Warburg respirometer. All determinations were made in duplicate.

From Table 1 it is seen that the measured xanthine oxidase activity of rat liver is decreased approximately 50 per cent. when the protein in the animals' diet is reduced from 25 per cent. to 20 per cent. When the protein level is lowered to 10 per cent., the measurable xanthine oxidase activity is almost (if not completely) lost.

TABLE 1

EFFECT OF PROTEIN INGESTION ON LIVER XANTHINE OXIDASE ACTIVITY

Group	Number of determinations	Xanthine oxidase activity* Range	Average
Stock—25 per cent. protein	4	1,190–1,690	1,420
20 per cent. casein	4	675–918	745
10 per cent. soybean oil meal	4	0–168†	42
10 per cent. distillers' solubles	5	0–100†	20

* Xanthine oxidase activity is given in cu. mm of oxygen taken up in one hour (during the linear portion of the reaction—endogenous uptake subtracted) per gram of dry weight of tissue.

† In several instances the O_2 uptake for the endogenous sample was slightly greater than for the sample with added xanthine.

We wish to thank Miss M. Mueller for assistance in this study.

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THE INHIBITING EFFECT OF QUINONES ON THE GROWTH OF PENICILLIUM NOTATUM

IN the past few years different investigators have studied the inhibitory effect of certain substances on fungi,[1] both saprophytic and pathogenic. Special attention has been given to the inhibitory effect of antibiotic agents, as tyrothricin, pyocyanine and hemipyocyanine on pathogenic fungi.[2] The remarkable antibacterial action of quinones has attracted the attention of various authors.[3,4,5,6] These substances, especially vitamin K, have been suggested as a preventive agency against dental caries,[7,8,9] on account of their capacity to prevent the formation of acids in the buccal cavity.

While investigating the metabolism of *Penicillium notatum*, we became interested in studying the effects of certain quinones on the growth of this mold. The following quinones have been used: 2-methyl-1,4-naphthoquinone, hydroquinone and benzoquinone. We also included β-methylnaphthalene in view of its structural similarity to vitamin K.

The substances were added in the desired concentrations to the Czapek-Dox medium which was sterilized by the Seitz filter; the pH was 6.5. The flasks were inoculated with the strain of *P. notatum* 9178 and incubated at 25° C. Results are given in Table 1.

TABLE 1

THE INHIBITING EFFECT OF QUINONES ON THE GROWTH OF PENICILLIUM NOTATUM

	Chemical substances added (mg per 100 ml Czapek-Dox medium)					
	50	25	10	2.5	1.25	0.625
2-Methyl-1,4-naphthoquinone	0	0	0	0	0	1
Hydroquinone	0	0	0	0	1	3
Benzoquinone	0	0	0	1	2	3
β-Methylnaphthalene	2	3	3	3	3	3

0 = no growth; 1 = limited growth; 2 = regular growth; 3 = abundant growth.

In our experiments all the three quinones, even when highly diluted, revealed their capacity of inhibiting the growth of *P. notatum*. The synthetic vitamin K was more active than the other two quinones. Since hydroquinone and benzoquinone have no vitamin activity, our results also suggest that this inhibitory action is a quinone function independent of the capacity to act as vitamin.

β-methylnaphthalene, in spite of being structurally so similar to 2-methyl-1,4-naphthoquinone, had no inhibiting effect on the growth of the mold.

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SCIENTIFIC APPARATUS AND LABORATORY METHODS

FILTRATION OF CITRATED PLASMA

IT has long been apparent that filtration is the only safe and effective method for the sterilization of citrated plasma. However, all previous work has shown that it is practically impossible to filter large amounts of plasma through the usual bacterial filters.

[1] J. E. Kempf and W. J. Nungester, SCIENCE, 100: 411, 1944.

[2] J. L. Stokes, R. L. Peck and C. R. Woodward, *Proc. Soc. Exp. Biol. and Med.*, 51: 129, 1942.

[3] S. A. Waksman and H. B. Woodruff, *Jour. Bact.*, 44: 373, 1942.

[4] A. E. Oxford and H. Raistrick, *Chem. and Ind.*, 61: 189, 1942.

[5] A. E. Oxford, *Chem. and Ind.*, 61: 128, 1942.

[6] W. D. Armstrong, W. W. Spink and J. Kahnke, *Proc. Soc. Exp. Biol. and Med.*, 52: 136, 1943.

[7] L. S. Fosdick, O. E. Fancher and J. C. Calandra, SCIENCE, 96: 45, 1942.

[8] J. C. Calandra, O. E. Fancher and L. S. Fosdick, *Jour. Dent. Res.*, 23: 31, 1944.

[9] W. D. Armstrong and J. W. Knutson, *Proc. Soc. Exp. Biol. and Med.*, 52: 307, 1943.

