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Abstracts

ABSTRACTS

EFFECT OF HYALURONIDASE ON URINE AND ITS POSSIBLE SIGNIFICANCE IN RENAL LITHIASIS. In 1950, it was observed that subcutaneous injections of hyaluronidase (wydase), mixed with isotonic sodium chloride solution, resulted in clearing of urine in patients who previously had turbid urine with much sedimentation. The effect of hyaluronidase was manifest within 30 minutes after injection and persisted for 24 to 72 hours.

In attempting to establish a mechanism by which the hyaluronidase produced this effect, urine specimens were examined under a microscope equipped with a standard dark-field condenser to ascertain whether hyaluronidase caused a change in the colloid-chemical condition of the urine. Preliminary observations appeared to establish a correlation between the injection of hyaluronidase and the number of colloidal particles discernible in the urine sample. Certain colloidal phenomena (e.g., adhesion) made the statistical validity of this method questionable. In addition, considerable dispute as to the significance of such examination is already apparent. Since that time, however, a technique of preparing urine samples for examination with the Leitz "Ultropak" microscope has been developed. With this method we have been able to offer visual proof that the injection of hyaluronidase results in the release into the urine of a protective colloid which not only disperses crystalline matter already present but also inhibits the formation and growth of new crystalline matter.

Since, in the initial studies, the addition of hyaluronidase to voided urine did not bring about the same alteration in colloidal properties that the injection of hyaluronidase did, it was suggested that hyaluronidase acted indirectly by releasing hyaluronate from the site of injection and that further amounts of hyaluronate were excreted into the urine during the period of restoration of hyaluronate at the site of injection. We have since established that potassium hyaluronate is a powerful peptizing and dispersing agent. The evidence thus far is very suggestive that a hyaluronidase substrate is a component of normal urine and that it plays an important part in maintaining the proper colloid-crystalloid balance.

It is accepted, although not conclusively proved, that the formation of kidney stones is the result of an imbalance of the colloidal and crystalloidal matter present in the urine. Since hyaluronidase seems to influence this balance, an investigation of the possibilities offered by employing hyaluronidase as a therapeutic agent in the treatment and prevention of renal calculi seemed to be of interest.

It was concluded that subcutaneous injection of hyaluronidase, mixed with isotonic sodium chloride, pronouncedly increases the protective urinary colloids and causes clearing of turbidity and sediment in the urine of the majority of cases studied. Hyaluronidase therapy has been effective in preventing calculus formation or reformation during a period of 11 to 21 months in 19 of 24 patients, 79 percent in

whom kidney stones previously formed at a rapid rate.

Butt, A. J., M.D.; Hauser, E. A., Ph.D.; Seifter, J., M.D., Effect of Hyaluronidase on Urine and Its Possible Significance in Renal Lithiasis. The Journal of The American Medical Association. 150:1096-1098 (November) 1952.

ANTIBIOTIC SYNERGISM AND ANTAGONISM. Fixed synergistic drug combinations against specific organisms do not exist. The author found that a broad division of antibiotic agents into two groups would permit formulation of certain predictions as to their combined drug action. The two groups are as follows:

Group I: Penicillin; streptomycin; bacitracin; and neomycin.

Group II: Aureomycin; chloramphenicol; and terramycin.

Combinations of the first group were found to be frequently synergistic, occasionally indifferent, but never antagonistic. Combinations of the second group were neither synergistic nor antagonistic, but produced often simple additive effects in the clinical tests. This effect could presumably likewise be obtained by increasing the dose of the single member.

When, on the other hand, a member of group II was combined with one of group I, their combined effect depended apparently on the susceptibility of the micro-organism to the group I agent. According to the results of the experiment, antagonism between the two groups may be expected with a micro-organism susceptible to a group I drug, and synergism may result if the organism is resistant to a group I drug.

This scheme has proved helpful in the selection of drug combinations for the treatment of specific infections.

[Jawetz, E., M.D., Ph.D., Antibiotic Synergism and Antagonism. Archives of Internal Medicine. 90:301 (September) 1952.]

TREATMENT FAILURE WITH PENICILLIN. Clinical experience has shown that large doses of penicillin may be ineffective in overcoming an infection, despite the fact that in vitro tests show the infective organism to be sensitive to the antibiotic. In some cases, refractoriness may be attributed either to inadequate concentrations of penicillin reaching the pathogenic organisms because of a walling off of the focus of infection or to the development of resistant organisms. Another explanation for refractoriness, namely, that in older foci of infection the organisms are no longer multiplying or metabolizing as actively as in the fresh infection, has recently been explored by Eagle.

