ACCORDING to a recent vote of the council, the next meeting of the Society of American Bacteriologists will be held in Detroit, Mich., on May 21–24, 1946. The headquarters will be at the Book-Cadillac Hotel. Plans for the program include reports on recent research from members of the society together with addresses by at least two speakers on topics of general interest. Round-table and symposia sessions on a variety of problems, including war-time research in bacteriology, will be included in the program. There will also be scientific and commercial exhibits. Members of the society should note that March 4, 1946, is the deadline for acceptance of abstracts and requests for exhibits. All abstracts should be submitted to the chairman of the program committee, Dr. L. S. McClung, 420 Kirkwood Hall, Bloomington, Ind. Requests for exhibits should be addressed to Dr. Joseph A. Kasper, Bureau of Health Laboratory, Herman Kiefer Hospital, Detroit 2, Mich.

THE Division of High-Polymer Physics of the American Physical Society will hold its second regular meeting at Columbia University, on January 24, 25 and 26, as one of the features of the general, annual meeting of the society. On the program of the division meeting are approximately twenty-five papers on rubbers, plastics and other high-polymeric materials, covering both the analysis of physical behavior and experimental techniques.

THE Rocky Mountain Biological Laboratory, closed for the duration of the war, will reopen for classes for students next summer, beginning on July 15. The courses scheduled are ecology, field botany and parasitology. The laboratory is situated eight miles from Crested Butte, Colo., in the Gunnison National Forest at an altitude of 9,500 feet; surrounding mountains rise to an altitude exceeding 13,500 feet. Much of the area around the laboratory is almost virgin territory for the research biologist. Independent investigators are welcome to carry on research on alpine biological problems. Communications should be addressed to Dr. John C. Johnson, director of the laboratory, Box 262, Edinboro, Pennsylvania, or to Dr. A. O. Weese, professor of zoology, University of Oklahoma, Norman, president of the board of trustees of the laboratory.

THE correspondent at Delhi, India, of *The Times*, London, announces that the establishment of an Indian National Research Council, authorized to initiate immediately a five-year program of development in the field of scientific and industrial research, is recommended to the Government of India in a report by the Industrial Research Planning Committee. The plan includes the building and equipment of national chemical and physical laboratories and of nine specialized research institutes—for food technology, metallurgy, fuel, glass and silicate, oils and paints, buildings and roads, leather and tanning, industrial fermentation and electro-chemistry; the all-round strengthening of existing research organizations; and the obtaining of seven hundred research workers to man the laboratories by the award of scholarships tenable in India and abroad. All the provinces and larger states are advised to set up laboratories for the investigation of scientific questions of local interest. The committee remarks that current scientific research in India does not represent the bare minimum, whether judged by international standards or by the requirements of India in its present state of industrial development.

SPECIAL ARTICLES

ORAL PENICILLIN—A COMPARISON OF VARIOUS MODES OF ADMINISTRATION[1]

IT has been demonstrated by Free, Leonards, McCullagh and Biro[2] that orally ingested penicillin is absorbed from the gastrointestinal tract in significant amounts. This finding has been confirmed by many laboratories and György, Vandergrift, Elias, Colio, Barry and Pilcher[3] and Free, Huffman, Trattner and Brown[4] have shown that gonorrhea may be successfully treated by orally administered penicillin.

The relative effectiveness of oral and parenteral penicillin in the treatment of disease has not been definitely established, but the general feeling is that perhaps 4 to 5 times as much oral penicillin is required to produce the same therapeutic effect as parenteral penicillin. Most investigators have ascribed this difference to the destruction of penicillin by gastric acid when it is given orally. The present report describes studies of the destruction of penicillin by gastric acidity and the efficacy of different forms of oral penicillin.

The subjects used in the first part of the present study were healthy young adults with both sexes equally represented. The subjects reported at the laboratory after an overnight fast voided and were

[1] From the Departments of Biochemistry and Medicine, School of Medicine, Western Reserve University, the Medical Service of University Hospitals, Cleveland, Ohio, and the Ben Venue Laboratories, Inc., Bedford, Ohio.

[2] A. H. Free, J. R. Leonards, D. R. McCullagh and B. E. Biro, SCIENCE, 100: 431, 1944.

[3] P. György, H. N. Vandergrift, W. Elias, L. G. Colio, F. M. Barry and J. D. Pilcher, *Jour. Am. Med. Asn.*, 127: 639, 1945.

[4] A. H. Free, L. F. Huffman, H. R. Trattner and H. B. Brown, *Jour. Lab. and Clin. Med.*, 30: 738, 1945.

then given the penicillin. Quantitative urine samples were collected at the end of 1 hour, 2 hours, 4 hours and 6 hours. The penicillin content of the urine was determined by the cylinder plate method on specimens suitably diluted with phosphate buffer.

