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More on the Legacy of Atropos, with Special Reference to *Datura stramonium*

To the Editor:—The following material is meant to complement Holzman's article on Atropos.¹ *Datura stramonium*, from the Greek *strychnomanikon* (causing madness),² is another of the atropine-containing herbals.

It is said that Apollo's priestess Pythia, under the influence of *Datura*, had her incoherent responses interpreted by a priest.³ Dioscorides was also familiar with *Datura*⁴:

The root being drank with ye quantity of a dragm, hath ye power to effect not unpleasant fantasies. But 2 dragms being drunk, make one beside himself for three days & 4 being drank kill him. But ye remedy of this is Melicrate, much being drank, & vomited up again.

Porta's *Magia Naturalis* mentions the belladonna alkaloids as useful for making people "... mad for a day, without injuring their health in anyway, for the amusement of guests at feasts."⁵

One must be careful extrapolating animal data to humans. Cat, rat, and rabbit livers have a rapid rate of atropine metabolism. In addition, 20-25% of rabbits have an atropine esterase⁶ capable of inactivating from 1 mg to 20 mg of atropine/cm³ serum. No human correlate exists.⁷

Atropine's mydriatic effects have been used clinically. Hughlings Jackson distinguished belladonna poisoning from postepileptic delirium by placing a drop of the patient's urine into a cat's eye. Subsequent rapid dilatation of the cat's pupil confirmed the diagnosis.⁸ Birds may not be substituted, as their irides are composed of striated muscle.⁹

Atropine toxicity therapy had a surreptitious origin. During medical school, Forrer¹⁰ saw a patient become comatose after receiving presumed procaine for local anesthesia. He later initiated atropine toxicity therapy (32-200 mg atropine sulfate, 4 days a week, for 6-30 treatments) for psychiatric therapy. Patients often had hallucinations and disturbing illusions before going into coma.¹¹ Similar treatments were also used for Parkinson disease,¹² with up to 195 mg hyoscine (scopolamine) used.¹³

In 1700, the founder of American psychiatry dealt with *Datura*.¹⁴ Sixty years later, Storck hinted at the psychiatric use of *Datura*:

If the thornapple, by disordering the mind, causes madness in sound persons, may we not try whether, by changing and disturbing the ideas and common sensory, it might not bring the insane, and persons bereft of their reason, to sanity, or soundness of mind, and, by a contrary motion, remove convulsions in the convulsed.¹⁵

The classic description of anticholinergic poisoning is: "hot as a hare, blind as a bat, dry as a bone, red as a beet, and mad as a hen."¹⁶

Several of *Datura* nicknames have dark overtones: Devil's apple, Devil's trumpet, herbe aux sorciers au de diable.¹⁷

Gerard notes that *Datura* is "of greater use in surgery" and "of a drowsie and numming, qualitie, not inferior to Mandrake." He also relates Theocritus' observations: "... even all the Colts and agile Mares in mountains mad do fall."¹⁸

Other examples of atropine in the popular literature are Castaneda's use of *Datura inoxia* ointment¹⁹ and Hawthorne.²⁰

Finally, *Datura* was used as an anesthetic²¹ 42 years and 3 days before the famous events of the Ether Dome.²²

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Anesthetic Uses of Hyoscine and Atropine Alkaloids in Surgical Arabic Book

To the Editor:—I read with interest Dr. Holzman's recent article concerning the history of atropine alkaloids.¹ This is a very important comprehensive review dealing with old myths that captured the imagination of ancient physicians. The actual use of these alkaloids was not very clear and the article did not give a definite account of their role in surgical practice. For that reason, I would like to note that almost 700 yr ago, an Arab surgeon wrote a complete chapter on pain relief and described the use of *Opium* (Afune), *hyoscine* and atropine alkaloids (Al-Banj). He did not mention mandrake as such. The surgeon was Abul Faradj Ibn Mouafak Eddin Yakoub Ibn Issasc Ibn Al-Koff (born 1232 A.D.) and his book was *Al-Omdah Fi Sinaat Al-Jirabah*.² His words go like this:

And you ought to know that relief for pain is of two types; true and untrue. The former is opposing the cause of pain. . . . With regards to the untrue type it is the anesthetic, it is the one that the surgeon needs in this situation. . . . The first pain reliever, the one which is the true type, is the beneficial with good consequence. With regards to the second pain reliever, even though pain relief occurs with it, and ability to treat is made possible, as much as it decreases pain, it weakens the strength and freezes the substance that causes pain and fixes to the organ, therefore the surgeon shouldn't use it except in a great matter.^{3,4}

This quotation represents a modification of the previously held views, paving the way for "rational" use of these drugs. His remarks are based on previous observations on patients. There are no controlled or statistical arguments in his accounts. However, he does document the

poisonous nature of these agents. He still advocates its use for great tasks (surgery) or "the ability to treat" (by the surgeon, *i.e.*, surgery) to be obtained.

Thank you for this excellent review.

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In Reply:—A sincere thanks to Drs. Lai and Takrouri for supplementary information. Although it is inevitable that an article tracing the mythology and pharmacology of the alkaloids omits much more than it includes, it also affords the author and other interested readers an opportunity to pursue offshoots of the thesis. Dr. Lai's references to the foresight of Dioscorides and Giambattista della Porta are a reassur-

ing reminder that physicians have long yearned to provide pain relief. His mentioning of Dr. Forrer's¹ use of atropine toxicity therapy, which, for the sake of brevity, I only touched upon, is a fascinating preview of our current efforts at trying to understand cholinoreceptors in the central nervous system. The *Datura stramonium* referred to by Dr. Lai has poisonous seeds and berries, with hyoscine a major constituent.