of the topics and classes of compounds presented, or the discussion of those which are included.

In the book under review, the authors have been guided by their evident desire to follow the former of the above alternatives and reduce the list of topics rather than the thoroughness of their treatment. This has been achieved mainly by totally ignoring one of the three major divisions of the subject, namely, that of the heterocyclic compounds. A more accurate title for the volume, therefore, would be "Aliphatic (Acyclic) and Carbocyclic Organic Chemistry."

Another sacrifice in the interest of brevity has been the omission in the text of citations to the original literature. In their place, a select list of reading references is given at the close of each chapter. Space has also been economized by the insertion of numerous tables of compounds and of their physical and chemical properties. Apparently one object of this rather severe limitation of the topics, classes and compounds to be considered has been to provide space for what the authors regard as the most novel feature of their book—that is, the inclusion, for optional reading, of a certain number of chapters pointing out the importance of organic chemistry in technology, industry, biology and medicine. Such general reading would probably comprise the chapters on Rubber, Microbiological Processes, Role of Carbohydrates in Biological Processes, Metabolism of Fats, Metabolism of Proteins and Amino Acids, Synthetic Fibers, Synthetic Plastics and Resins, Accessory Dietary Factors and Advances in Chemotherapy.

The underlying plan of the work has been first to make clear to the reader the elements of the subject by a discussion of the chemistry of such relatively simple groups as the aliphatic hydrocarbons, alcohols and acids, and then to lead him forward gradually through more intricate and difficult fields; simultaneously replacing the older empirical theoretical explanations by more modern and more scientific ones.

All organic chemists are familiar with the splendid contributions which Dr. and Mrs. Fieser have been making for many years in the lecture room and laboratory, and as authors. No one is better qualified to prepare an exceptionally fine general treatise in this branch of science, and the result of their labor is a book which, in thoroughness and clarity of presentation, authoritative and up-to-date information, and the fascination of the world it discloses, is unexcelled. It should be in the possession of every one interested in organic chemistry. It is to be hoped that the authors will find time later for a companion volume devoted to the heterocycles.

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SPECIAL ARTICLES

THE URINARY EXCRETION OF PENICILLIN AFTER ORAL ADMINISTRATION TO NORMAL HUMAN SUBJECTS[1]

EARLY studies on the absorption and excretion of penicillin[2] suggested that oral administration was not effective in attaining adequate blood levels that were required for the treatment of severe infections. The destruction of penicillin by the acid gastric contents appeared as a possibility to account for the results obtained.[2,3] Until quite recently only very limited amounts of penicillin have been available and it has been highly desirable to use it in the most efficient manner possible. However, it would appear that the supplies of penicillin will be enormously increased[4] so that it becomes possible to consider less efficient but more convenient means of administering the drug. Certainly oral administration is the method of choice in the majority of instances from the standpoint of both the patient and the attending physician. For this reason it seemed desirable to re-examine the urinary excretion of penicillin after the oral ingestion of relatively large doses in order to ascertain if therapeutically effective quantities might be absorbed from the gastrointestinal tract. The present report describes studies of the urinary excretion of penicillin following its oral ingestion, either alone or along with sodium bicarbonate by normal human subjects.

A solution of the sodium salt of penicillin containing 500 Oxford units per milligram of total solids was employed in these studies. In all cases the subjects were fasting for 3 to 6 hours but not longer than this. All assays were carried out by the cylinder plate technique on suitably diluted urine specimens.[5] Table 1 shows the amount of penicillin excreted in the urine by two males (A and C) and one female (B) following the oral ingestion of 100,000 Oxford units. Two studies were made on subject A. It will be seen that from 8 to 33 per cent. of the quantity taken by mouth was excreted in the urine. The average rate of urinary

[1] From the Ben Venue Laboratories Inc., Bedford, Ohio, and the Department of Biochemistry, School of Medicine, Western Reserve University, Cleveland, Ohio. This article was received on June 3, 1944. It has now been released for publication.

[2] C. H. Rammelkamp and C. S. Keefer, *Jour. Clin. Invest.*, 22: 425, 1943.

[3] C. H. Rammelkamp and J. D. Helm, Jr., *Proc. Soc. Exp. Biol. and Med.*, 54: 324, 1943.

[4] R. D. Coghill, *Chemical and Engineering News*, 22: 588, 1944.

[5] W. H. Schmidt and A. J. Moyer, *Jour. Bact.*, 47: 199, 1944.