Table 1 shows the urinary excretion of penicillin following the administration of 100,000 units either

TABLE 1

AVERAGE URINARY EXCRETION OF PENICILLIN FOLLOWING ADMINISTRATION OF 100,000 UNITS

Number of subjects	Mode of administration	0–1 hr.	1–2 hr.	2–4 hr.	4–6 hr.	Total
11	Intramuscular injection	38210	16350	5720	700	60980
13	Orally-dissolved in water	4740	5410	2780	720	13650
8	Intraduodenally by tube	10240	7220	4170	1200	22830
7	Orally-dissolved in sodium citrate solution	5820	10210	5630	1400	23060
6	Orally-suspended in oil	4570	5500	2680	1700	14450
5	Orally-dissolved in milk	4100	7100	5460	1280	17940
6	Orally-sealed gelatin capsules	2650	7360	4530	920	15460
6	Orally-enteric coated capsules	1800	7030	4270	1140	14240
4	Orally-mixed with raw egg	4600	6660	3440	1650	16350
3	Orally in solution with bile salts	6220	3730	1830	690	12470

intramuscularly, intraduodenally, orally with water or orally along with various other substances. The amount of penicillin excreted after intramuscular injection was approximately 60 per cent. of the administered dose. These results are in agreement with most of the data in the literature. In the same group of subjects the ingestion of 100,000 units orally dissolved in 250 cc of water resulted in an average excretion of approximately 14,000 units. These results are in agreement with earlier data obtained by the authors[2] but are somewhat greater than some of the values obtained by other laboratories. In 8 of the same subjects a tube was passed into the duodenum and the position of the tube was determined either by fluoroscopic examination or by the character of the aspirated contents, as indicated by an alkaline reaction, the presence of bile and the presence of pancreatic enzymes. In these subjects 100,000 units of penicillin dissolved in 100 cc of water was instilled into the duodenum at a constant rate over a period of 15 minutes. Following this the tube was pulled back into the stomach and the gastric contents aspirated. In no instance did the gastric contents contain any regurgitated penicillin as indicated by either pigment or assay. The excretion of penicillin following intraduodenal administration averaged approximately 23 per cent. of the ingested dose. This is somewhat greater than after oral ingestion but does not approach that observed following intramuscular injection. In 7 of the subjects the oral administration of penicillin in a solution containing 5 gm of sodium citrate resulted in a urinary excretion quite comparable to that following direct instillation of the penicillin into the duodenum. However, the total excretion again does not compare with that following intramuscular administration. These results with sodium citrate confirm the findings of Charney, Alburn and Bernhart.[5]

Other modes of administration of penicillin included solution in milk, mixed raw egg or bile salts solution, suspension in sesame or corn oil, and in sealed gelatin capsules and enteric coated capsules. The advantages of any of these modes of administration over simple aqueous solution is in no instance

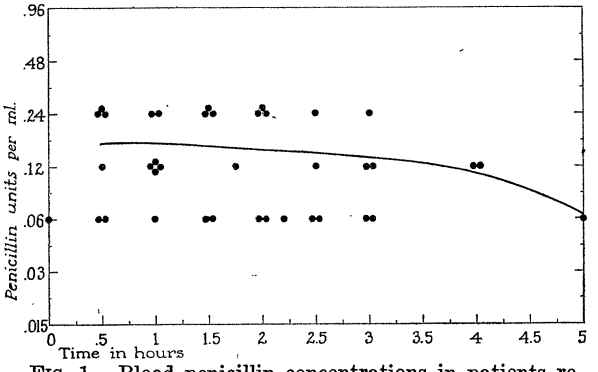

FIG. 1. Blood penicillin concentrations in patients receiving 100,000 units of penicillin orally.

marked although from the point of view of taste the gelatin or enteric capsules were quite advantageous.

In the second part of the study, penicillin was administered orally to patients on the wards of Lakeside

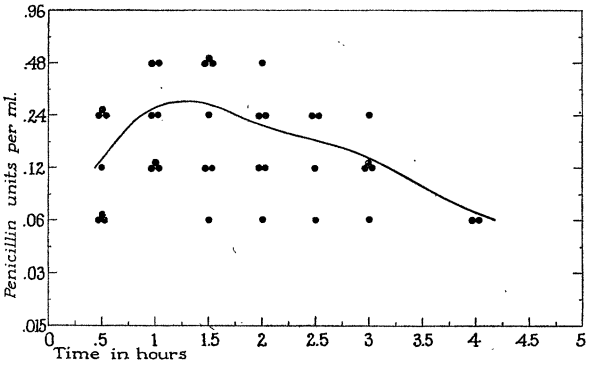

FIG. 2. Blood penicillin concentrations in patients receiving 100,000 units of penicillin orally along with potassium citrate.

