Journal of the Minnesota Academy of Science

Volume 19 | Number 1 Article 4

4-1951

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In two additional operations on the right side, the return of blood was not interrupted but, instead, a running suture was passed on each side of the site of the incision. By tying the ends of each suture together they were looped, and were crossed so that traction exerted on them closed the incision, which was 15 to 20 mm. in length. The other features of the operation were the same.

It is fortunate that the anatomic relationships of the heart and thorax of the dog are such that the right ventricle can be explored from either the right or left side. If it is desirable to inspect the pulmonary artery, the approach through the left side is preferable

The operation has been done on the right side in five animals. In all operations except one, worms were removed. Larvae were present in the blood smears of all animals before and after the operation. A second operation was done on the left side of the thorax in all of the dogs. A few worms were removed from each of two animals. In two others worms were not found. The fifth dog did not yield any worms at either operation. After the second operation this dog was killed. Thorough examination of the heart and pulmonic vessels did not disclose any heartworms. Three other dogs of the series were killed. Six worms were found in one dog at necropsy; examination of the other dogs gave negative results.

One of the series of five dogs is still alive after nearly three years, and still has larvae of *Dirofilaria immitis* in the blood.

This work has amply demonstrated that the surgical removal of heartworms is a feasible procedure. It remains to be seen whether the operation will become a practical method of removal of the worms from a heavily infected valuable animal to which the administration of a vermifuge might be considered too great a risk. A combination of the operation with a vermifuge might offer certain advantages, since most of the worms could be removed by surgical means and the small number that might be missed at operation could be killed with anthelmintic agents without too serious risk to the animal.

THE PRESENT STATUS OF THE SEARCH FOR ANTITUBERCULOSIS SUBSTANCES

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The demonstration by Robert Koch almost three fourths of a century ago that tuberculosis is caused by a micro-organism provided reason for belief that a specific treatment of the disease could be found. During the following years a great deal of effort and

money was expended in the search for a chemotherapeutic agent capable of inhibiting the growth of the tubercle bacillus in tissue, with resultant arrest and cure of the disease. Failures and discouragement prevailed for almost sixty years, and interest in the specific therapy of tuberculosis began to wane until the beginning of the last decade, when it was demonstrated that experimental tuberculosis of animals could be beneficially affected by treatment with certain agents which are derivatives of a simple chemical compound known as "diaminodiphenyl-sulfone."[1] Although these agents, promin, diasone and promizole, were not acceptable for clinical use because of their toxicity or low activity in human tuberculosis, nevertheless they gave ample evidence that experimental tuberculosis in animals was finally open to attack. This aroused again a world-wide interest in the specific treatment of tuberculosis. Many laboratories are now engaged in the synthesis of new compounds, and also are searching for chemotherapeutic agents of microbial origin: the antibiotics. Methods for evaluating proposed antituberculosis agents by animal experimentation have been devised.[2] In addition to animal tests for the determination of antituberculosis properties of new materials, extensive pharmacologic and toxicologic studies are being made.

In 1944, when streptomycin became available, the previous experience with the sulfones in experimental tuberculosis permitted rapid evaluation of its antituberculosis effects in animals and its introduction into clinical trials.[3] At present streptomycin, including its derivative, dihydrostreptomycin, is the most potent antituberculosis agent known. It has, however, definite limitations. In chronic, long-standing tuberculosis this antibiotic agent has little promise of effecting healing of large destructive lesions. In certain instances it produces damage to the vestibular apparatus, causing impairment of balance. Tubercle bacilli may become resistant to the effects of streptomycin. These limitations prompted search for other antituberculosis substances.

Para-aminosalicylic acid (PAS) is of particular interest because it is the only chemotherapeutic agent developed on a theoretic basis. It was known that salicylates played some part in the oxidative processes of the metabolism of the tubercle bacillus. It was thought that a derivative of salicylic acid might interfere with the metabolism of the tubercle bacillus and thus inhibit growth. The derivative

[1] Feldman, W. H.: "Chemotherapy of Tuberculosis"—Including Use of Streptomycin: Harben Lecture, 1946; Evaluation of Efficacy in Tuberculosis of Sulfonamides, Sulfones and Certain Other Substances. J. Roy. Inst. Pub. Health & Hyg. 9:297–324 (Oct.) 1946.

[2] Rake, Geoffrey [Editor]: The Chemotherapy of Tuberculosis—The Experimental Approach. Ann. New York Acad. Sc. 52:627–787 (Dec. 14) 1949.

