other toxic ingredients which are present in the Indians' arrow-poison, and after extensive animal experimentation a product was obtained which seemed safe for human trial. This substance was offered to the medical profession for experimental study under the name of 'Intocostrin'. . . . The typical curare action consists essentially of an interruption of nervous impulses to muscle, this interruption taking place at the termination of the nerve fibres at the muscle cells, and probably consists in a neutralization of the acetylcholine reaction which is the fundamental neuro-muscular stimulation mechanism. . . . There is a good deal of individual variation in patients as to the duration of effect, and this depends also to some extent on the depth of anaesthesia present. Curare affects only the neuro-muscular junction and it is in no sense an anaesthetic agent. . . . Intocostrin is marketed in 5 cc. vials of a sterile aqueous solution which contains 20 mgm. of the pure curare substance to each cc. We have found that 5 cc. (or 100 mgm. of curare substance) is an adequate dose for the average adult. . . . The drug prostigmin, which is allied chemically to physostigmine, apparently bears the closest resemblance to a true physiological antidote of curare. . . . During recent months we have not used curare very frequently, and our total series has grown only to 90 cases simply because we were satisfied with its efficacy and wished to keep it for cases in which it was really needed. . . . According to our present knowledge, curare is simply a powerful but short acting adjuvant to anaesthetic agents, to be used in an unconscious patient to tide one over an emergency situation where complete relaxation is demanded." 10 references.

J. C. M. C.

WALTON, R. P.: *Sublingual Administration of Drugs.* J. A. M. A. **124**: 138–143 (Jan. 15) 1944.

"Recently there were recommendations, both in this country and in England, that morphine be administered sublingually in those wartime emergencies in which hypodermic injections were not possible. The recommendation was challenged and, fortunately, has not been generally accepted. . . . Morphine, codeine and dilaudid have low distribution coefficients (less than 2) and are very slightly soluble in oil. From observations with trained Thierry fistula dogs it has been demonstrated that they do not pass through the oral mucosa to any significant degree. . . . Diacetyl morphine is the only morphine derivative in this group which might reasonably be expected to be effective by this sublingual route. . . . Diacetyl morphine, which by in vitro and by animal experiments clearly indicated the highest degree of penetrability, was not satisfactorily effective in human subjects with relatively extreme doses, and in special mixtures which in some cases were too irritant for ordinary use. . . . Strychnine and picrotoxin both produced convulsions in dogs when simply applied to the oral mucosa. . . . Dangerously large doses would be needed in order to obtain penetration of effective doses through the oral mucosae of human subjects. Epinephrine by sublingual application in dogs does not produce effects in doses two hundred and fifty times greater than the intravenous dose producing recognizable effects. . . . In human subjects, sublingual doses of 3 mg. were without effect although the same subjects showed definite responses to one-tenth that amount by subcutaneous injection. . . .

"Ephedrine exhibits more promising solubility characteristics than epinephrine, but a limited number of

experiments with dogs and with human subjects showed that its degree of penetration was low. Metrazol and hydrocyanic acid can be shown to produce their typical effects in dogs by sublingual administration, but the degree of penetrability is not striking and no effects were obtained in human subjects with relatively large doses. . . . The fat-water distribution coefficient of drugs is a dominant factor in determining their penetrability through the oral mucosa. . . . The majority of drugs . . . do not penetrate the oral mucosa in significant amounts, and it is unsound practice to rely on this technic with any drug whose effectiveness by this route has not been conclusively demonstrated." 50 references.

J. C. M. C.

GUNDERSEN, TRYGVE, AND LIEBMAN, S. D.: *Effect of Local Anesthetics on Regeneration of Corneal Epithelium.* Arch. Ophth. 31: 29–33 (Jan.) 1944.

"Clinically it has been observed from time to time that local anesthetics have an inhibitory influence on the regeneration of corneal epithelium. . . . Heretofore no attempt has been made to determine experimentally whether or not local anesthetics affect the regrowth of corneal epithelium. . . . Guinea pigs (4 for the study of each drug) were used as test animals. . . . The drugs used in these experiments were fresh preparations similar to those in daily use in the clinic of the Massachusetts Eye and Ear Infirmary. These drugs were solutions of 10 per cent cocaine hydrochloride, 4 per cent cocaine hydrochloride, 1 per cent butacaine sulfate, 4 per cent larocaine hydrochloride, 1 per cent phenacaine hydrochloride and 0.5 per cent tetracaine hydrochloride, all containing 0.5 per cent chlorobutanol. One per cent phenacaine hydrochloride and 0.5 per cent tetracaine hydrochloride in ointment form were instilled into the right eyes of the two other groups of guinea pigs. The left, or control, eyes of these animals were treated with ointment base containing no local anesthetic. The experiments for the 10 per cent cocaine hydrochloride and the 1 per cent phenacaine hydrochloride were carried out in duplicate series, and the eyes of the second series of animals were removed at varying intervals for histologic examination. Further studies were carried out to evaluate the influence of tonicity of the cocaine and the tetracaine solutions on the regeneration of corneal epithelium. . . . All of the local anesthetics tested had some delaying effect on the healing process of the corneal epithelium of the guinea pig. This effect is modified in degree by the concentration and the tonicity of the anesthetic agent. The pH is probably not a determining factor, since buffered solutions at a pH comparable to that of the anesthetics used showed relatively little inhibitory action. Of the various anesthetics tested, 1 per cent phenacaine hydrochloride and a hypertonic 0.5 per cent solution of tetracaine hydrochloride were the least toxic to the regenerating epithelium." 3 references.

J. C. M. C.

CHAPMAN, W. P.; ARROWOOD, JULIA G., AND BEECHER, H. K.: *The Analgetic Effects of Low Concentrations of Nitrous Oxide Compared in Man with Morphine Sulphate.* J. Clin. Investigation 22: 871–875 (Nov.) 1943.

"The purpose of this study is to report, on the basis of quantitative studies, that nitrous oxide in low concentration (consciousness not impaired, beyond a slight euphoria) has power to relieve pain comparable to that of morphine and yet does not have the undesirable side effects which limit the use of morphine. . . . Fifteen healthy