

the tank so that either cell may be rolled into position in front of the windows for observation. Spherical joints can be added to pre-existing equipment if the supports for the electrode vessels are given slight horizontal freedom. A method for making cells has been published (5). Pyrex glass plates, of course, must be used for cementing to the spherical joints.

The cells and holders have been used successfully for several years in an electrophoresis apparatus using parabolic mirrors in the optical system, as described elsewhere (4).

References

1. LONGSWORTH, L. G., CANNAN, R. K., and MACINNES, D. A. *J. Amer. chem. Soc.*, 1940, **62**, 2580.
2. LONGSWORTH, L. G., and MACINNES, D. A. *Chem. Rev.*, 1939, **24**, 271.
3. SVENSSON, HARRY. *Ark. Kem. Min. Geol.*, 1946, **22A**, No. 10.
4. SWINGLE, S. M. *Rev. sci. Instr.*, 1947, **18**, 128.
5. WRIGHT, G. G., JR., and SWINGLE, S. M. *Science*, 1943, **97**, 564.

Administration of Micronized Therapeutic Agents by Inhalation or Topical Application

GEORGE V. TAPLIN and FRED A. BRYAN

Department of Medicine, University of Rochester School of Medicine and Dentistry, and Medical Clinics, Strong Memorial and Rochester Municipal Hospitals, Rochester, New York

There are many disadvantages to the present method of administering therapeutic agents by the aerosol principle. The major objections are: (1) the wasteful, expensive, and unnecessary use of oxygen merely as a source of pressure; (2) the fact that the manual methods are time consuming and tiring (20-30 minutes/dose); and (3) the fact that the penicillin solutions used deteriorate rapidly and must be kept refrigerated to retain full potency for one week.

A small ball mill (Fig. 1) has been built, using readily available materials, which will grind various therapeutic agents to a micronized state in two hours. The material is then bolted through fine-meshed silk bolting cloth. When 40-50 grams of the mixture is prepared by use of this apparatus, the loss is less than 10 per cent.

Several modifications of the apparatus for administration of the smoke have been devised. The final apparatus is shown in Fig. 2. The lower chamber contains drierite, which is a dehydrating substance (anhydrous calcium sulfate), with an indicator which turns from blue to pink when it has picked up all the moisture it can. The lower chamber is filtered on both ends to prevent the drierite from being blown into the smoke-producing chamber or from being drawn into the air-intake opening. The smoke chamber has been built with a small surface area to increase the emptying efficiency. The air vents into this compartment are placed at an acute angle to force the powder into a spiral path in order to create turbulence. The outlet tube is likewise made of small internal caliber to reduce the amount of precipitate on the walls of the tube. Various adapters (nasal, oral, dental, vaginal, etc.) can be fitted to the outlet tube. This equipment can be used as it stands or fitted with a rubber mouthpiece. In other words, no bulb is necessary, but the exit tube or rubber mouthpiece can be placed in the mouth, and, by inhaling through the apparatus, the finely divided therapeutic agents can be drawn into

the lungs. Efficiency studies indicate that, when used correctly, the apparatus will deliver in the smoke form 95 per cent of the

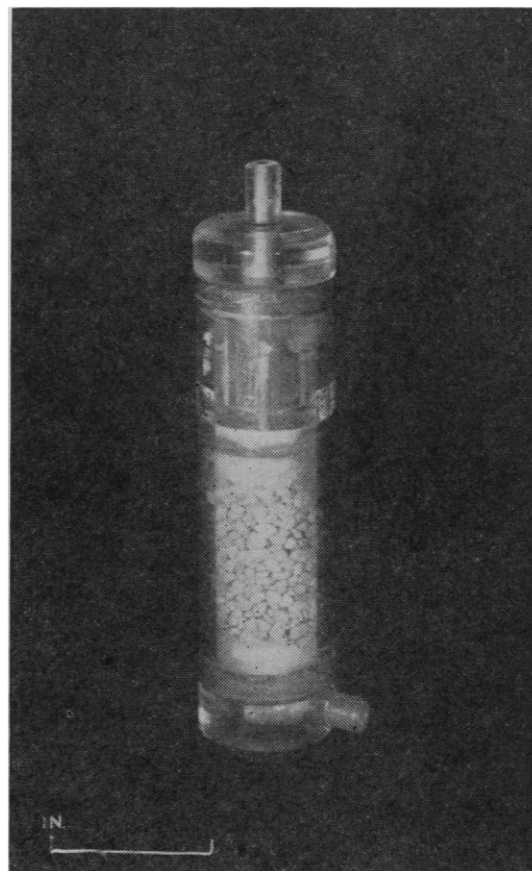


FIG. 1. The ball mill.

therapeutic agent originally placed in the cup and may be administered by the patient in from two to four minutes.

