

no effect on the skeletal neuromuscular blockage. An oxime increases the effectiveness of drug therapy in poisoning by some, but not all, cholinesterase inhibitors. Unlike atropine, it acts by reactivating the inhibited enzyme at nicotinic as well as muscarinic sites and therefore relieves the skeletal neuromuscular block (2, 3). The guidance put out by the Department of Defense on the treatment of anticholinesterase poisoning stresses the fact that an oxime is to be used as an adjunct to atropine (4).

Also, we have found that the iodine salt is not the oxime of choice because of its comparatively low solubility in water and because of the possibility of producing iodism. The chloride salt (pralidoxime chloride) has been evaluated extensively and is the oxime of choice for use in combination with atropine (2).

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22 June 1970

My article discusses a basic problem of the molecular biology of excitable membranes. The casual remark referring to the existence of a highly efficient and successful antidote against intoxication by organophosphate insecticides (OPI) was prompted by the present interest in environmental control of pesticides and by the article in *The New Yorker* (1) describing the treatment of an accidental victim of OPI intoxication.

In contrast to atropine, which is toxic in milligram concentrations, pyridine 2-aldoxime methiodide (PAM) is harmless to humans at a concentration of 1 to 2 g. Oximes are widely accepted to be the antidote that repairs the specific biochemical lesion caused by OPI; they reverse the block of acetylcholinesterase, the basic cause of the fatal effects. Atropine helps by protecting the receptor protein against excess acetylcholine, one of the indirect effects of acetylcholinesterase block, but it does not

reverse the inactivation of the enzyme. We demonstrated that animals injected with 10- to 20-fold sure (100 percent) lethal doses of OPI survived when treated with PAM in combination with atropine (2). Also, a series of articles [see, for example, the paper by Namba and Hiraki (3)] have been published describing the success of PAM when applied to severe cases of OPI intoxication of agricultural workers. (In the commercial product, the iodine salt of PAM was replaced by the chloride many years ago.)

A recent article in *Science News* (4) about treatment of OPI poisoning refers to PAM as the "key antidote." Van Sint, the scientific director of the Army's Chemical Warfare Center, emphasizes the crucial role of PAM, whereas in his comment (5) Sim stresses the role of atropine and refers to PAM as an "adjunct" to atropine. The recent deaths caused by parathion (6) would most likely have been prevented if the

physicians had not used atropine alone as the antidote (according to the report), but had used PAM in conjunction with atropine. Although widely used in many other countries, PAM is surprisingly little known to physicians in this country. The article in *Science News* is most timely and fortunate, drawing attention to the lifesaving role of PAM instead of playing it down.

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23 September 1970

Lesch-Nyhan Syndrome: Preventive Control

Our paper "Lesch-Nyhan syndrome: Preventive control by prenatal diagnosis" (1) contained an error drawn to our attention by Dr. Walter E. Nance. The last two sentences should read:

"Thus the diagnosis of index cases is of practical, rather than theoretical, importance in that this information will lead to the identification of heterozygotic mothers who are at risk of bearing additional affected children and raises the need for examination of such mothers as well as other female relatives for evidence of cell mosaicism for the HGPRT enzyme. Theoretically, new mutations not reflected in the

mothers' somatic cells could account for as many as one-third of cases. However, mosaicism has been found in all of the ten mothers so far examined in this laboratory. This disease may now be added to the list of disorders detectable by prenatal diagnosis (13)."

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25 September 1970

Lateralization of Bird Song

Nottebohm (1) has recently published results of experiments in which the hypoglossal nerves serving the syrinx of chaffinches were sectioned unilaterally. When the left nerve was sectioned either of two results occurred, many song elements disappeared completely although a few remained, or alternatively, in place of the absent elements were new patterns which were interpreted as distortions of those formerly present. In contrast, when the right nerve was sectioned

alone only a few elements disappeared.

From these results Nottebohm then speculates on the lateralization of control of song within the central nervous system, and secondly, on the control of song through means independent of the need of proprioceptive feedback once development has terminated. This latter suggestion was made since some elements of the songs appear unchanged after sectioning. It is particularly this latter interpretation which I question.