

Clinical Trials

Dr. MARC DANIELS spoke on "The Clinical Evaluation of Potential Chemotherapeutic Agents in Pulmonary Tuberculosis." Considerable progress in this type of work had been made during the past five years; it was now possible, in a relatively short space of time, to evaluate scientifically the clinical effectiveness of a new drug for tuberculosis. Before embarking on a large-scale clinical trial of a drug found effective in the experimental animal, it was useful to have preliminary small clinical investigations to study toxicity in man, and to gauge the effect of the drug in observable superficial tuberculous lesions. If results of these pilot trials were promising, a fully organized clinical trial might be justified. The basic methods of trial in pulmonary tuberculosis were: comparison with clinical course before treatment, comparison with untreated controls, comparison with the effect of a known drug, and study of the effect of combination with streptomycin in preventing streptomycin-resistance. This latter method had become a most valuable one; fewer cases were needed than for a trial measuring clinical effect. Dr. Daniels described the various rigorous procedures and the team-work necessary for the proper conduct of a clinical trial. The Medical Research Council trials in England had been made possible only by the voluntary co-operation of a great many expert clinicians and pathologists.

At the final session Mr. T. J. D. LANE described a small trial of B.283 in genito-urinary tuberculosis. Twelve patients had been treated, nine of whom had had nephrectomy. In eight cases not rendered bacteriologically negative by streptomycin four had become negative on treatment with B.283; two, however, had later relapsed. The dose was 1 to 4 grammes a day. The drug, a dark red powder, made patients the colour of a "technicolour Indian." No trial had yet been made of streptomycin in association with B.283. Another drug, B.53, produced by Dr. Barry, had shown some effect in tuberculous cystitis.

Preparations and Appliances

A MACHINE-MILKER FOR THE BREAST

Dr. R. A. RATCLIFF, paediatrician, Oxford Regional Hospital Board, writes: Existing mechanical means of extracting milk from the lactating breast are described as breast "pumps," and by that description they are also condemned. Modern dairy science emphasizes the distinction between lactogenesis and galactopoiesis, and this differentiation has stimulated the study of the latter process, which is the flowing of the milk as distinguished from its secretion. Normal galactopoiesis is characterized by a rise of pressure within the breast, produced by contraction of the alveoli, causing an active flowing of milk from the nipple. Any means of emptying the breast can be physiological only if it promotes this natural reaction.

To devise a mechanical appliance which will have a baby-like action and cause physiological alveolar contraction, completely and comfortably emptying the breast, has occupied my attention for some years. I believe that the response of the lactating breast is the only permissible test of such an appliance, and I have therefore relied solely on the opinion of my patients in its development, not being content with the design until they all declared the action to be "just like a baby." Seven machines of the kind described here have been successfully operated in differing circumstances during the last eighteen months.

The appliance consists of: (1) A cabinet measuring 15½ by 13 by 8 in. (39 by 33 by 20 cm.) containing a vacuum pump operated by a small electric motor running off the mains or off a 12-volt car battery (Fig. 1). Sterilizing equipment is

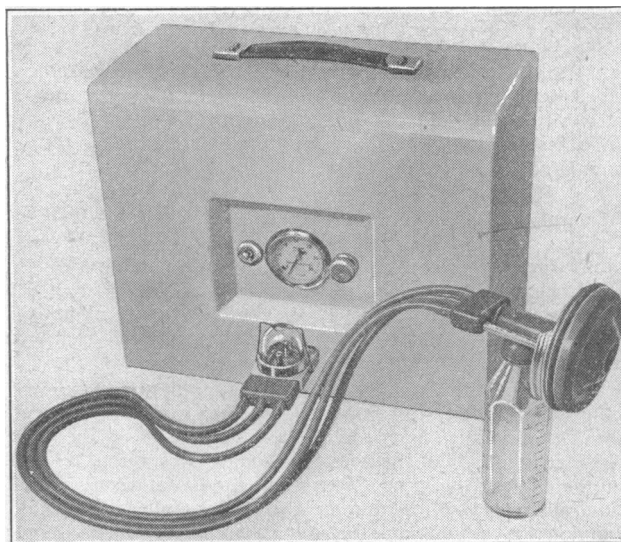


FIG. 1.