When filter candles were employed, it was found that the plasma tended to clot during filtration and that the pores of these filters quickly became clogged, even though every effort was made to clarify the plasma before filtration. When the so-called "Seitz" or asbestos-composition pads were used, a laborious system for washing the pads or an arrangement of multiple pads was necessary to filter relatively small amounts of plasma without fear of clotting.

Bushby, Buttle and Whitby reported that with a 14 cm Seitz filter, an "S. B. Sterilmat" pad and a negative pressure of 20–25 mm mercury, approximately 500 cc of plasma could be filtered without clotting.[1] Very soon after this amount had been exceeded, clots began to appear in the filtrate; and if as much as 1,500 cc was filtered, the pad became completely blocked with clots. But the amount that could be filtered might be increased by preliminary clarification of the plasma, by wetting the pads before they were autoclaved, by washing the pads with sodium citrate solution before and between the filtration of amounts of about 500 cc and by using a combination of positive and negative pressures.

Macfarlane, Mainwaring, Macsween and Parish described a method for the filtration of citrated plasma which required a large number of asbestos pads.[2] Using fourteen 20 × 20 cm pads, they found that not more than 16 liters of citrated plasma could be filtered if clotting was to be prevented. This amount represents only 3 cc of plasma per square centimeter of filtering surface.

With a specially prepared asbestos-composition pad which permits rapid filtration without clotting, we have developed a method for the filtration of plasma on a large scale.[3] Using a single 14 cm pad and a pressure of 15–20 pounds, we have been able to filter as much as 15–18 liters of plasma without any evidence of clotting. A 14 cm pad has an effective filter surface of 126.6 square centimeters so that this amount would represent approximately 120 cc–145 cc of plasma per square centimeter of filtering surface. Accordingly, if six 20 × 20 cm pads having an effective filter surface of 2,103 square centimeters are arranged in a filter press, it should be possible to filter at least 249 liters of citrated plasma or 41.5 liters through a single 20 × 20 cm pad.

The technique for the filtration of citrated plasma described below was developed primarily for fresh plasma, plasma separated from the red and white cells within 48 hours from the time of bleeding and intended either for freezing or drying.

Blood is received in the standard Red Cross Donor bottles which contain 50 cc of a 4 per cent. solution of sodium citrate for each 500 cc of blood. It is handled in the manner prescribed by the National Institute of Health.[4]

After centrifugation, the plasma is drawn off and pooled. A preservative is added. Then the material is filtered. The final yield of plasma from a bleeding is approximately 300 cc, of which 50 cc is citrate.

A 2,800 cc standard stainless steel Hormann filter, utilizing a 14 cm pad, has been used in this work.[5] However, there is no reason why multiple-plate filters can not be used. A clarifying pad (designated as a K6) and a sterilizing pad (designated as an S6) are placed together in the filter, the K6 pad on top of the S6 pad.[6] The pads need not be washed before they are used. To prevent the asbestos from flaking, a stainless steel screen is placed over the K6 pad. Another stainless steel screen is set on the outlet plate under the S6 pad to insure support. A two-holed size 11½ rubber stopper, one hole for the filter outlet plate and the other for a stainless steel bend to which is attached a bacteria-excluding cotton air filter arrangement, completes the filter unit assembly. The filter unit assembly has been designed to fit into a 20-liter carboy. (See Fig. 1).

The entire filter unit is wrapped and sterilized by autoclaving at 125° C. for one hour. It is advisable to leave the unit loosely assembled during autoclaving in order to avoid distortion of the pads. After autoclaving, the filter and the rubber stopper are introduced under aseptic precautions into a sterile 20-liter carboy. The unit is tightened before the plasma is allowed to flow into the receiving chamber. It should be tightened again soon after the plasma has wetted the pads.

The plasma that is to be filtered is placed in a water bath and warmed to 35°C.–37° C. Warmed to this temperature, plasma under pressure of 15–20 pounds filters rapidly, usually at the rate of 5–7 liters per hour. Vacuum is applied through the air filter arrangement whenever plasma is being introduced into the receiving chamber. After the chamber has been filled, pressure is applied and the vacuum may or may not be continued. Being treated thus, the plasma does

[1] S. R. M. Bushby, G. A. H. Buttle and L. E. H. Whitby, *Lancet*, 239: 131–132, 1940.

[2] R. G. Macfarlane, B. R. S. Mainwaring, J. C. Macsween and H. J. Parish, *Brit. Med. Jour.*, 1: 377–381, 1942.

[3] We are indebted to Mr. Warren F. Moore, of Republic Filters, Paterson, N. J., for his cooperation in the development of these pads. In the process of manufacture the pads are treated in such a manner that they have a calcium content of less than 0.01 per cent.

[4] "Minimum Requirements for Unfiltered Normal Human Plasma." 4th revision, May 1, 1944. These minimum requirements must be observed by all processors of normal human plasma for the Military.

[5] Manufactured by the F. R. Hormann Company, Brooklyn, N. Y.

