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MEDICAL INTELLIGENCE

NUTMEG INTOXICATION*

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WITH the geometric multiplication of drugs available for use in the 1960's and with the corresponding increase in side effects, toxicity and complications, it is refreshing to report anew a toxic state attributable to a common household spice — nutmeg — used since the Middle Ages. Nutmegs were introduced into Europe by the Arabs in the middle of the twelfth century,[1] and poisoning with this spice was probably documented as early as 1576.[2]

Nutmegs are the dried seed kernels of a tall evergreen tree, *Myristica fragrans,* indigenous to the Molucca Islands of the South Pacific, and now widely cultivated on the Caribbean islands of Grenada and Trinidad. Between 1900 and 1910 the British medical literature contained repeated references to nutmeg poisoning, usually secondary to unsuccessful attempts at abortion; these reports are representative.[2-6] McCord and Jervey[7] recently described an acute case. In the 2 cases presented below, the confessed motivation for ingesting the spice differed from those previously recorded.

CLINICAL SUMMARY

Two male college students, 19 and 20 years of age, were seen in the Student Health Service about 6 hours after each had ingested 2 tablespoonfuls (about 14 gm. or roughly the equivalent of 2 grated nutmegs) of commercially available powdered nutmeg suspended in a glass of milk. This proce-

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dure had been recommended by a "beatnik" acquaintance as providing a mental state somewhat akin to ethanol intoxication, without requiring the use of alcohol.

Approximately 5 hours after swallowing the powdered nutmeg each had the onset of a significant pharmacologic effect, heralded by a leaden feeling in the extremities and a nonchalant, detached mental state described as "unreal" or "dreamlike." Rapid heart rates and palpitation were noted, and both complained of dry mouth and thirst. Onlookers observed that 1 student became quite hyperactive and agitated, and talked incoherently. It was noted that the facies of both were "as red as beets." Nausea, vomiting and abdominal cramps were absent.

Physical examination at this point disclosed 2 hyperactive young men in no acute distress. The skin was quite flushed about the heads and shoulders, but pale and somewhat clammy on the extremities. Pupils were of normal size in 1 and dilated but reactive in the more hypertensive patient. Visual accommodation was not affected. The remainder of the physical examination, including a careful neurologic check, was within normal limits. There were no apparent hallucinations or delusions, but both students were agitated and quite apprehensive throughout the examination. One described a sense of impending doom, as if he were "breaking up inside."

The blood pressures were 170/90 (30 minutes later, 140/84) and 152/84. The pulses were 130 and 148 per minute, and the rhythm strong and regular in both. Temperatures were normal, and the respirations were rapid.

Unfortunately, no initial laboratory studies were obtained. Detailed laboratory studies in the recent case of acute nutmeg poisoning reported by McCord and Jervey[7] were within normal limits. Four weeks after the acute episodes described here, complete blood counts, urinalyses and serum chemical findings — including cholesterol, bilirubin, cephalin flocculation and alkaline phosphatase — were entirely within normal limits.

The initial clinical impression, based upon the history of nutmeg ingestion and the physical findings of flushing, absence of salivation, tachycardia and the dilated pupils seen in 1 patient, was atropine poisoning. Fortunately, the 1st thought — to give pilocarpine — was changed in favor of observation and administration of Epsom salts to empty the bowel of unabsorbed nutmeg.

Extreme drowsiness occurred about 12 hours after ingestion and lasted for the next 24 hours. Both patients stated emphatically that a sense of unreality persisted for 48 to 60 hours from the time of 1 oral dose of nutmeg. Along with decreased salivation, this mental detachment was the last symptom to disappear. Subsequent recovery was uneventful. Regarding the problem of addiction it is pertinent to state that neither would care to repeat this experience, and both described it as unpleasant and somewhat frightening.

