AIR FILTERS FOR SMALL-SCALE ASEPTIC UNITS

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In the last few years the importance of air hygiene has become increasingly recognised; many procedures now need to be carried out in dust-free atmospheres and in some cases in air completely freed from micro-organisms. This importance is reflected in numerous publications, in particular in the Medical Research Council Special Report, "Studies in Air Hygiene[1]," in the American Association for the Advancement of Science monograph, "Aeriobology[2]," and in the symposium "Air Disinfection and Sterilisation" organised by the Microbiology Group of the Society of Chemical Industry[3]. Although much attention has been given to other aspects of sterilisation procedures, relatively little work seems to have been done on the performance of filters for supplying bacteria-free air and it is the purpose of this paper to consider the efficiencies of some available commercially, particularly of those used in small units, e.g., for the single unit "sterile" room.

Filtration is one of the several methods which might be considered and is the one which has proved most practicable for this purpose. Other methods include washing with water containing a germicide, electrostatic precipitation, high pressure compression with filtration and treatment with ultra-violet radiations or with a bactericidal aerosol or vapour. The first three of these require large and expensive installations; ultra-violet light treatment is unsuitable because of its relative slowness in action, its limited range of activity and ineffectiveness against bacterial spores and other protected organisms (see, for example, Bourdillon *et al.*[4] and Mellors[5]), and bactericidal aerosols are impracticable when required for continuous use.

A filter for the purpose under consideration should have a high filtration efficiency combined with an adequate air flow capacity and low back pressure, and those most generally used are of a fibrous construction. Glass wool, cotton fibres and slag wool are the materials usually used, and there is little doubt from the published work of Terjesen and Cherry[6] and later of Cherry, McCann and Parker[7] that slag wool is the most effective. However, it suffers the considerable disadvantage of having a high resistance to air flow, and is thus unsuitable for many installations and is precluded from the present discussion.

The interstices of all fibrous filters are relatively coarse in terms of the sizes of particles to be filtered and it follows, therefore, that the mechanism of filtration is not dependent simply on mechanical sieving. Considerable theory on the factors governing the efficacy of filtration of aerosol particles has been proposed in recent years. Of all those considered, the most important according to Stairmand[8] are the impingement and diffusion factors. Efficiency of filtration may be expected, therefore, to vary with rate of air flow as well as with mass or size of particles to be filtered. The published experimental evidence in support of the theories, particularly with bacteria used as test particles, is unfortunately scanty. Phillips[9] claimed that bacteria-free air supplies could be obtained continuously over periods of several months with glass-wool filters with flow capacities of from 1 to 600 cu. ft./minute; Yaglou and Wilson[22] claimed an efficiency of 40 to 60 per cent. with oiled glass or steel wool filters against normal air-borne organisms; DallaValle and Hollaender[11] with several commercial filters found efficiencies of 65 to 80 per cent. against spores of the hay bacillus, and Decker *et al.*[12] obtained a 98 per cent. efficiency with a special spun glass filter and later claimed an efficiency of over 99 per cent. with a similar filter with a flow capacity of 250 cu. ft./minute against *Serratia indica* and *Bacterium coli* bacteriophage. The considerable discordance between these results arises probably because they were obtained somewhat empirically under fixed conditions of air flow, bacterial infection, etc., and no attempt was made to examine the filters systematically. On the other hand, Terjesen and Cherry[6], working with a specially constructed oiled glass silk filter, and Kluyver and Visser[13], working with carbon granule filters, both found variation in efficiency with rate of air flow.

EXPERIMENTAL

The filters examined in these experiments were confined to those available commercially, and were constructed of oil-treated glass fibres, oil-treated fine wire gauze or cotton fibres. Tests were carried out with each filter with different sources of infection and over a wide range of air flows. The apparatus used was the same in principle as that described by Terjesen and Cherry[6] and is shown diagrammatically in Figure 1.

