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The toxic action of nitrobenzene, with special reference to the cerebellum.**By M. DRESBACH and W. L. CHANDLER.***[From the Department of Physiology and Biochemistry, Cornell Medical College, Ithaca, N. Y.]*

The toxic action of nitrobenzene has been comparatively little studied in an experimental way. The investigations here reported have been in progress about two years. Dogs, cats, rabbits, guinea pigs, white rats and mice, hens, pigeons, frogs, and certain insects and blood parasites have been used. The animals have in all cases been exposed to air saturated with the vapor of the nitrobenzene at various temperatures in a special metal box of forty cubic feet capacity, and so arranged that good ventilation was insured. The periods of exposure varied from one to twenty-four hours, or even longer, as in case of rabbits and guinea pigs; with other animals the exposure was usually much shorter. The effects obtained vary with the type of animal somewhat. In dogs and birds the nervous system disturbances predominate, with lighter dosage, while in the other mammals used blood changes are more prominent, especially in severe poisoning. The details of these variations will be published later. At this time we give only the central nervous system reactions. These are of a type that are associated with cerebellar disturbance especially. Thus, in dogs an early asthenic condition in the limb and neck muscles, staggering gait, typical cerebellar nystagmus, unequal pupils, "circus" movements may be seen. In birds a body attitude and rotating motion of the head are strikingly similar to those in birds with cerebellar lesions. The animals may recover, sustain permanent disturbance of muscular coördination, or die. Symptoms develop at any time up to three or four days after exposure to the vapor.

Histological study of various parts of the brain and cord revealed remarkable chromatolytic changes, apparently confined to the Purkinje cells of the cerebellum, in all animals showing

disturbed coördination. The chromatolysis in these cells seems to be roughly proportional to the intensity of symptoms. In general, the cytoplasm and nuclei swell, often to several times the normal size, the tigroid substance becomes faint and collected around the nucleus, or disappears altogether. Often the entire cell shrinks and disappears completely. In one dog with disturbed motor function resulting from exposure to the vapor several months before the sectioning of the brain no Purkinje cells at all could be found in some parts of the cerebellum. All signs pointed to a permanent lesion. A hen showed a similar permanent effect. In these two cases the fatigued or weakened muscle activity in the legs resembled closely the type said to be associated with lesions of certain cerebellar tracts.

Since the Purkinje cell axones are the only efferent paths from the cerebellar cortex and since the nitrobenzene attacks these cells especially, if not selectively, the results are suggestive. While we cannot claim a specific and direct effect of nitrobenzene on these cells, as far as chromatolysis may indicate it the action is not much in evidence, if at all, in other parts of the nervous system.

Animals poisoned in this way illustrate nicely cerebellar disorders for teaching purposes. They also show in a striking way an instance of delayed development of toxic action of a substance stored in the body. This latent period in nitrobenzene poisoning forms one of its most interesting features and is being studied by the writers. Other interesting problems have been opened up by the work.

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A method for the simultaneous fractional analyses of gastric and duodenal contents.

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It is possible to study simultaneously the duodenal and gastric secretions by the following method: An Einhorn tube is passed into the duodenum of the patient, using the technic of Einhorn. Next