Summary and Conclusions. Experiments in the rat show that continuous exposure to non-specific damaging agents elicits a characteristic 3-stage general adaptation syndrome which is of considerably shorter duration in the adrenalectomized animal than in the normal. During the first stage, the blood chlorides and blood sugar are decreased; during the second stage, both these values return to normal in spite of continued treatment and the general condition of the animals is considerably improved. During the final third stage of exhaustion, hypoglycemia and hypochloremia reappear and general resistance decreases again. These experiments are in agreement with the conception that the primary cause of the adrenal insufficiency syndrome is a disturbance in the mechanism of adaptation and more particularly a decrease in the ability to maintain adaptation once it is acquired. The decrease in blood sugar, blood chlorides, blood volume, thermoregulating ability, muscular efficiency, etc., as well as the increase in blood potassium, are probably all simply the consequences of this primary disability.

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In vitro and *In vivo* Effect of Sulfanilamide on *Brucella abortus* and *Brucella suis.*

BEN D. CHINN. (Introduced by S. A. Koser.)

From the Department of Bacteriology, Medical College of the State of South Carolina, Charleston.

In vitro Experiments. Various concentrations of para-aminobenzene sulfonamide* were added to dextrose broth, veal-infusion broth, and 10% serum-veal-infusion broth. The effect of the chemical on the growth-rates of *Br. abortus* and *Br. suis* was relatively the same regardless of the medium used.

The strains used had been under artificial cultivation for over 2 years but were still pathogenic for guinea pigs. The cultures grew quite well on veal-infusion agar and in the various liquid media mentioned above after incubation for 48 hours at 37°C under ordinary atmospheric conditions.

One-tenth cubic centimeter of a 1:100 dilution of a 48-hour broth culture was seeded into flasks containing 100 cc of broth; sterile

* The para-aminobenzene sulfonamide (prontylin) was kindly supplied by the Winthrop Chemical Co., New York.

1% solution of *p*-aminobenzene sulfonamide was added to obtain concentrations of 1:1000, 1:10,000, 1:100,000, and 1:1,000,000. Control cultures did not contain any sulfanilamide.

Plate counts were made before the sulfanilamide was added, 10 minutes after its addition and after 24, 48, and 72 hours' incubation at 37°C. The initial counts were between 1000 and 3000 organisms per cc. Within 10 minutes after the sulfanilamide was added a marked reduction in the number of viable cells was found in the 1:1,000, 1:10,000, and 1:100,000 dilutions. All the organisms were destroyed during this short period in the 1:1000 dilution, for no colonies appeared on plates subsequently made from both the *Br. abortus* and *Br. suis* cultures in this dilution. Most of the organisms were destroyed in the 1:10,000 dilution after 10 minutes' exposure and those remaining were either killed or inhibited by the drug after further incubation. After 72 hours the counts were less than 10 organisms per cc.

In the 1:100,000 dilution the bactericidal effect was less marked but there was a definite bacteriostatic effect throughout the incubationary period. The count after 72 hours was 35,000 per cc for *Br. abortus*. With the *Br. suis* strain there were 500 cc after 24 hours and none after 72 hours. The 1:1,000,000 dilution was slightly bactericidal after 10 minutes and definitely bacteriostatic thereafter. There were 1,200,000 organisms per cc in the *Br. abortus* culture and 2,500,000 in the *Br. suis* culture after 72 hours. The control cultures contained 3,000,000 and 45,000,000 organisms per cc for *Br. abortus* and *Br. suis* respectively after 72 hours.

These experiments demonstrate the bactericidal and bacteriostatic effect of *p*-aminobenzene sulfonamide on *Br. abortus* and *Br. suis* *in vitro*. Similar results have more recently been obtained with *Br. melitensis*.

In vivo Experiments. *Br. abortus* and *Br. suis* infections in guinea pigs generally produce a chronic type of disease if small doses are inoculated. In 4 to 6 weeks the most characteristic pathological change is an enlarged, nodular spleen and a nodular liver but lesions may also be found in the testicles, kidneys, and other organs. The invading bacteria can usually be isolated from these tissues.

In order to determine the protective effect of *p*-aminobenzene sulfonamide in experimental infections, 6 guinea pigs were inoculated intraäbdominally with a culture of *Br. abortus* and 6 with *Br. suis*. One-half cc of an agar-slant culture suspended in 5 cc of saline was injected into each animal.

Three animals in each group were given a single oral dose of

100 mg of sulfanilamide daily. Treatment was started 2 hours after inoculation. The other 3 guinea pigs, used as controls, were not treated. After 30 days the 12 animals were killed, the gross lesions noted and cultures made from livers and spleens.

The spleens of the untreated guinea pigs were, in most cases, large and nodular. The spleens of the 6 treated animals appeared normal on gross examination and their average weight was 0.87 g. The average weight of 5 normal guinea pigs' spleens was 0.98 g. The average weight of the spleens from the 6 untreated guinea pigs was 1.54 g. During the 30-day period the loss of weight of the untreated animals was somewhat greater than that of the treated animals. Cultures from the spleen and liver of the treated guinea pigs were negative while cultures of Brucella were obtained from all of the untreated animals.

From these results it is apparent that the oral treatment of Brucella infections in guinea pigs with *p*-aminobenzene sulfonamide is effective in preventing a generalized infection when treatment is begun immediately after infection. It appears from these experiments that most or all of the organisms are destroyed before any extensive invasion can take place or that the sulfanilamide inhibits the multiplication of the organisms in the tissues.

The therapeutic effect of *p*-aminobenzene sulfonamide in Brucella-infected guinea pigs is under investigation.

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Effect of Sodium Citrate and Sodium Bicarbonate on Ethyl Alcohol Acidosis.

BYRON B. CLARK AND ROBERT W. MORRISSEY. (Introduced by H. E. Himwich.)

From the Department of Physiology and Pharmacology, Albany Medical College, Albany, New York.

It has been shown by Himwich, *et al.*,[1] that an acidosis follows the ingestion of large quantities of ethyl alcohol. This paper reports the action of sodium citrate and sodium bicarbonate on the changes in alkaline reserve and blood lactic acid resulting from large doses of ethyl alcohol in dogs.

[1] Himwich, H. E., Nahum, L. H., Rakieten, N., Fazekas, J. F., DuBois, D., and Gildes, E. F., *J. Am. Med. Assn.*, 1933, **100**, 651.