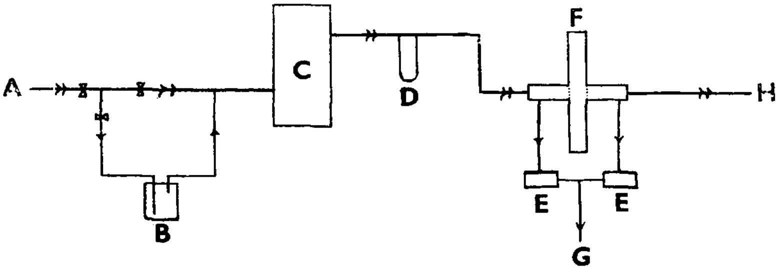

FIG. 1. Arrangement of apparatus for testing air filters.

A. Air input.
B. Source of infection.
C. Mixing tank.
D. Flow meter.
E. Slit sampler.
F. Test filter.
G. Vacuum.
H. Exhaust.

It consisted essentially of a controlled source of air and of bacterial infection, a mixing tank, the test filter, and air sampling devices immediately before and after the filter. The air supply was taken from a service main and was practically free from bacteria. The bacterial infection was introduced into the main air stream through a venturi throat system from either a sprayed aerosol of a culture of *Chromobacterium prodigiosum*, or a spore-infected dust maintained in a state of constant but gentle agitation to ensure evenness of infection during an experiment. The bacterial cloud density of the sprayed culture varied between 100 and 500 cells per cu. ft. and of the dust mixture between 50 and 500 cells per cu. ft., but the level was maintained constant for any one experiment. Two sources of infected dust were used, (1) from pellicle cultures, and (2) from centrifuged shaken cultures of *Bacillus subtilis*, ground and diluted with French chalk. These mixtures gave different responses in the filters, as will be seen from Table I, due to the different state of separation of the organisms. Standard Bourdillon-type slit-samplers were used for testing the air, samples of 1 cu. ft. being taken before, and up to 15 cu. ft. after, filtration.

TABLE I

VARIATIONS IN EFFICIENCIES OF FIBRE FILTERS WITH AIR FLOW RATE

	Percentage filtration efficiency with								
	Glass fibre filter			Wire gauze filter			Cotton fibre filter		
Air flow rate (ft./minute)	Aerosol	Dust 1	Dust 2	Aerosol	Dust 1	Dust 2	Aerosol	Dust 1	Dust 2
864	40	96							
665			92	34		84	55		95
576	19	92		29		75	45		
475			82	20		72	45		92
380		79	63	14		64	41		85
288	7		58	10		59	45	99	90
184	1	82	52	19		54	46		88
123			48	20		43	48		82
92	15	70						97	
60			49	25		46	56		81
30	46	74	40						79
18			46					97	84
12		71							88
6			53						90
2		85							

Each individual filtration experiment was run for a period of at least 3 hours, but in some cases it was continued for several days; this did not seem to affect any of the results obtained. At intervals during each experiment, slit sampler counts were taken of the air before and after filtration. At least 3 such observations were made and from their means the percentage efficiency of the filters were calculated.

The smallest filter obtainable commercially was 10″ × 10″ × 2″ deep, and as this was larger than was convenient for much of our experimental work, the majority of the filter was blanked off on both sides leaving a test area near the middle of only 4½ sq. in. This enabled considerable air velocities to be employed without demanding abnormally large volumes of air. Air flows were always measured in terms of velocities in preference to volumes per unit of time.

RESULTS

The standard glass wool filters examined were made from long glass fibres treated with a light adhesive oil. Their mean diameter was 180 μ, but ranged from 92 μ to 360 μ. In addition, 3 others supplied specially by one of the makers of these filters were also examined. The cotton fibre filters consisted of a thin layer of cotton wool spread evenly over a cotton gauze and held rigid on a wire gauze mount. This mount was bent in the filter frame into a multi-"V" form, presumably to afford a greater filtration area within the frame of the filter. On close examination, both of these types of filter exhibited small variations in evenness and density of packing, a factor which was manifested in differences between the performances of filters of the same type or of areas of the same filter. The wire filter was built up of several layers of 18 mesh, oil-treated wire gauze, alternate layers being bent in multi-"V" form. The pressure differences across all of these filters were negligibly small, observed values being less than 0·2 in. except at very high air-flow rates.

The first experiments were of a preliminary nature to determine whether a bacterial aerosol gave the same responses as dust-borne bacteria. The aerosol of *Chr. prodigiosum* had a particle size of about 1 μ and the spore-infected dust from 2 μ to 30 μ, the majority lying between 2 μ and 15 μ. Typical comparative results from the same filter under otherwise identical conditions were:—

Glass fibre filter—14·7 per cent. efficient against the aerosol, 70 per cent. efficient against infected dust.

