onic acid excretion. The detection of free rutin in the urine of rats makes it appear that Fukuda's(1) observations on rabbits and Garino's(2) observations on dogs are correct although the routes of administration were different. Our inability to detect hesperidin methyl chalcone in the urine indicates that Kirtley and Peck(6) were correct in assuming that the compound was not excreted in the urine in a free state. Furthermore, the small amount of the compound detected in conjugated form indicates that the compound is either stored or completely destroyed. Our results are contrary to those of Clark and MacKay(5) but the methods of administration of rutin differed. They showed that most of the rutin remained unabsorbed in the intestine after oral administration, whereas we were able to show complete absorption after subcutaneous administration. Such absorption leads to either excretion or biological destruction, and our results indicate that the latter process is the most important in the handling of hesperidin, hesperidin methyl chalcone and naringin and equivalent to excretion in the handling of rutin.

Summary. A study has been made of the metabolism and urinary excretion of rutin, hesperidin. hesperidin methyl chalcone, naringin and phloroacetophenone. Whereas the latter compound is to a large extent excreted either free or combined, the flavonoids, with the exception of rutin, are probably destroyed in the body or converted into other compounds which were not detected by the methods used. Rutin is partially destroyed in the body and partially handled by the usual phenol excretion pathways of sulfate and glucuronide.

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Chronic Toxicity of Ammonia Fumes by Inhalation.* (19857)

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The frequent exposure of industrial workers to ammonia fumes for long periods of time appears to have led to the impression that if the concentration is not sufficient to cause acute damage, then no damage need be anticipated. However, the author has been unable to find in the literature any substantiating evidence from controlled experimentation. In view of the fact that Fazekas(1,2) found that the administration of 50-80 cc of 0.5% ammonium hydroxide orally to rabbits either daily or on alternate days for periods of several months caused a marked increase in size of the suprarenal glands, it would appear desirable to investigate the potential toxicity of ammonia by inhalation. Accordingly, this was done.

Experimental methods. Twelve male guinea pigs were used for experimentation and 6 for controls. All animals were fed Purina rabbit chow supplemented with greens. The con-

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trols were denied food and drink during the periods that the experimental animals were in the gas chamber. All animals were weighed weekly. Exposure to ammonia was for 6 hours per day, 5 days per week. At intervals of 6 weeks 4 experimental and 2 control animals were sacrificed, and hearts, lungs, livers, stomachs, small intestines, spleens, kidneys, and suprarenal glands were removed for microscopic examination. Anhydrous ammonia gas was led from the cylinder of liquid ammonia through a flow-meter into the gas chamber where it was discharged into the air stream from a centrifugal blower. Concentration of ammonia in the chamber atmosphere was measured 2 or 3 times daily by chemical analysis. A chamber concentration of 170 parts per million by volume was sought. By actual analyses the concentration varied between 140 and 200 p.p.m., with only occasional values falling beyond these limits. Henderson and Haggard(3) report the least concentration necessary to be detectable by odor as 53 p.p.m. and to cause immediate throat irritation as 408 p.p.m. Five or 6 members of the laboratory staff inhaled the exhaust fumes from the chamber, and all were of the opinion that no person would remain in such an atmosphere voluntarily for any appreciable period of time because of the disagreeable odor and respiratory distress. Therefore, it appears probable that such a concentration represents an approximate maximum which one might have to contend with as a potential cause of chronic intoxication.

Results. Animals sacrificed after 6 and 12 weeks of exposure showed no abnormalities which could be attributed to ammonia. There were the minor lesions of one sort or another which are common in most laboratory animals and of no special significance. However, those animals which had been exposed to ammonia for 18 weeks exhibited changes which were not observed in the controls nor in others sacrificed after the shorter periods of exposure. There was considerable congestion of spleens, livers and kidneys, and early degenerative changes in the suprarenal gland. The spleens consistently contained larger than normal quantities of hemosiderin, which is taken to indicate increased blood destruction. The upper tubules of the kidneys and in 2 of the 4 animals the lower tubules as well showed fairly marked cloudy swelling with precipitated albumen in the lumens and some casts. In 2 of the animals there was a brownish discoloration of the blood in the vessels of the medulla between the connecting tubules suggestive of the formation of hematin. The changes in the suprarenal glands were not marked, and consisted of swelling of the cells with degeneration of the cytoplasm of the cells of the mid and inner zones. This degeneration was of the nature of a loss of normal granular structure of the cytoplasm giving to it a more nearly homogeneous appearance. The suprarenal glands were not of abnormally large size. Histological studies were made by Dr. G. Z. Williams, Prof. of Pathology, in this institution.

Summary. Exposure of male guinea pigs to an atmospheric concentration of 170 p.p.m. of ammonia for periods of 6 hours per day, 5 days per week for as long as 12 weeks gave no significant evidence of chronic intoxication. However, such exposure for 18 weeks resulted in relatively mild though definite changes in spleens, kidneys, suprarenal glands, and livers, with severity of the changes being most prominent in spleens and least in livers. Hearts, lungs, stomachs, and small intestines showed no consistent changes suggestive of chronic intoxication.

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