol and viomycin.

**EXPERIMENTAL**

The intraperitoneal route for the administration of antibiotics and fungal inoculum was selected to fulfil requirements simulating those found in human infections, namely the presence of a therapeutic agent and fungal inoculum at the surface of a host membrane.

(a) Antibiotics and their levels of tolerance.

The following antibiotics were administered intraperitoneally to mice of the outbred strain: — Streptomycin (Calcium Chloride Complex), Penicillin G, Viomycin Sulphate, Chloramphenicol B.P. Toleration of the drugs was estimated at levels lying between 50 mg. and 0.1 mg. in the case of streptomycin, viomycin and chloramphenicol in aqueous solution or suspension. Immediate toxic effects, recognisable by collapse, shallow rapid breathing and death within fifteen minutes, occurred with streptomycin at dosages of 50 mg. and 5 mg. Dosages of 2.5 mg. and 0.1 mg. resulted in a mild state of collapse followed by recovery. Viomycin was lethal at 50 mg. and showed mild toxicity at 5 mg., followed by recovery. Chloramphenicol was well tolerated at 50 mg., and penicillin at 5,000 units. Of 107 animals of outbred strain, 8 served as controls for the estimation of the long term effects of antibiotic treatment. Each animal received 2 injections of a given antibiotic followed by 0.5 ml. sterile water, 24 hours later; 2 received penicillin 500 units; 2 received 0.1 mg. streptomycin; 2 received 5 mg. chloramphenicol, and 2 received 0.5 mg. viomycin at each injection.

(b) Fungal isolates.

2 isolates of *C. albicans* from human sources, E₁ and C₂ (BLYTH, 1958), were used in the experiments. 17 animals were selected for estimating the pathogenicity of the isolates. 5 animals received