

analytical data as a basis for unquestionable conclusions regarding the origin of the nitrogen.

The suggestion of Lang (3) involves the assumption that the argon of a natural gas is derived from the atmosphere and that argon and nitrogen are not substantially separated from each other as the gas collects. If such an assumption is correct, it follows that nitrogen in natural gases originates both in the atmosphere and in chemical processes. In some gases, such as Samples IV, V, VI, and X, most of the nitrogen appears to be of chemical origin and in others, such as Samples I, II, III, and IX, of atmospheric origin.

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## The Intestinal Absorption of Penicillin G

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Investigators are in general agreement that the oral dosage requirements of penicillin are four or five times the parenteral requirements in order to obtain comparable serum concentrations and equal therapeutic effectiveness (2, 3, 5). It has also been shown by Free, Parker, and Biro (3) and others that this approximate oral/parenteral ratio is substantiated by measurements of total urinary excretion of penicillin after administration by the two routes. Destruction by gastric acidity was found to account for only a minor portion of the loss of an oral dose.

In a survey of the problem Cutting, *et al.* (1) suggested that lack of intestinal absorption and subsequent destruction in the bowel by penicillinases may be of importance. The present work is an effort to obtain more specific information on the absorbability of penicillin from the intestine in order to evaluate this view.

Forty-four healthy adult mongrel cats, fasted for 24 hours previous to the experiments, were used for the study. Pure crystalline sodium penicillin G was

used in order to make the results more referable. Under dial-urethane anesthesia (.7 cc./kg. dial with urethane, Ciba) .1 millimole penicillin/kg. body weight was placed in the ligated duodenum, the abdominal incision sutured, and absorption allowed to take place for various periods of time up to 3 hours. The penicillin had been dissolved previously in 2.5 cc. normal saline solution/kg. of cat in order to standardize intestinal fluid volumes and osmotic influences. At the end of the test period the incision was reopened, the duodenum removed, and the contents thoroughly washed out and analyzed for penicillin by the cylinder-plate method. Preliminary experiments showed that the duodenal contents of 24-hour fasted cats under dial-urethane anesthesia contained no substances interfering with the penicillin assay and that the duodenal contents alone gave no ring of inhibition with the test organism. Control recoveries of penicillin from injected loops removed and washed out immediately averaged 98 per cent of the injected quantity.

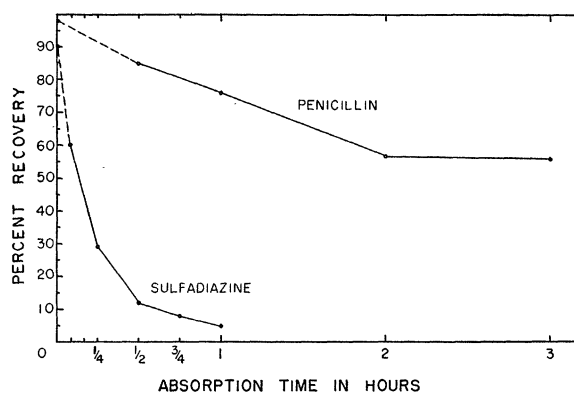


FIG. 1. Recoveries of sodium penicillin G and sodium sulfadiazine from the ligated duodenum of cats after various periods of absorption. Each point represents the average of four experiments.

As a comparison, the absorption of sulfadiazine, a chemotherapeutic agent known to be satisfactorily absorbed from the gastrointestinal tract, was studied under the same conditions. The dose used was .1 millimole sodium sulfadiazine/kg., and the administration, absorption, and recovery procedures were also the same as those used for the penicillin experiments. Sulfadiazine determinations were made by the colorimetric method of Marshall and Litchfield (6). Preliminary experiments showed that the duodenal contents of 24-hour fasted cats under dial-urethane anesthesia contained no substances interfering with the colorimetric assay for sulfadiazine. Control recoveries of sulfadiazine from injected loops removed and washed out immediately averaged 90 per cent of the injected quantity. Results are shown in Fig. 1.