Cotton fibre filter—45 per cent. efficient against the aerosol, 92 per cent. efficient against infected dust.

Wire gauze filter—19 per cent. efficient against the aerosol, 54 per cent. efficient against infected dust.

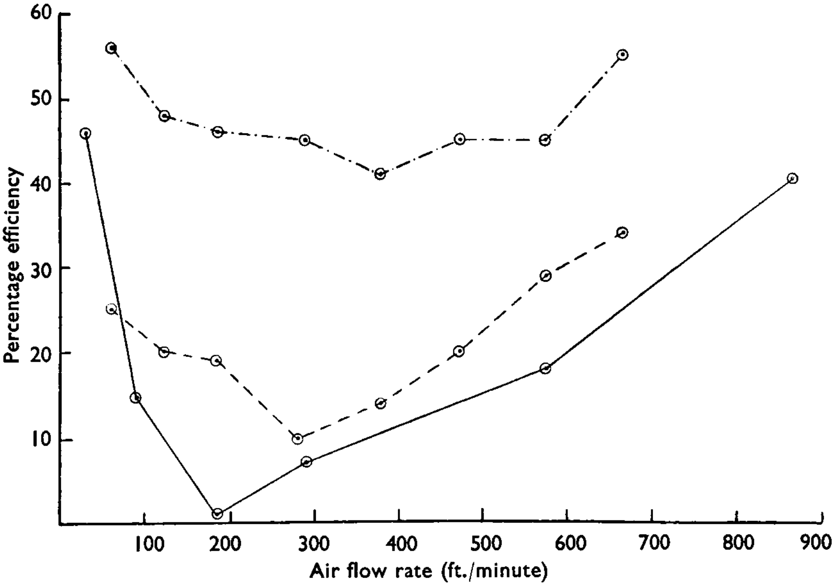

FIG. 2. Variation in efficiencies of filters with air flow rate using a bacterial aerosol.
—— Glass fibre filter.
– – – Wire gauze filter.
–·–·– Cotton fibre filter.

The significance of the differences in particle size was immediately evident, thus making it imperative that both types of infection should be included.

Examination of the influence of air flow rate on the efficiency of filtration showed it to be highly significant. With each type of filter the pattern of response was similar but was operative at different levels. Typical results are quoted in Table I and illustrated in Figures 2 and 3

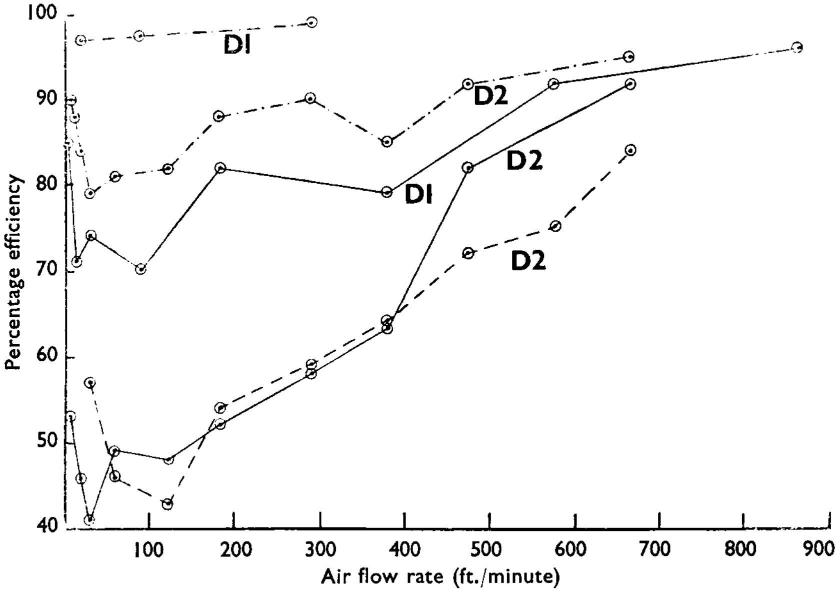

FIG. 3. Variation in efficiencies of filters with air flow rate using spore-infected dusts.