A disposable apparatus containing the principles of the smoke chamber may be molded very inexpensively by the

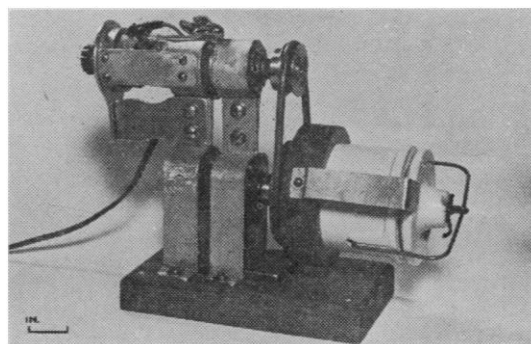


FIG. 2. The apparatus.

use of one of the transparent plastics. This apparatus may be used as both container and dispenser for the penicillin or other therapeutic agents.

Blood penicillin concentrations were determined by the

method described by Wolahan and Cutting (1). Results on the blood levels in subjects inhaling various doses of the micronized potassium penicillin-glucose preparation are shown in Table 1.

TABLE 1

Patient	Dosage (units of crystalline penicillin)	Interval after administration	Concentration (units/cc. citrated whole blood)
C*	30,000	$\frac{1}{2}$ hr.	.03
		1 "	.03
T*	30,000	$\frac{1}{2}$ "	.06
		1 "	.03
R*	50,000	$\frac{1}{2}$ "	.03
		1 "	.03
		2 "	.015
S*	50,000	$\frac{1}{2}$ "	.06
		1 "	.03
		2 "	.03
		3 "	.03
L	25,000	$\frac{1}{2}$ "	.015
		1 "	.015
		2 "	.015
M	30,000	1 " 20 min.	.06
		2 "	.06
P	30,000	1 "	.06
		2 "	.03
B	160,000	1 "	.06
		2 "	.03
		4 "	.03
		6 "	.03
		8 "	.03
		10 "	.03
		12 "	.00
O'N	90,000	$\frac{1}{2}$ "	.125
		1 "	.06
		2 "	.06
		3 "	.03
		4 "	.06
H	90,000	$\frac{1}{2}$ "	2.000
		1 "	.125
		2 "	.125
		3 "	1.000 (P)
		4 "	.060
		5 "	.060

* Normal controls. Penicillin and penicillinase controls were performed.

In all cases except one (L) where 25,000 units or more were administered, a therapeutic concentration was obtained in $\frac{1}{2}$ hour and maintained for about 3 hours. After large doses (B and O'N) the therapeutic levels are maintained for approximately 10 hours. In two cases studied it was found that 10-15 per cent of the dose administered was excreted in the urine in the first hour.

Any soluble therapeutic agent which can be produced in the solid state or which can be chemically precipitated or physically combined with glucose, β -lactose, lactose, etc. may be micronized and used in the manner described. Some of the agents meeting these requirements are: the sulfonamides; antibiotic agents such as penicillin and streptomycin; hormones such as insulin and estrone; antihistamine drugs such as

Benadryl; vasoconstrictors such as neosynephrine and ephedrine; narcotics such as codeine and dilaudid; biologicals such as immune human globulin, vaccines, etc.; various medicinal compounds such as cough mixtures; and numerous others. These materials may be used individually or in compatible combinations, with or without a vehicle.

In certain diseases principally those in which a high local concentration of the agent at site of the infection or reacting organ is of great importance, this method of therapeutics is particularly advantageous. These include certain diseases of the respiratory tract, topical application where indicated, allergic states, and urinary tract infections. The method is also useful in the prophylaxis of venereal diseases, acute rheumatic fever, common carrier states, and the prevention of postoperative pulmonary infections.

This method of administering penicillin glucose mixtures has been used in more than 40 cases of various diseases where penicillin therapy was indicated. The clinical and bacteriological response to treatment has been excellent. Patients prefer this type of treatment to injections or aerosol. By the incorporation of from 2 to 5 mg. of Benadryl/dose of penicillin glucose mixture (200 mg.) there have been no local sensitivity reactions to penicillin in the last 35 cases.

This preliminary report is presented for the purpose of stimulating further study of the method described. Several studies of the suggested applications of the method are in progress at the University of Rochester School of Medicine and Dentistry by members of various departments of the University.

References

1. WOLAHAN, M. B., and CUTTING, W. C. *J. lab. clin. Med.*, 1945, 30, 161.

A Simple Device to Increase Background Contrast in Photomicrography

ROY J. PENCE¹

*Division of Entomology,
University of California, Los Angeles*

In the photography of small insects it has been considered necessary in this laboratory to find a means of intensifying the blackness of the background. A simple microscope attachment was therefore constructed to make possible the desired contrast between the photographed object and the background. This device, which is essentially the physicists' "black body," consists of a cavity with a small opening and with interior walls of low reflectance. The opening is placed beneath the specimen to be photographed and provides a background of very nearly zero reflectance, since the light that enters the opening is absorbed within the cavity.

To construct this cavity, it was found convenient to use the black bakelite cover of a microtessar lens container, but any cylinder of comparable dimensions and lined with a nonreflective black substance should be satisfactory. A disk of black photographic paper with a $\frac{1}{4}$ -inch hole cut in its center was glued over the open end to provide the small opening referred to above. This simple device will ride on the condenser lens and can be elevated into position immediately below the

¹ The writer wishes to thank R. E. Worley, of the Physics Department at this University, for his review and criticism of this paper.