Discussion

After early descriptions in pharmacology textbooks of the toxic states associated with the ingestion of nutmeg the literature was sparse for the next fifty years. Dale,[3] in 1909, demonstrated that cats were very sensitive to the toxic effects of myristicin, the chief active principle in nutmeg. Central-nervous-system excitation preceding coma and accompanying fatty degeneration of the liver followed feeding of relatively large amounts to cats. Thus, ironically, a "nutmeg liver" resulted from nutmeg poisoning in cats (Fig. 1)! However, in the case reported by Green,[8] biopsy of the liver revealed no pathologic change. Power and Salway,[9] in 1908, had contributed substantially to the pharmacology of nutmeg. Indeed, Dr. Power[10]

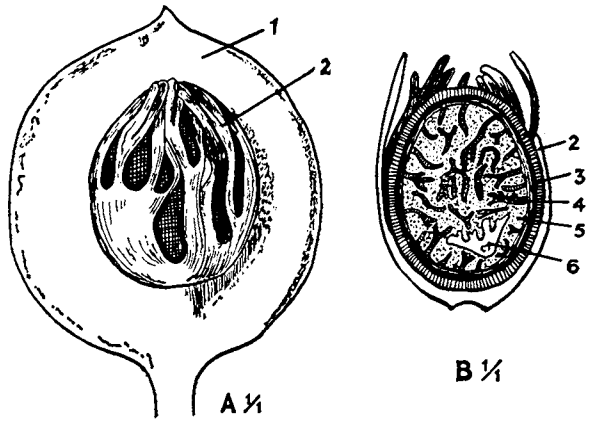

Figure 1. *"Nutmeg Liver" Resulting from Nutmeg Poisoning in Cats (Reproduced from Trease[1] with the Permission of the Publishers).*

A = *the fruit of* Myristica fragrans, *with half the pericarp removed (1), and the aril (2), which in dried form provides the rarer companion spice, mace.*

B = *longitudinal section of nutmeg, showing the reticulated appearance that led to the term "nutmeg liver."*

suggested elsewhere that myristicin alone was not responsible for all the effects of whole nutmeg.

Within the past ten years several scattered references to nutmeg toxicity have appeared in the literature.[7,8,11,12] Symptoms usually appeared three to six hours after the ingestion of one to three whole nutmegs, or 5 to 15 gm. of the grated spice. Striking features common to all these cases, which may be confused with the signs of atropine poisoning, include flushing of the skin, tachycardia, absence of salivation and central-nervous-system excitation. A useful differential clue (not present in the cases reported above but found in most reports) is the early pupillary constriction of myristicin, contrasted with the dilated pupils of the belladonna-type drugs.

An excellent pharmacologic review by Truitt et al.[11] emphasized the bizarre disorder of the central nervous system and pointed out that this effect, which led to the intentional ingestion by the 2 young men described above, was not wholly related to myristicin but to some other volatile principles present in nutmeg. These include eugenol, isoeugenol, geraniol, safrol, borneol and linalool. These writers pointed out the similarity of the structural formula of myristicin, with its indole group, to reserpine and adrenochrome, both serotonin antagonists. Weiss[12] also documented nicely the hallucinogenic and euphoria-inducing effects of nutmeg in prison inmates.

Since the earliest pharmacologic classification of myristicin as an ecbolic oil, or abortifacient, reports in the literature have extensively documented cases of toxicity with uniformly unsuccessful efforts at abortion. Folk medicine has also held that oral ingestion of nutmeg was effective for menorrhagia, boils

and eczema, but the test of time has shown this useful spice to have little medicinal value.

Finally, one wonders if the age-old custom of adding nutmeg to the traditional Yuletide cup of eggnog arose from the psychopharmacologic effect described in these 2 cases.

Summary and Conclusions

Two cases of nutmeg poisoning are reported in college students who took the powdered spice to produce a sense of exhilaration and intoxication. Apparently, this odd pharmacologic effect is fairly well known among the more bohemian elements of the population, as well as alcoholic patients and narcotic addicts whose regular supplies are exhausted. The clinical findings and courses are briefly described. These cases are reported as an interesting example of toxicity caused by a usually benign household condiment.