——— Glass fibre filter D1. Dust 1.
– – – – Wire gauze filter D2. Dust 2.
–·–·– Cotton fibre alter.

showing that, starting with low initial velocities, increasing air speeds resulted in a fall in efficiency followed by a continuous rise which was maintained over the remainder of the range examined. It is of interest to note that one manufacturer recommends that glass fibre filters be used at an air velocity of about 300 ft. per minute (equivalent to 200 cu. ft. per 10 in. square filter) at which rate the efficiency of filtration against bacteria is near its minimum. The tests also illustrate the anticipated different responses of the relatively coarse glass fibre or wire gauze filter materials against the finer cotton fibre filter.

One disadvantage found with the cotton fibre filter was the rapidity with which it became clogged when used against dust. For this reason, and also because the use of two filters in series is often recommended, experiments with more than one filter were carried out. Table II shows the results of tests using two filters with air flows of about 300 ft. per minute against spore-infected dust 1. With two glass fibre filters the response showed practically no improvement over that from one; with a glass fibre filter followed by a cotton one, the response was the same as that from the cotton filter alone. In this case, the cotton filter showed no sign of clogging even after several days continuous use.

TABLE II

EFFICIENCIES OF TWO FILTERS IN SERIES

Filters used	Percentage efficiency of filtration	
	Test 1	Test 2
One glass fibre	89	84
Two glass fibres	90	90
One glass fibre and one cotton fibre . .	98·5	98
One cotton fibre	99	—

Tests against spore-infected dust

Further evidence of the lack of improvement with multiple glass filters is shown in Table III, when three filters were tested in series against the aerosol and against spore-infected dust 2. Air samples were taken after each filter and in every case the majority of the infection removable by these filters under the conditions given was taken out by the first one, the effect of the second and third filters being negligible or only small.

TABLE III

EFFICIENCIES OF THREE GLASS FIBRE FILTERS IN SERIES

Air flow rate (ft./minute)	Bacterial infection	Percentage efficiency of filtration after		
		1 filter	2 filters	3 filters
864	Aerosol	52	50	44
576	,,	35	44	46
465	Dust 2	49	61	66
288	,, ,,	40	45	54
184	,, ,,	32	30	33

In Table IV are shown the results of tests with the 3 specially made filters against spore-infected dust at 3 different air flows. Filter A was more densely packed with a normal grade of glass fibre; Filter B had graded fibres, coarse ones on the input side graduating to finer ones on the outlet; filter C was a normal filter but had been treated with a different adhesive oil. No great differences in performance were evident under the conditions chosen, but it appeared that each of the specially made filters was slightly better than a normal one taken from stock.

TABLE IV

EFFICIENCIES OF DIFFERENT GLASS FIBRE FILTERS

Air flow rate (ft./minute)	Percentage efficiency of filtration of filter			
	A	B	C	Normal
360	95	95	94	88
270	86	89	89	86
180	82	87	81	80

A = more densely packed filter.
B = graded fibre filter.
C = normal filter with different adhesive oil.

Filters installed in aseptic rooms. A few experiments with some of the filters were carried out under actual working conditions in an aseptic filling room. This room measured about 12 feet cube and was fitted high in one wall with a fan supplying controlled normal air through the test filters. The air escaped naturally through door gaps, etc., thus giving a transverse-downward air flow. In these experiments a normal air contamination was allowed to develop with two operators moving about freely for some time. The room was then vacated, and flushed with an air flow equivalent to 8 changes per hour, the air being sampled at intervals by means of the slit sampler. With either a glass fibre, cotton fibre, or a glass fibre followed by cotton fibre filter, the bacterial content was reduced to 3 to 6 organisms per cu. ft. in about 30 minutes and this level remained practically unchanged after further prolonged flushing. This order of result is borne out in the very many observations taken over a number of years in aseptic filling rooms whilst normal activities were in progress, when counts of 5 to 10 organisms per cu. ft. have been regularly obtained. They support the findings of Yaglou and Wilson[10] and of Coulthard[14], who reported low bacterial counts in rooms flushed with filtered air.