The high recovery of penicillin from the ligated duodenum (an average of 76 per cent after 1 hour, 57 per

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cent after 2 hours, and 56 per cent after 3 hours) indicates a definitely slow rate of absorption as compared to sulfadiazine absorption, in which case an average of only 12 per cent was recovered after  $\frac{1}{2}$  hour and 5 per cent after 1 hour of absorption. It therefore becomes increasingly evident that the major portion of an oral dose of penicillin passes through the upper portion of the intestinal tract unabsorbed. When it reaches the lower portions of the tract, where bacteria are more numerous and inactivating enzymes more likely to be present, destruction occurs before complete absorption can take place. Work to be published later confirms the assumption of a progressive rate of penicillin destruction downward in the gastrointestinal tract.

The slow absorption of penicillin from the intestine can be added to evidence of its passage with difficulty through certain other body membranes (4).

Efforts to increase the efficiency of oral administration should be directed toward increasing its penetration through the intestinal mucosa.

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### Toxicity of DDT Isomers to Some Insects Affecting Man<sup>1</sup>

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Isolation of o,o'-DDT [1-trichloro-2,2-bis(o-chlorophenyl)ethane] from technical DDT by a method involving preferential dehydrochlorination with ethanolic sodium hydroxide of the more reactive p,p'-DDT [1-trichloro-2,2-bis(p-chlorophenyl)ethane] and o,p'-DDT [1-trichloro-2-o-chlorophenyl-2-p-chlorophenyl-ethane] and oxidation of the resulting olefins with chromic anhydride, leaving the unreactive o,o'-DDT isomer, has recently been reported (2). Isolation of the other two isomers, p,p'-DDT, the major and most active constituent of technical DDT, and o,p'-DDT, the major impurity, has previously been reported (4).

As there has been considerable interest and specu-

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lation on the possible insecticidal activity of the o,o'-DDT isomer, we wish to present data as to the action of the substance against the fourth-instar larvae and adults of the common malaria mosquito (*Anopheles quadrimaculatus* Say) in America and against the housefly (*Musca domestica* L.) and the body louse (*Pediculus humanus corporis* Deg.). For comparison, results on the p,p' and o,p' isomers are also included. The compounds used had the following melting points: o,o'-DDT, 92-93° (cor.) (2); p,p'-DDT, 108.5-109.0° (cor.) (4); o,p'-DDT, 74.0-74.5° (cor.) (4).

The tests against the mosquito larvae were carried out by the beaker method in acetone-water suspension (3). Tests were made in triplicate, 20 insects being used in each test. Results are given in Table 1.

TABLE 1  
TOXICITY OF DDT ISOMERS TO FOURTH-INSTAR LARVAE OF *A. quadrimaculatus*

DDT isomer	Dosage (ppm)	48-hr. mortality (%)
o,o'	5.0	17
	7.5	100
p,p'	0.00125	7
	.0025	32
	.005	74
	.01	100
o,p'	0.005	6
	.01	16
	.03	85

Spray tests were made against adult houseflies and mosquitoes. One ml. of a 1-per cent solution of each of the isomers in refined kerosene (Deobase) was sprayed into a 100-cubic-foot chamber in which the insects were exposed in small screen-wire cages and tested by a pendulum-swinging method. The tests were conducted in triplicate. Approximately 300 insects were used in each test. Results are given in Table 2.

TABLE 2  
TOXICITY OF DDT ISOMERS TO ADULT HOUSEFLIES AND *A. quadrimaculatus*

DDT isomer	Houseflies			Mosquitoes		
	Knockdown in 10 min. (%)	Knockdown in 30 min. (%)	Kill in 24 hr. (%)	Knockdown in 10 min. (%)	Knockdown in 30 min. (%)	Kill in 24 hr. (%)
o,o'	0	0	1	5	6	15
p,p'	0	14	50	20	69	89
o,p'	0	0	0	6	8	20

In tests against body lice by the beaker test method (1), o,o'-DDT and o,p'-DDT gave no kill at 0.2 per cent, whereas p,p'-DDT gave 100 per cent mortality at this concentration.

As compared with p,p'-DDT, the o,o'-DDT isomer was found to be of a very low order of toxicity against the adult and fourth-instar larvae of the common