[6] These specially treated pads are available through Mr. Warren F. Moore, Republic Filters, Paterson, N. J.

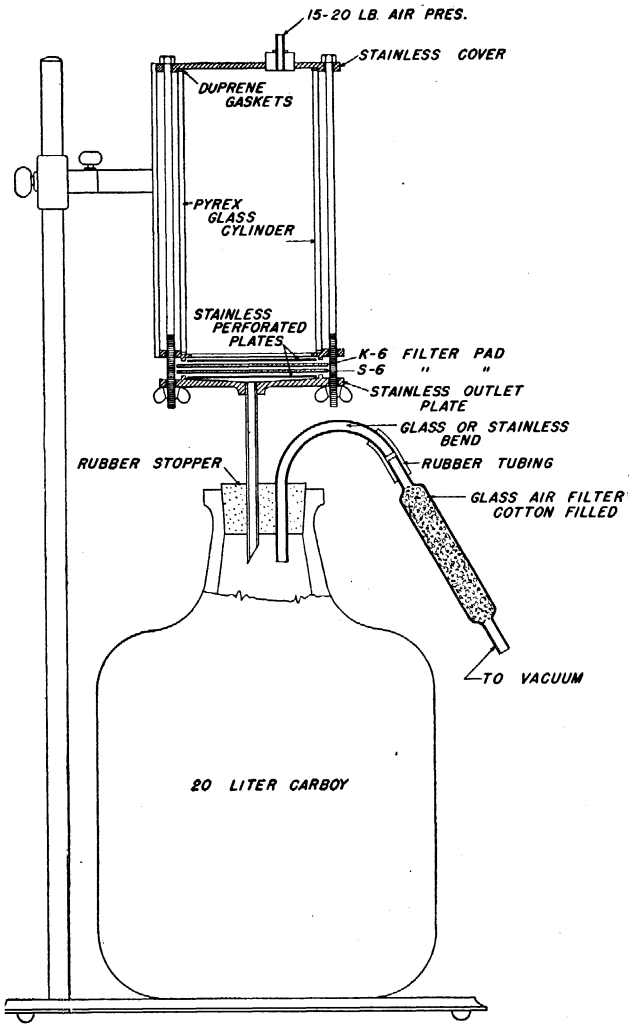

FIG. 1

not remain in contact with the filter pad for any great length of time, an additional precaution to avoid clotting.

When filtration has been completed, the plasma is immediately transferred to final containers and frozen. It has been found desirable that the filling and freezing processes be done within 3–4 hours after filtration.

Over 200 lots, each lot consisting of 15–18 liters of citrated plasma, have been filtered by this method without a single contamination of the final bulk material.

Chemical studies indicate that there is no apparent difference between filtered and unfiltered citrated normal human plasma. These studies will be reported in detail later, but one interesting point may well be mentioned here. It is found that this method of filtration removes traces of red cells so fine that they escape detection by the naked eye.

Summary: Large amounts of fresh citrated plasma can be filtered easily through specially prepared asbestos-composition pads without clotting. A description of the technique is given.

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EFFICIENT HANDLER FOR SMALL MAMMALS

THE author devised this apparatus shown in Fig. 1 which has proved to be extremely useful when rats are

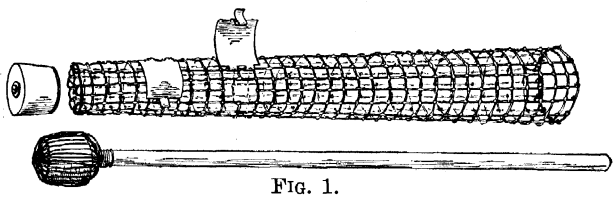

FIG. 1.

wild and hard to manage. It was first used to handle large numbers of rats and mice in feeding and inoculating experiments without the use of anesthetics. The device has been used for a number of years at the University of Illinois and is now being used in several other universities.

The gadget consists of a wire cloth cone 18 inches long of half-inch mesh for use with rats; a quarter-inch mesh is better for mice. The large cone here described is $2\frac{3}{4}$ inches in diameter at one end and tapers to $1\frac{3}{4}$ inches at the opposite end. Wires are clipped out at convenient places near the small end and a sheet metal door with a fastener covers this opening. A wooden plunger handle to which is screwed a large plunger cork tipped with a sheet metal disk and another large stopper cork with metal disk complete the essential equipment. To insure free movement in the cone the plunger cork may be wrapped with wire.

To use the instrument insert the stopper cork in the small end of the cone and place the large end into the animal cage so as to crowd the animal into a corner. Slip the end of the cone over the head of the rat or mouse while holding the cone at about a 45° angle. In attempting to escape the animal will run quickly up the incline to the stoppered end. The plunger is inserted at once and the animal is ready for use. The animal is freed into its cage by pulling the stopper cork and if necessary by stimulating its exit by means of the plunger.

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