For many operations the screen has become an indispensable part of the sterile room equipment. A logical development of the foregoing observations was to apply it to the screen itself and flush it with a continuous supply of sterile filtered air. Since the volume of the screen is comparatively small, it is not difficult to provide a much faster air flow rate than in the whole room. In practice a flow rate of one to two changes per minute has been found most satisfactory and has proved to be the most efficient way of using the screen. Many hundreds of bacterial air counts taken under such screens have always shown the superiority of this adaptation over the normal method.

DISCUSSION

Although the manufacturers do not claim that their various filters are completely effective in removing bacteria from the air, nevertheless several types are used extensively for this purpose. Our experiments have shown their efficacy as bacterial filters to be dependent on the nature of the filter material, on the size of particles to be filtered and on the rate of air flow through the filter; packing density and depth of filter must also play a significant rôle. In particular, each type of filter appears to possess a minimal efficiency at an air flow rate which varies with particle size and according to the nature of the filter bed. These observations find a ready explanation in Stairmand's theory of filtration[8] in which he postulates that impingement forces exert the greatest effect at high velocities and diffusion forces at low velocities.

Efficiency due to impingement, or inertial, forces will naturally increase with velocity since the faster the speed of a particle the more likely it is to strike a fibre of the filter and be held there. Again, the greater the mass of a particle the more likely it is to strike against a fibre and be held, hence the greater efficiences of these filters against dust-borne infection than against bacterial aerosols. With diminishing air flow rates the impingement effects must decrease so that, if no other effects were operative, efficiency would reach zero. However, diffusion effects become more significant with lower flow rates and thus retard the decline in efficiency, and eventually reverse it. In practice, as is seen from experimental results, this does not occur until well below the normal working range of the filters. It is not improbable that forces such as electrostatic attraction, humidity and the condition of the particle also play a significant part in determining filtration efficiency. These aspects do not as yet seem to have been investigated.

Throughout the tests, greater variation in efficiencies with changes in flow rate was found with the larger fibre filters, and the greatest was obtained with the smallest particles. Again applying Stairmand's theory, the impingement efficiency of a single fibre is shown to be a function of the expression $\frac{Dg}{Vf}$ (where D = diameter of the fibre, g = gravitational constant, V = velocity of approach and f = free falling speed of the particles). When D is large, as with the glass fibres, the variation in efficiency with flow rate, V, will be greater than when D is small, as with cotton fibres. Similarly, if f is small, as in the case of an aerosol, greater variation will be found than with a dust where f is greater. This explains, for example, why steeper slopes were obtained with the coarser fibre filters. From this theory can also be deduced why two or more filters of the same type used in series did not give any significantly enhanced efficiency over a single filter; the first filter would appear to remove all particles down to a certain size, the residue of which then pass practically unchecked through the subsequent filters.

In practice, nearly all air-borne bacteria are carried on dust particles. Hence a filter is not generally called upon to remove the smaller bacterial particles of 1 μ or less. Under these conditions, a glass fibre filter is adequate for many purposes, but where a higher efficiency of filtration is necessary, the cotton fibre filter is superior. Unfortunately, this type of filter becomes fairly rapidly choked with dust, hence a combination of a glass fibre filter followed by a cotton one would seem to be the choice, the glass filter to remove the larger dust particles and the cotton filter to remove the finer ones. Such an arrangement has been run under experimental conditions with a heavily dust-laden air flow for several days without any sign of choking and has maintained an efficiency of 98 to 99 per cent.

SUMMARY

1. Comparisons of commercially available glass fibre, wire gauze and cotton fibre filters against a bacterial aerosol and spore-infected dusts have shown the cotton fibre filter to be the most efficient.

2. Variation in efficiencies of all filters with air flow rate and with size of particles to be filtered has been found. Previously proposed theories have been used to explain this.

3. No advantage was gained from using two or more glass fibre

filters in series, but a glass fibre followed by a cotton fibre filter had certain advantages.

4. Under working conditions, many observations have proved the glass filter effective in maintaining a satisfactory low level of bacterial air infection in aseptic filling units.

5. Screens flushed with sterile filtered air are recommended for small-scale sterile operations.

Thanks are due to Mr. G. A. B. Maxfield for his technical assistance.