Mice were given intramuscular injections of known numbers of a highly virulent strain of group A streptococci, and treatment with penicillin was begun at varying intervals after inoculation. Animals were then killed at either one, two, four, or eight hours after treatment and the inoculated muscle emulsified and subcultured to determine the residual viable organisms.

Preliminary experiments with untreated animals revealed a rapid increase in number of organisms recovered from muscle during the first nine hours after inoculation, with only a moderate increase occurring in the next 15 hours. In animals treated with penicillin during the first six hours of the infection, a rapid bactericidal effect was noted and no deaths occurred in animals set aside for mortality studies. If treatment was delayed 12 hours, however, the same dose of penicillin exerted only a slow and irregular bactericidal effect and the mortality rate did not differ significantly from that of untreated controls. In order to effect a cure when treatment was delayed, it was found necessary to continue treatment for six to eight days.

In discussing these results, Eagle draws attention to the well-known fact that penicillin kills bacteria most effectively in vitro when they are actively metabolizing a favorable medium and suggests that in older infections the organisms have multiplied to such an extent that they exhaust the surrounding tissue of nutrilites faster than they can be supplied by the blood stream. Furthermore, as inflammation sets in, the leukocytes may compete with these bacteria for the nutrilites, while

local accumulation of products toxic to the bacteria may further reduce their metabolic activity. This concept is strengthened by the observation that, when larger inoculations were used, the time during which penicillin exerted a rapid bactericidal effect was shortened.

The author suggests that exhaustion of favorable foodstuffs may explain the paradoxical treatment failure sometimes observed with penicillin. Since the physiological state of the organisms rather than the concentration of the penicillin appears to be the limiting factor in such a refractory state, prolongation of treatment or the use of penicillin in combination with an antibiotic, the effectiveness of which is not restricted to actively metabolizing organisms, would appear at times to be a more logical approach to successful therapy than the use of increased dosages of penicillin.

[Editorial, Treatment Failure with Penicillin. The Journal of The American Medical Association. 151:301 (January) 1953.]

SOME PROPERTIES OF THE CAUSATIVE AGENT OF TRANSMISSIBLE GASTROENTERITIS IN SWINE. Transmissible gastroenteritis, a cause of deaths in many thousands of baby pigs, has been reported in all the Midwestern states. Because this disease spreads and kills young pigs so rapidly, treatment and control have been very discouraging.

In order to clarify some of the characteristics of the causative agent in this disease, these studies were made. (1) The survival of the causative agent under various conditions; (2) the effect of centrifugation on the concentration of the etiological agent; (3) the susceptibility of laboratory animals to the causative agent; and (4), the effect of treatment. The animals used for these studies included 96 baby pigs, 19 guinea pigs, 43 mice, 4 hamsters, and 5 rabbits.

A summary of the results of this study revealed the following: (1) The causative agent remained infective for young pigs after three days drying at 67° to 70°F. (2) Supernatant fluid from centrifuged ground gastrointestinal tract containing .05 percent formalin was not infective. (3) Ground gastrointestinal tract produced disease after being stored for three years and six months at —28°C. (4) Centrifugation of filtrates at 15,000 to 18,000 revolutions per minute for thirty to sixty minutes apparently concentrated the causative agent to some extent. (5) No host except swine has been found for the causative agent of transmissible gastroenteritis. (6) Under the conditions of this study, none of the therapeutic agents used was of any value in the treatment of transmissible gastroenteritis. They included streptomycin, aureomycin, chloromycetin, penicillin, sulfadiazine, sulfathaladine and sulfamethazine.

[Bay, W. W., D.V.M., M.S.; Doyle, L. P., D.V.M., M.S., Ph.D; Hutchings, L. M., D.V.M., M.S., Ph.D., Some Properties of the Causative Agent of Transmissible Gastroenteritis in Swine. American Journal of Veterinary Research. 13:318-321 (July) 1952.]

The objectives of the Public Health Subcommittee of the National Brucellosis Committee are: (1) To inform the American farmer of the danger to himself and the public of brucellosis infection; (2) To recommend procedures which will lessen the danger of human infection. The following outline was submitted for the approval of the committee:

1. That universal pasteurization of milk and all dairy products be encouraged.
2. That only disease-free herds be permitted a Grade A classification for milk and milk products.
3. That steps be taken to educate farmers of the danger, to themselves and their families, of keeping infected animals.
4. That educational materials be made available to personnel in the animal-handling industries, other than the livestock farmer, pointing out the dangers of occupational brucellosis, and the means whereby infection may be avoided.
5. That the subcommittee review new public health problems and suggestions as they are received, and encourage private and governmental agencies to develop methods of public health education.