

predict the therapeutic equivalence of oxytetracycline.

However, it is apparent that predictions of therapeutic availability cannot be made with precision from *in vitro* experiments in this case. On the basis of our work, acceptable performance in a clinical blood level experiment appears necessary to establish the adequacy of the dosage forms of oxytetracycline.

Comment:—The 16 lots of oxytetracycline tested were procured from commercial sources. They were certified by the Food and Drug Administration and met official specifications. It is of considerable concern, therefore, to find not only significant differences in serum antibiotic levels among these lots, but numerous instances where blood levels achieved are well below the range generally accepted to be clinically effective. We have reported the results to the Food and Drug Administration and have discussed these results with them.

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1. Varley, A.B.: The Generic Inequivalence of Drugs, *JAMA* 206:1745-1748 (Nov 8) 1968.

2. Calesnick, B.; Katchen, B.; and Black, J.: Importance of Dissolution Rates in Producing Effective Diazoxide Blood Levels in Man, *J Pharm Sci* 54:1277-1280 (Sept) 1965.

3. Searl, R.O., and Pernarowski, M.: Biopharmaceutical Properties of Solid Dosage Forms: I. Evaluation of 23 Brands of Phenylbutazone Tablets, *Canad Med Assoc J* 96:1513 (June 10) 1967.

4. Friend, D.G.: Generic Drugs and Therapeutic Equivalence, *JAMA* 206:1785 (Nov 18) 1968.

Fabry's Disease

To the Editor:—The following is a case report of Fabry's disease. The report is submitted for the purpose of aiding in establishing the incidence of the malady. The disease is becoming recognized with increasing frequency.

Report of a case:—This 24-year-old white man relates that he has had a rash about his leg and inguinal areas since early childhood. The patient has been aware of easy tiring and lack of sweating. In addition, he has described episodes of "bone pain" involving the arm and leg, which are brought about by temperature changes and by exercise and generally are relieved by rest. The patient does not recall any episodes of unexplained fever as a child.

The patient's mother, brother, one male cousin, and two great-uncles (one of which died at age 45 of unknown cause) have bone pains and a skin rash allegedly similar to that of the patient. All of the above individuals have descended from the great-grandmother of the patient.

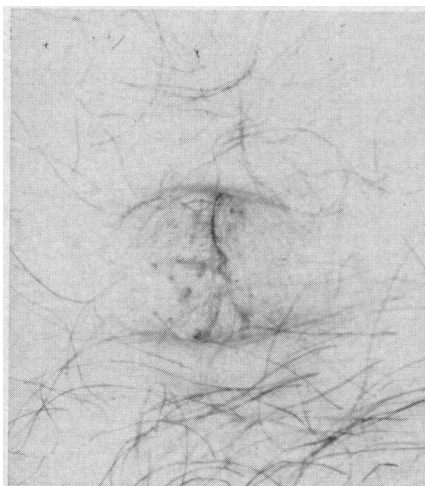


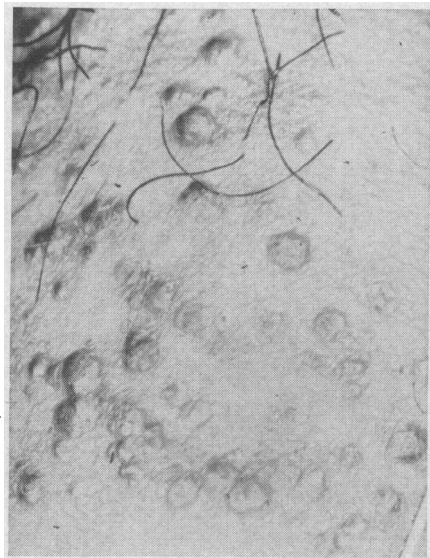
Fig 1

The blood pressure was 130/80. Angiomata were noted in the pubic and perineal areas and were also present in and about the umbilicus (Fig 1 and 2). In addition, angiomata were noted on the oral mucosa and there were telangiectatic lesions of the bulbar and palpebral conjunctiva with tortuosity of the retinal vessels. Slit-lamp examination gave negative results.