TABLE 1

URINARY EXCRETION OF PENICILLIN FOLLOWING THE ORAL INGESTION OF PENICILLIN

Subject	Total excretion following ingestion of 100,000 Oxford units	Total excretion following ingestion of 100,000 Oxford units and 10 gm Na HCO3
A	22,200	12,700
A	33,600	
B	8,800	1,950
C	16,300	4,300

excretion for the three subjects is indicated by Fig. 1. The maximum excretion occurred during the first hour and all penicillin had essentially disappeared from the urine by the end of 6 hours. No untoward reactions were noted in any of the three subjects.

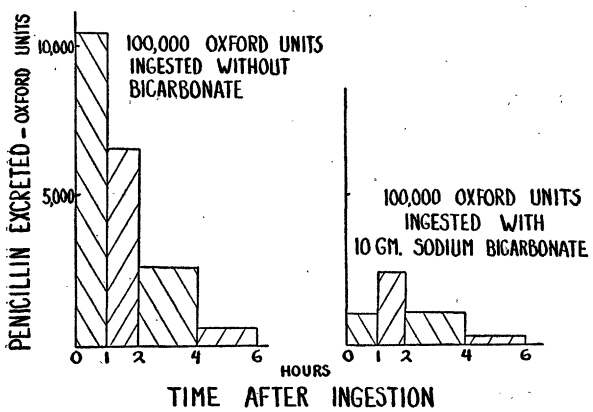

FIG. 1. The rate of urinary excretion of penicillin following its oral ingestion by human subjects.

It has been suggested[3] that the simultaneous administration of sodium bicarbonate might decrease the amount of destruction of penicillin in the gastrointestinal tract. Results of studies in which 100,000 Oxford units of penicillin were ingested along with 10 grams of sodium bicarbonate are also shown in Table 1. It will be seen that in each of the three subjects the amount of penicillin excreted was quite definitely decreased. In subject A the amount of penicillin excreted was approximately half of that noted when the penicillin was ingested alone, whereas the excretion of penicillin by subjects B and C was only 20 to 25 per cent. as great when the bicarbonate was taken along with the penicillin. The reason for the decrease in penicillin excretion is not readily apparent. In the first place the bicarbonate may sufficiently decrease gastric emptying so that there is more destruction of the substance in the stomach. This is consistent with the results indicated in Fig. 1 which show that the maximum penicillin excretion occurred in the first hour when the penicillin was ingested alone, but when sodium bicarbonate was also ingested the maximum penicillin excretion was delayed and occurred between 1 and 2 hours. A second possibility is that the alkaline urine which is excreted following bicarbonate ingestion causes a destruction of the compound while the urine is in the bladder.

Comparison of the quantity of penicillin excreted after oral ingestion with that after intravenous administration suggests that some of the compound is destroyed in the intestinal tract. However, it would appear from the above data that if the doses of penicillin administered orally are larger than those that are effective by intravenous administration, then one might reasonably expect that an adequate amount of the drug will be absorbed and will provide a therapeutic effect in the treatment of infections by susceptible organisms. For instance, the amount of penicillin excreted by each of the subjects after oral ingestion was of the same order of magnitude or larger than the quantity used in many single clinical intravenous or intramuscular injections. A possible added advantage of oral administration is that the absorption continues over some period of time so that the effects of an elevated blood level of penicillin will be prolonged.[6]

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PROLONGING EFFECTIVE PENICILLIN ACTION[1]

"PROLONG penicillin" has now become a slogan for clinical research workers seeking to extend the effective action of this wonder-working but evanescent drug. When administered in saline solution by intramuscular injection, over half of the penicillin is soon excreted in the urine, requiring renewed dosages every two or three hours. Effective levels have recently been prolonged by using a penicillin beeswax-peanut oil mixture.[2] The authors of this report have tried a new approach to the problem involving the well-known principle of chilling, in order to slow down the circulation in and around the site of the intramuscular injection..

MATERIALS AND METHODS

This simple method was first tried, beginning Sep-

[6] Since completion of the above study 10 additional studies have been made of the excretion of penicillin following the oral ingestion of 100,000 Oxford units. The excretion pattern and total excretion of penicillin corresponded with the results described above.

[1] The opinions and views set forth in this article are those of the writers and are not to be considered as reflecting the policies of the Navy Department.

[2] "A Method of Prolonging the Action of Penicillin," by M. J. Romansky and G. E. Rittman. SCIENCE, vol. 100, No. 2592, p. 196, Sept. 1, 1944.