Hospital. It was put up in gelatin capsules and was routinely given in 5 doses a day at 2 and 7 P.M., midnight, and 5 and 10 A.M. with 100,000 units as the standard dose. Blood was taken at intervals after

[5] J. Charney, H. E. Alburn and F. W. Bernhart, SCIENCE, 101: 251, 1945.

at least one of the doses for assay. The results are given in Figs. 1 and 2. It will be seen that 100,000 units of penicillin given alone produces a satisfactory blood concentration for several hours. With the addition of potassium citrate the peak concentration is raised, but there is little difference in the duration of an appreciable blood concentration. The results of administration of penicillin simultaneously with aluminum hydroxide gave essentially similar results.

Fig. 3 indicates the blood level of penicillin of a patient who received 100,000 units intravenously.[6]

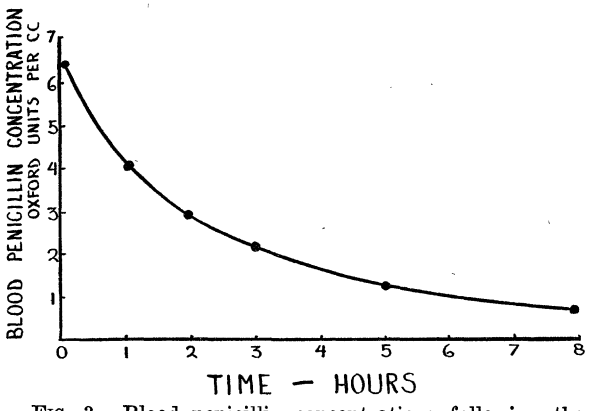

FIG. 3. Blood penicillin concentrations following the intravenous injection of 100,000 units into a patient with complete anuria.

This white female, 46 years of age, had 3 days previously taken a lethal dose of mercury bichloride. At the time the penicillin was injected a complete anuria existed so that no urinary excretion was possible. The blood concentration, however, decreased at a rate which suggested that the half life of penicillin in the body was approximately 2 hours. This indicates that penicillin is destroyed, inactivated or excreted by some route in addition to the kidneys. This disappearance of penicillin in the body proper is also indicated by the fact that only 60 per cent. of intramuscularly administered penicillin is excreted. It has also been noted when the urinary excretion rate is decreased by diodrast[7] or para-amino hippuric acid[8] that the total amount of excreted penicillin decreases from approximately 60 per cent. to 30 per cent.

The destruction of penicillin in the body proper may be the basis for the difference in the excretion of penicillin when administered orally or intraduodenally as compared with the excretion of parenterally administered penicillin. In the one instance the excretion is exceedingly rapid during the first few minutes after injection so that the exposure time to "destructive" influences is quite short. On the other hand, penicillin absorption from the gastrointestinal tract results in a more uniform rate of entry of penicillin into the circulation and in general the rate of excretion is fairly uniform during the first 2 hours after ingestion. This results in a longer exposure of penicillin to possible destructive influences. It may be significant that orally or duodenally administered penicillin enters the portal circulation and is exposed to the metabolic activities of the liver, whereas parenterally administered penicillin is not nearly so completely exposed to this influence. It is also known that certain of the bacteria of the intestinal flora elaborate penicillinases which rapidly inactivate penicillin. However, the site of absorption of penicillin and the location of significant amounts of the enzyme in the intestine are not sufficiently defined to indicate whether or not such destruction may be of significance.

[6] The studies on this patient were done in collaboration with Dr. Max. Miller, of the Department of Medicine, School of Medicine, Western Reserve University, and the Medical Service of University Hospitals, Cleveland, Ohio.

[7] C. H. Rammelkamp and S. E. Bradley, *Proc. Soc. Exp. Biol. and Med.*, 53: 30, 1943.

[8] K. H. Beyer, L. Peters, R. Woodward and W. F. Verwey, *Jour. Pharm. and Exp. Therap.*, 82: 310, 1944.

SUMMARY

A comparison of penicillin excretion when equivalent quantities of the drug are given orally or parenterally indicates that approximately 60 per cent. urinary excretion occurs after parenteral administration, whereas 14 per cent. urinary excretion occurs following oral ingestion. That destruction by gastric acidity is not primarily responsible for this difference is indicated by the fact that administration of penicillin directly into the duodenum does not greatly alter the amount of penicillin excretion. Evidence indicating that the majority of orally administered penicillin is destroyed by the body proper is discussed.

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IMPAIRMENT OF REPRODUCTION IN RATS BY INGESTION OF LEAD

ACCIDENTAL contamination with lead of an experimental diet for rats led to results which appear confirmatory of the thesis that sterility, high incidence of abortion and excessive infant mortality in human populations may be caused by chronic lead poisoning.[1] Report of our results is of interest because Calvery and associates in an extended series of papers[2] were unable to reproduce such effects of lead poisoning either in rats or dogs by feeding lead acetate or lead arsenate. It may be significant that our animals ingested lead largely in metal form.

[1] R. M. Hutton, "Lead Poisoning; a compilation of present knowledge." Provincial Board of Health of Ontario, Toronto. 1923.

[2] *Jour. Pharmacol.*, 64: 364–464, 1938.