(*8*) were made of the T agglutinin titer of patients with various virus diseases. A significant rise in T agglutinin titer was observed only in patients with primary atypical pneumonia. These workers were observing only the T agglutinin; but, as has been shown here, there is more than one panagglutinin in sera and the panagglutinin titer for cells such as PTC may be increased without being detected if only the T agglutinin is observed.

It is possible that agglutinins for altered red cells are implicated in the pathogenesis of various diseases and, for instance, may sometimes be the cause of intravascular agglutination ("sludged blood" [*6*]). However, as there may be many different agglutinins acting on cells altered by different agents, these agglutinins would not be observed if the sera were tested with cells altered by a single agent. As an example, the tubercle bacillus may form an enzyme which alters some of the infected host's red cells and these altered red cells could then serve as antigens, having become "foreign" to the body. The antibodies produced against these altered cells may then act on other altered cells, causing intravascular agglutination. The agglutinins produced in such cases need not necessarily be panagglutinins, since they may agglutinate only red cells altered by the specific agent. In this hypothetical case, the specific agent is an enzyme produced by the tubercle bacillus, and thus the agglutinin for red cells altered by this agent may be found only in individuals suffering from tuberculosis. If a specific altering agent was produced by an organism such as the staphylococcus, the agglutinin acting on red cells altered by this agent may be found in all sera, due to the staphylococci normally present in the body, but it may increase in titer in individuals with staphylococcal infections. It is conceivable that an endogenous abnormal enzyme system may also produce the general picture described here.

Friedenreich (*4*) tested most of the common bacteria for the ability of their culture filtrates to render red cells panagglutinable, but found that only a few were able to do so. However, Chu (*3*) recently found that filtrates of the cultures of many common bacteria did render red cells panagglutinable. Chu did not describe the manner in which he grew his organisms, and differences in the media and conditions of growth may explain the differences in their results. He also did not report any cross-absorption studies to see if different agglutinins were responsible for the agglutination in the various cases. The organism with which Friedenreich did most of his work produced active filtrates only if it was grown at 22° C; the filtrates were inactive if the organisms were grown at 37° C. In this laboratory and in other laboratories (*11*) active filtrates are routinely obtained when the organisms are grown at 37° C. Thus the conditions necessary for the production of active filtrates probably vary with different organisms. Studies are under way in this laboratory on the ability of filtrates of cultures of pathogenic bacteria grown under various conditions to render red cells agglutinable by normal sera and by sera from patients with infections caused by the specific bacteria.

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Reduction of Mortality from X-Radiation by Treatment with Antibiotics[1]

C. Phillip Miller, Carolyn W. Hammond, and Marianne Tompkins

Department of Medicine and the Institute of Radiobiology and Biophysics, University of Chicago, Chicago

A preceding communication (*1*) presented results of blood and spleen cultures on mice subjected to a single exposure of 600 or 450 roentgen units total body x-radiation. The results showed an incidence of bacteremia which rose and fell during the second postirradiation week roughly parallel with the daily death rate. This finding suggested that infection might be a significant factor in death from radiation injury. An attempt, therefore, was made to reduce the mortality from x-radiation by controlling the bacteremia by the administration of antibiotics. As the bacteremia was found to be caused by microorganisms (mostly Gram-negative bacilli) normally inhabiting the lower intestinal tract of these mice, it was realized that to be effective an antibiotic must be active against a wide variety of bacterial species.

Methods. Male Swiss mice were exposed to a single dose of 450 r x-radiation delivered at 20 kv, 15 ma, at a distance of 27 in., using ½-mm copper and 3-mm Bakelite filter.[2] The dose rate was approximately 20 r per min. Their LD_{50} (30 days) was about 400 r.

After irradiation, they were divided into control and treated groups, so that each therapeutic trial contained a group of control mice that had received the same dose of irradiation on the same day. From the 4th to the 28th day after irradiation, the treated mice were injected

[1] This investigation was initiated as part of the U. S. Army Contract No. W39-007-MD-425 and has been continued under Contract No. At(11-1)-46 between the U. S. Atomic Energy Commission and the University of Chicago.

[2] Most of the mice were irradiated at the Argonne National Laboratory with the assistance of Mr. Joseph Trier and Mr. Emil Johnson. Some were irradiated by Dr. James W. J. Carpender of the Section of Roentgenology, Department of Medicine, University of Chicago.

subcutaneously with 0.5 ml of saline containing the antibiotic[3] in the doses indicated in Table 1. Control mice received daily injections of 0.5 ml saline subcutaneously for the same period of time.