provided, and this is stored inside the cabinet. There is also space for storing the other external parts. The pump supplies both a constant and a pulsating partial vacuum. An interceptor to prevent the milk accidentally entering the pump is fitted between the facepiece and the vacuum pump. (2) Three ¼-in. (0.32-cm.) bore rubber tubes carry the vacuum, one constant and two pulsating alternately. (3) The facepiece, which has parts corresponding to the baby's throat, gums, mouth, and face, is built up on a metal base and holds a standard feeding-bottle, so that the constant vacuum reaches the throat and mouth through the bottle (Figs. 2 and 3). On the other side of the metal base is fixed an oval piece of moulded rubber which corresponds to the baby's gums, being moved by the suction operating alternately inside and out. Over all a thin diaphragm of moulded rubber is stretched from the throat behind through the mouth, shaped for the lips, and carried out to the rim, forming the face.

The degree of vacuum is adjustable by the mother, who usually seems to prefer 4 to 5 in. (10 to 12.5 cm.) of mercury. Clear instructions are given that she must not allow the least degree of discomfort.

The constant vacuum sucks milk through the short wide throat into the bottle, and the pulsating vacuum moves the gums and provides: (a) the massaging action of the baby's face; (b) the biting action of the gums; and (c) the regular

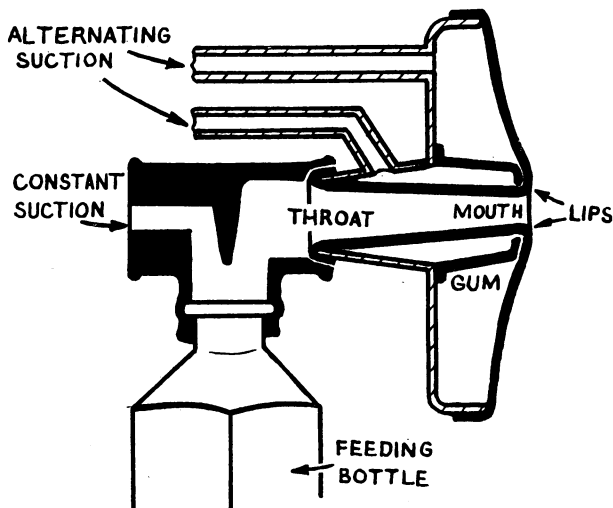


FIG. 2.

squeeze on opposite sides of the nipple produced between the baby's tongue and hard palate. This movement, together with the constant suction along the throat, is exactly that illustrated by F. Charlotte Naish.* Careful attention has been paid to easy thorough cleaning and sterilization by an untrained person, and in this respect the apparatus is designed in accordance with advice obtained from the National Institute for Research in Dairying. The short milk

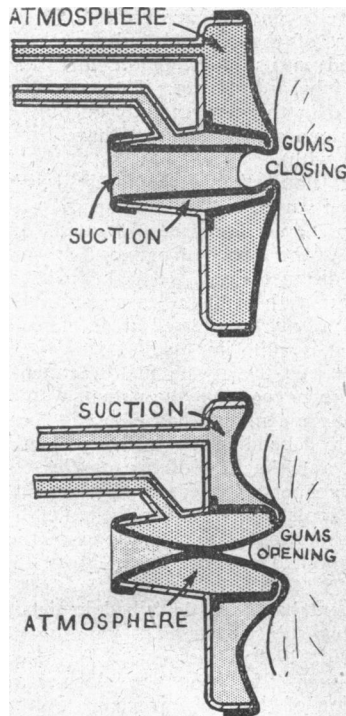


FIG. 3.

passages have no recesses or corners where milk residues may collect, and all parts in contact with milk are readily replaceable. In use, feeds are taken from the breast just as if the appliance were a real baby, but one, moreover, possessing the virtues of patience and gentleness. This feeding is a very comfortable process even in early lactation; the breast is completely emptied, and the yield is steadily increased. A premature baby can be left in hospital after the mother has gone home, and by feeding only to the machine at home the supply of milk is steadily increased. This milk is free from any contamination for taking to the hospital, while the physiological "let down" encouraged by the appliance makes the baby's feeding very easy even at the first attempt. Similarly, the appliance will comfortably maintain lactation if a baby requires admission to hospital without his mother or if a baby cannot suckle by reason of cleft-palate or other causes.

Where such abnormalities as delayed lactation, depressed nipples, or mastitis are present the painless action has been found to save the breast-feed in cases in which it would otherwise have been lost.