[3] Riggins, H. M. and Hinshaw, H. C.: Streptomycin and Dihydrostreptomycin in Tuberculosis; Reports of Research Including Studies Sponsored by the American Trudeau Society (Medical Section, National Tuberculosis Association). New York, National Tuberculosis Association, 1949, 554 pp.

of salicylic acid, PAS, was found to do this.[4] Animal experimentation revealed that PAS has a marked therapeutic effect on infections caused by streptomycin-resistant tubercle bacilli. Furthermore, it was found that the combined use of PAS and streptomycin or dihydrostreptomycin in patients delays or prevents the appearance of drug-resistant tubercle bacilli. This drug also has definite limitations. Its therapeutic effect is observed to be slow. It is poorly tolerated by many patients. Tubercle bacilli resistant to PAS may appear.[5] Many attempts are being made to alter the chemical structure of PAS to reduce its undesirable effects and to increase its therapeutic efficiency, but at present no effective derivative has been made.

The thiosemicarbazones are known to be of some value in reversing progressive tuberculous disease in experimental animals, but the toxicity of presently available compounds of this group limits the clinical application. Many actinomycetes produce antibiotic substances which are active against tubercle bacilli growing in test tubes, but most of these materials prove to be too toxic for experimental animals and are not considered for clinical trials. Two such agents, however, neomycin and viomycin, hold considerable interest since both have been found to be active against streptomycin-resistant tubercle bacilli in experimental animals and, for guinea pigs, at least, have low toxicity. Neomycin has been found to be very toxic for human patients and its place in the therapeutic regimen against tuberculosis will depend on the success of current attempts to produce neomycin of lower toxicity. Viomycin as yet has not been adequately studied to determine whether or not it can be accepted as an adequate chemotherapeutic agent.

The approach to the search for antituberculosis agents is largely empiric. Antibiotic agents from hundreds of cultures of actinomycetes are being tested routinely against tubercle bacilli in test-tube cultures. Those that suppress growth are then tested for toxicity and therapeutic activity in experimental animals. The vast majority are found to be of little or no value. Synthetic agents are being sought in much the same manner. Chemists are attempting to increase the potency of known weakly active agents or are trying to alter the toxicity of known active but toxic materials. These procedures are largely trial-and-error methods.

Another approach to the problem is to study the enzymes of tubercle bacilli in an attempt to disclose the factors which may be responsible for virulence, for growth and for the ability of tubercle bacilli to become resistant to drugs. If certain enzyme systems can be elucidated, it may be possible to block some such system with

[4] Lehmann, Jörgen: Kemoterapi av tuberkulos: p-Aminosalicylsyra (PAS) och närstående derivats bakteriostatiska effekt på tuberkelbacillen jämte djurexperimentella och kliniska försök med PAS. Svenska läk.-tidning. 43:2029–2041 (Aug. 16) 1946.

[5] Chemotherapy and Antibiotics (Special Issue): Dis. of—Chest. 16:633–913 (Dec.) 1949.

an agent nontoxic for patients and thus obtain a potential antituberculosis substance.[6]

Great strides have been made in a very short time. The direction for research to pursue in this field is now well mapped. Experience has afforded methods of evaluation and criteria for the acceptance of new antituberculosis drugs. The ideal is not now at hand, although streptomycin and PAS are greatly beneficial in many cases. Investigations are expanding, and there is now reason to believe that new and better antituberculosis agents will be made available to physicians for the treatment of tuberculosis.

THE EFFECT OF THE REMOVAL OF THE ADRENAL GLAND IN PIGS

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SOME OBSERVATIONS ON THE CIRCULATORY SYSTEM OF LUMBRICUS TERRESTRIS

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A PRELIMINARY REPORT OF A SURVEY OF THE AQUATIC INSECTS OF THE AMITY CREEK (WEST BRANCH OF LESTER RIVER)

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ABSTRACT

Weekly bottom samples (one square yard) were collected at six stations from April 15 to November 15, 1950. Factors such as pH, temperature of air and water, light (direct and reflected), various types of stream bottoms were studied in relationship to the bottom fauna. Dipterous larvae were the most dominant group, Trichoptera ranked second and Ephemeroptera composed the third largest group.

[6] Zeller, E. A., Owen, C. A., Jr. and Karlson, A. G.: Diamine Oxidase of Mycobacterium Smegmatis: Effect of Streptomycin and Dihydrostreptomycin. J. Biol. Chem. 188:623–630 (Feb.) 1951.