Laboratory Data:—Values of complete blood count, electrolytes, blood urea nitrogen, and liver function studies were within normal limits. Urinalysis revealed 2 to 3+ proteinuria and mulberry cells were seen on two separate occasions. Twenty-four hour protein loss was 2 gm/day and a creatinine clearance was calculated to 130 ml/min. A methacholine sweat test revealed little or no sweating as compared to a normal control. Bone marrow examination revealed vacuolated macrophages.

Although Fabry originally described this disorder as a dermatologic

Fig 2



disease only, it has been shown to involve bone marrow, kidneys, and small and medium arteries. Death frequently occurs by the fourth decade and the cause of death is commonly uremia.

The disorder has been shown to be X-linked recessive with complete penetrance in the hemizygote male and there is variable penetrance in the heterozygote female.

Brady et al¹ recently showed the disorder was secondary to a deficiency of a single enzyme, ceramidetrihexosidase, and this deficiency resulted in the accumulation of ceramidetrihexoside which is a breakdown product of globoside, the major glycosphingo lipid in the red cell membrane and kidney. Thus, Fabry's disease takes its place along side other lipid storage disorders, such as Gaucher's disease.

Finally a report of a family in France with a renal disorder with similar histologic and electron microscopic findings to Fabry's disease but without the skin lesion has been reported.² It will be interesting to note if the latter disorder is also due to the same enzyme deficiency.

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1. Brady, R.O., et al: Enzymatic Defect in Fabry's Disease, *New Eng J Med* 276:1163-1167 (May 25) 1967.

2. Hamburger, J., et al: *Nephrology*, Philadelphia: W. B. Saunders Co, 1968, p 811-816.

Catnip and Related Psychedelic Compounds

To the Editor:—Physicians will find in the article (207:1349, 1969) that catnip (*Nepeta cataria*) has been described in the US Dispensary as a treatment for various disorders including amenorrhea. It was official in the *United States Pharmacopeia* from 1840 to 1880 and it was used as a mild stimulant, as an emmenagogue, an agent that induces menstruation, and for its quieting effect on the nervous system.¹

Drugs have been used empirically for the treatment of disease from time immemorial and the lay public is confused by reports of tried but unproven medications. For marihuana, confusion is rampant. In a recent book widely read by enthusiasts and by young people in high school who are seeking information, the editor takes the view that marihuana should be legalized and says in his foreword:

First, marihuana should be accorded the medical status it once had in this

country as a legitimate prescription item.² After 1937, with the passage of the Marihuana Tax Act and subsequent federal and state legislation, it became virtually impossible for physicians to obtain or prescribe marihuana preparations for their patients. Thus the medical profession was denied access to a versatile pharmaceutical tool with a history of therapeutic utility going back thousands of years.

This outlook is bolstered in the text by reference to the use of marihuana for neuralgia, chronic alcoholism, mental depression, hysteria, softening of the brain, nervous vomiting, cough, St. Vitus' dance, spasm of the bladder, migraine, tetanus, locomotor ataxia, uterine bleeding, eczema, and hydrophobia. My reaction on reading the material was, "Quick, bottle it for sale before it loses its effect." Notwithstanding, it is not today a "drug on the market." If definitive, clinical, experimental work substantiates marihuana's therapeutic usefulness, and if it also appears to be superior to other drugs available to the physician, I would suggest that it then be accorded the medical status it once had.

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1. Henkel, A.: *American Medicinal Leaves and Herbs*, Washington, DC: Government Printing Office, 1911.

2. Solomon, D. (ed.): *The Marihuana Papers*, New York: New American Library, 1968.

To the Editor:—The authors mention that catnip is a member of the mint family, Labiatae; thyme and marjoram also belong in this family, and these items are the principal substances used as fillers in cheap or low-grade marihuana. In the same way that lactose is used to cut heroin to increase the monetary return, these substances may be added to marihuana. Some individuals who have never seen or smelled marihuana could not detect any differences when confronted with containers of either of the substances commonly used as spices. In fact, in an experiment conducted by this writer, a group of law-enforcement agents became convinced that the substance they were looking at and handling was marihuana when it was in reality, thyme.