I am indebted to Dr. Edward McG. Hedgpeth, director of the Student Health Service at the University of North Carolina, for giving me the opportunity to see these 2 patients and for his co-operation in the preparation of this report.

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ACCIDENTAL GLUTETHIMIDE INTOXICATION IN CHILDREN*

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GLUTETHIMIDE is a sedative and hypnotic drug that has gained widespread use since its introduction in 1955. When used in therapeutic doses it appears to be relatively free of adverse effects. However, its margin of safety is rather narrow, coma having resulted in adults from as little as ten times the therapeutic dose.[1] Recently, an unusual neurologic syndrome manifested by cerebellar ataxia, nystagmus, dilated pupils and rapid fluctuations in state of consciousness was observed in 2 children who accidentally ingested only two to four times the therapeutic dose of glutethimide.

Case Reports

Case 1. A 6-year-old girl was admitted to the Children's Hospital Medical Center, Boston, on June 19, 1961, because of drowsiness and ataxia. Three days earlier she had fallen off a fire hydrant and had struck her head in the occipital region. She was not concussed. On the evening before admission unsteadiness of gait was noted. The next morning she was drowsy, and during the ensuing hours several episodes of deep sleep were observed. When aroused, she was unable to sit or stand. There was no vomiting or complaint of headache. The child had been taking penicillin tablets by mouth twice daily for rheumatic-fever prophylaxis. A bottle of glutethimide,‡ containing 500 mg., had been kept next to the penicillin tablets. The mother reported that 1 tablet of the former might have been given by mistake on the afternoon before and 1 on the morning of admission.

On examination the patient's mental status varied from stupor to mild drowsiness. The patient weighed 18.1 kg. The mucous membranes were dry. Both pupils were widely dilated and reacted sluggishly to light. There was marked horizontal nystagmus on lateral gaze in both directions. Vertical nystagmus on upward gaze was noted on 1 occasion. Muscle tone was diminished. There was marked truncal ataxia, the child being unable to sit or stand. Intention tremor of the hands was present bilaterally. Tendon reflexes were hypoactive, and plantar responses were flexor. The response to pinprick was generally diminished.

The temperature was 99.6°F., and the pulse 76 per minute. The blood pressure was 110 systolic, 60 diastolic.

No fracture was observed on roentgenograms of the skull. An electroencephalogram obtained while the patient was stuporous showed an excessive amount of diffusely fast activity (20 to 30 per second), suggesting drug intoxication. The glutethimide blood level, determined by a modification of the method of Goldbaum,[2] was 0.7 mg. per 100 ml. 6 hours after the assumed ingestion of the 2d 500-mg. tablet. The cerebrospinal fluid was clear and under a pressure of 180 mm.

The child improved rapidly. On the next day she was only mildly drowsy and was able to walk. A slight intention tremor and nystagmus were still present, but had cleared completely over the next 24 hours.

Case 2. A 5-7/12-year-old boy (M.G.H. 120-07-78) was admitted to the Massachusetts General Hospital on August 9, 1962, because of lethargy and ataxia. He had been in good health until the afternoon of admission, when he fell from his tricycle. Upon arising he staggered wildly and had to be carried home. He complained of feeling dizzy. The family physician found him to be lethargic and unsteady on his feet and referred him to the hospital.

On admission the patient was awake and euphoric. His speech was slurred. The weight was 18.9 kg. Both pupils were widely dilated and reacted sluggishly to light. Coarse horizontal nystagmus on right lateral gaze and vertical nystagmus on upward gaze were present. There was truncal ataxia, the patient being unable to sit without support. Past pointing and marked unsteadiness were present on finger-to-nose and heel-to-shin testing. The tendon reflexes were symmetrically hypoactive, and the plantar responses were flexor. X-ray films of the skull showed no fracture.

The temperature was 99.2°F., and the pulse 88. The blood pressure was 120/80.

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‡In the form of Doriden, Ciba Pharmaceutical Company, Summit, New Jersey.