The machine is made for me by Gascoignes (Reading) Ltd., Reading.

**Breast Feeding*, p. 26. 1948. Oxford University Press, London.

The world's population has increased by 826,000,000 since the beginning of the present century, nearly half of this total being contributed by Asiatic countries, according to a statistical study made by the World Health Organization. In addition, the study shows that the world population has nearly quadrupled in the last three centuries and that two-thirds of this increase has occurred within the last century alone. Of the 52 countries listed, only one—the Republic of Ireland—has actually shown a decrease (7%) during the first half of this century. The population went down from 3,200,000 to 3,000,000. The largest percentage increase of all was registered in Argentina, where the population rose by 251%. Argentina is followed by Cuba (231%), Colombia (217%), and Brazil (191%). On the whole, the American continent has recorded the greatest relative increase during the past fifty years, whereas the rate of increase has been slower in Europe than anywhere else. The population of Europe rose only 36% (not including the U.S.S.R.) during the half-century under review.

Correspondence

Lung Carcinoma Statistics

SIR,—In answer to a Parliamentary question (June 28) the Minister of Health is reported (July 7, p. 60) to have replied: "Deaths recorded as due to carcinoma of the lung were 2,121 males and 694 females in 1940 and 3,720 males and 807 females in 1949." This answer, it appears to me, will inevitably be misinterpreted and lead to confusion, for the figures given are very different from those published by the Registrar-General of England and Wales. For 1949 they are, in fact, less than half those given by the Registrar-General under the customary heading of "cancer of the lung and pleura."

The explanation of this difference cannot lie in the exclusion by the Minister of the few deaths specifically ascribed to the pleura, and it is impossible to believe that "carcinoma" would be interpreted in such a narrow pathological sense as to exclude deaths described on the certificate as due to "cancer." It must be presumed, therefore, that the Minister has omitted from his totals the large numbers of deaths which are attributed to cancer of the bronchus. This sub-group does not appear separately in the reports of the Registrar-General, for, as in the *International List of Causes of Death*, it has invariably been classed with cancer of the lung. Since, however, these descriptions are used interchangeably in ordinary medical parlance it is clearly necessary to take the two sub-groups together when considering the number of deaths "due to carcinoma of the lung."

The figures required to answer the question by Dr. Barnet Stross are, therefore, those published by the Registrar-General under "cancer of the lung and pleura"—namely, 4,047 males and 1,180 females in 1940 and 9,327 males and 1,945 females in 1949. Not only, it will be seen, are these figures very much greater than those given by the Minister, but they reveal also an appreciably steeper increase over the ten years.—I am, etc.,

London, W.C.1.

A. BRADFORD HILL.

** The Minister confirms that he excluded cancer of the bronchus from his totals.—ED., *B.M.J.*

Infective Hepatitis

SIR,—It may be of interest in connexion with Dr. L. E. Glynn's article (May 26, p. 1198) to note the frequent occurrence of bilirubinuria without significant elevation of serum bilirubin in the pre-icteric stage of infective hepatitis. This was described by Budd in 1846 (*Diseases of the Liver*, p. 368, Philadelphia, Lea and Blanchard), but it is unusual for bilirubinuria to be so gross as to be detectable on inspection of the urine. Using the simple tests for bilirubin in urine, this phenomenon has been observed (Pollock, M. R., *Lancet*, 1945, 2, 626) in as many as 86% of cases, and thus is of some diagnostic value. For this purpose the methylene-blue test has been used successfully (Gellis, S. S., and Stokes, J., jun., *J. Amer. med. Ass.*, 1945, 128, 782), and it has the merits of simplicity and high sensitivity; but the more complicated Fouchet test has the added advantage of freedom from false positive results.—I am, etc.,

Glasgow.

A. G. BAIKIE.

Combined Reductions of the Lower Jaw and Nose

SIR,—In their very lucid article (July 7, p. 26), Mr. P. Clarkson and his colleagues agree that a combination in one operation of bilateral osteotomies of the mandible together with a nasal reduction causes anxiety in the post-operative period. This combination of procedures is liable to cause extreme anxiety and is therefore contraindicated. These two operations can be performed with a suitable time interval, when a good airway can be maintained throughout treatment and the same final result obtained.—I am, etc.,

St. Thomas's Hospital, S.E.1.

RICHARD BATTLE.