TABLE 1

EFFECT OF ANTIBIOTIC THERAPY ON THE MORTALITY OF MICE EXPOSED TO 450 R X-RADIATION

Drug	Dose	Animals irradiated	% Dead at 30 days
Streptomycin	6,000 μg	128*	16
Controls†	.....	127*	81
Streptomycin	5,000 μg	101*	34
Controls†	.....	101*	89
Streptomycin	7,000 μg	88‡	30
Controls†	.....	88‡	77
Penicillin	10,000 units		
Streptomycin plus ...	5,000 μg	72‡	25
Controls†	.....	72‡	66
Chloramphenicol	2.0 mg	47‡	36
Controls†	.....	45‡	60

* Total in 3 experiments.

† Control mice were injected subcutaneously with 0.5 ml saline daily for the same period—24 days.

‡ Total in 2 experiments.

Results. The results, presented in Table 1, show that streptomycin administered subcutaneously once a day from the 4th through the 28th day after irradiation significantly reduced the mortality during the 30-day period of observation. In the group treated with 6,000 μg of streptomycin, 16% died, as compared with 81% of the controls. Doses of 5,000 and 7,000 μg of streptomycin showed less striking but still significant degrees of protection.

The group treated with a combination of 5,000 μg of streptomycin and 10,000 units of penicillin had a 30-day mortality of 25% compared with 66% for the controls.

Preliminary trials with other antibiotics have shown chloramphenicol (chloromycetin) to be somewhat less effective than streptomycin alone or in combination with penicillin. Chloramphenicol, as well as aureomycin, caused a considerable degree of irritation at the site of the injection. In some of the mice there was even necrosis of the skin. These deleterious effects are being obviated in current experiments in which the drug is administered in food.

Polymyxin B in doses of 0.2, 0.1, 0.05, and 0.02 mg failed to reduce the mortality. In fact, the death rate was increased by the larger dose, presumably because of its toxicity.

Results with aureomycin were irregular. One experiment showed a significant reduction in mortality but another experiment showed none, probably because infection with a strain of *Pseudomonas aeruginosa* insensitive to aureomycin appeared among the mice in that group.

[3] The streptomycin and polymyxin were provided by Chas. Pfizer & Co.; the penicillin by Commercial Solvents Corporation, Eli Lilly & Co., and Schenley & Co.; the aureomycin by Lederle & Co.; the chloromycetin by Parke-Davis & Co.

It seems evident, therefore, that, to be effective in reducing mortality from irradiation injury in mice, a chemotherapeutic agent must provide protection against infections by bacteria normally present in the animal, and also against all pathogens which might establish themselves within its body during the period when the animal's natural resistance to infection is markedly reduced. Among the antibiotics tested, streptomycin has provided the most effective protection.

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New Chemotherapeutic Agents in Enterohepatitis (Blackhead) of Turkeys

E. Waletzky, J. H. Clark, and H. W. Marson[1]

Chemotherapy Division, American Cyanamid Company, Stamford, Connecticut

The need for an economical chemotherapeutic agent for the treatment or prevention of enterohepatitis (blackhead) of the turkey and chicken encouraged the trial in enterohepatitis of compounds with suppressive activity in other protozoan infections. It seemed desirable to test a large variety of such agents in view of the wide taxonomic gap between *Histomonas meleagridis* and other pathogenic protozoa, and the generally limited correlation between activity in different protozoan infections, e.g., malaria and coccidiosis (*4*). Twenty-four compounds of 17 different structural types active in experimental cecal coccidiosis (*Eimeria tenella*) of the chicken, mainly at somewhat toxic or at uneconomically high concentrations (*5*), and six types of antimalarials were tested in young infected turkeys by the drug-diet method. Standardized enterohepatitis infections were obtained by the rectal inoculation of homogenates from livers with freshly formed lesions.

A high degree of suppressive activity in enterohepatitis at nontoxic diet concentrations was shown only by 2-amino-5-nitropyrimidine (*3*) (Enheptin-P),[2] a compound with a moderate degree of anticoccidial activity at slightly toxic concentrations in the chicken (0.15%). On the other hand, such highly active anticoccidials as the sulfanilamide derivatives or nitrophenide, and such antimalarials as chloroquine or chlorguanide, as well as the 18 other types of compounds tested, were inactive. 2-Amino-5-nitropyrimidine almost completely prevented mortality (12%) and the development of cecal and liver lesions in 164 birds when 0.1% concentrations of drug in the diet were given for 7 to 14 days and when treatment was begun not later than 3 days after rectal inoculation. The 215 untreated controls in these 13 tests suffered 80%

[1] The assistance of C. O. Hughes in the early phase of the biological work, and of M. C. Brandt, A. Bliznick, and S. Brackett in its later phase, is gratefully acknowledged.

[2] Enheptin-P is a trademarked product.