Other members of the mint family have been reputed to have hallucinatory properties. Several years ago, Gordon Wasson described a Central American member of this species which was being used by a local Indian tribe for visionary purposes.

Many members of this family yield volatile substances, but in addition they contain compounds with hydroxyl (both alcoholic and phenolic) radicals. Some of these have local anesthetic properties, eg, menthol, carvone, camphor, etc. Similar local anesthetic substances are known to have central stimulant or depressant properties when administered systemically, so it is not really too surprising when something like catnip is shown to have hallucinogenic properties.

Another member of the mints which may be remembered (and may have been prescribed) by some older practitioners is hedeoma or pennyroyal. This was used for years for its abortifacient properties, and as an emmenagogue. The active ingredient of this plant is pulegone, and it is converted by biochemical reduction to menthol. In smoking catnip (or marihuana for that matter) one is led to wonder what kind of conversions take place under those drastic circumstances of combustion.

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Gaspere Tagliacozzi— Plastic Surgeon

To the Editor:—One sentence in the editorial which might have been more understandingly presented was the statement (207:1343, 1969), "Although Tagliacozzi mentions the possibility of heterologous skin transplants, he found it more practical to select the skin from the patient's own body." If, after *practical*, the words "because of the difficulty in keeping two individuals attached to each other for the requisite length of time" were inserted, this would have given the reason more clearly. Tagliacozzi explains this in book 1, chapter 18, page 59 of his *De curtorum chirurgia per insitionem* (concerning the surgery of deformities by transplantation), Venice, 1597.

In the final paragraph of the editorial, a quotation said to be taken from "the first chapter of Tagliacozzi's treatise," really appears in the epilogue of Mrs. Gnudi's and my book, *The Life and Times of Gaspere Tagliacozzi, Surgeon of Bologna, 1545-1599*, page 331, first paragraph, which is a translation taken from book 1, Chapter 11, page 43, of Tagliacozzi's *De curtorum chirurgia* and not from the first chapter as

stated. Probably our note on page 331, "*De curtorum chirurgia*, I, II, p. 43" was misunderstood.

In the editorial, Tagliacozzi is *Gaspere* but on the cover caption his name is *Gaspari*. The year of his birth is given in the editorial correctly as 1545, in the cover caption as 1546. We expressly used the years 1545-1599 in the title of our book to ensure that 1545 would be recognized as being the year of his birth. We had determined the exact year of Tagliacozzi's baptismal record. Giovanni Antonio Magini's horoscope in *De Astrologica*, Venice, 1607, fixes the actual time of birth as Feb 27, 1545, at 2:33 A.M. The portrait is to be found in the Vittorio Putti (the late great Italian orthopedic surgeon) collection not the Patti collection.

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Pyriform Sinusotomy

To the Editor:—In reference to the letter which described pyriform sinusotomy, John A. Ritter, MD, (207:367, 1969) has described a very simple operation which has proven of tremendous value in the management of patients with carcinoma of the head and neck in their early postoperative phase. In addition, we have found it extremely useful in the long-term management with patients with stroke and any other disabling diseases that preclude insufficient oral intake.

Our technique which is essentially that described by Dr. Ritter, was first described in *Surgery Gynecology and Obstetrics* (125:127, 1967) and subsequently published in the *American Journal of Surgery* in October 1968. Others who have described similar techniques include Ketcham and Smith (*Amer J Surg* 104:682, 1962), C. T. Klopp (*J Cardiovasc Res* 21:490, 1951), Shumrick (*Arch Surg* 94:277, 1967), Weir et al (*Ann Surg* 165:142, 1967), and Woodburn and his co-workers (*Cleveland Clin Quart* 21: 231, 1964).

We certainly agree with Dr. Ritter that this is a valuable procedure but have not extended its use as he has to the management of infants.

Worthy of mention for those employing this technique is that the most crucial aspect is the method by which the tube is secured after placement. The most satisfactory method is a suture of heavy silk or nonabsorbable material near the