REFERENCES

1. "*Studies in Air Hygiene*," H.M.S.O., London, 1948. Special Report Series No. 262.
2. "*Aerobiology*," *Amer. Assoc. Adv. Sci.*, Lancaster, Penn., U.S.A., 1942.
3. *Chem. Ind.*, 1950, p. 805.
4. Bourdillon, Lidwell and Lovelock (with others), "*Studies in Air Hygiene*," H.M.S.O., London, 1948, pp. 173, 208.
5. Mellors, *J. appl. Chem.*, 1952, **2**, 68.
6. Terjesen and Cherry, *Trans. Inst. chem. Eng.*, 1947, **25**, 89.
7. Cherry, McCann and Parker, *J. appl. Chem.*, 1951, **1**, S108.
8. Stairmand, *Trans. Inst. chem. Eng.*, 1950, **28**, 130.
9. Phillips, *J. Bact.*, 1941, **41**, 270.
10. Yaglou and Wilson, "*Aerobiology*," *Amer. Assoc. Adv. Sci.*, Lancaster, Penn., U.S.A., 1942, p. 129.
11. DallaValle and Hollaender, *Pub. Hlth. Reps.*, 1939, **54**, 695.
12. Decker, Geile, Glick and Scharnhorst, *Bact. Proc.*, 1950, **1950**, 59.
13. Kluyver and Visser, *A. van Leewenhoek J. Microbiol. and Serol.*, 1951, **16**, 299.
14. Coulthard, *J. Soc. chem. Ind.*, 1948, **67**, 441.

DISCUSSION

The paper was presented by MR. G. SYKES.

DR. H. S. BEAN (London), referring to Figure 3, asked whether it meant that at a low air flow rate, for every 100 bacteria-carrying particles per unit volume of air before the filter, there were only 50 in the same volume of air after passing through the filter. The graph showed further that when the airflow was increased to 600 cu. ft. per minute, the efficiency of the filter increased to something like 90 per cent. By increasing the airflow there was a greater number of bacteria impinging on the filter but, at the same time, the increased volume of air passing into the room carried an increased number of bacteria-carrying particles. If that were the case, it would appear that the logical step was to take every precaution to prevent the air from the duct entering the screen.

MR. E. ADAMS (Plymouth) said that filtration alone was not completely satisfactory. If the requirement was to remove particles down to, say, 5 μ, it was fairly satisfactory, but if the requirement was to remove still finer particles it meant that the number of air changes had to be increased from, say, 10 to 20, in which case the draught from the fans and the noise became appreciable. Consequently, he found it difficult to appreciate the very great difference in efficiency at the different rates (Table I). He wondered how the results would appear if the determinations were carried out in an aseptic room, and whether there would be a similar divergence with different flow rates.

MR. N. D. HARRIS (London) said that there was an impregnated resin filter available which the manufacturers claimed would remove 99·9 per cent. of all particles down to 0·2 μ. If that were so it would seem to be very satisfactory

MR. D. N. GORE (Dorking) described a large filter which consisted of banks of undulating plates supporting a film of oil, the plates being arranged so that a large surface was produced upon which the air impinged. The filter was satisfactory except under conditions of high humidity, when the oil film seemed to be disturbed.

DR. W. P. KENNEDY (London) said that, with regard to impaction surface, one device which had given satisfactory results consisted of placing a flat tray about 1½ ft. square below the outlet from the filter and fan. The tray was filled with water to a depth of about ½ in. There was an increased efficiency of the sterilisation as judged by plate counts. He also referred to a circular container holding a filter paper about 1 ft. in diameter. The air impinged upon the paper, and on passing through flowed by an ultra-violet lamp.

MR. J. H. OAKLEY (London) described an apparatus for removing water from compressed air, in which droplets of moisture were continuously removed by centrifugal action. As the droplets would carry with them the bacteria-laden dust particles the apparatus seemed to have possibilities for clearing air and for reducing its bacterial content.

MR. E. W. SIMPSON (London) said that insufficient attention was given to the air after it had passed through the filter. Very often there was a long length of trunking which accumulated a great deal of fine particles, and if the rate of flow changed, those particles were carried through into the presumably sterile atmosphere. It was usual in a filtration system to operate the optimum rate of air flow. With a large filter a high rate of air flow produced the best results, but also produced a gale in the sterile room. This could be obviated and efficiency remain unimpaired if the frontage area of the filter were reduced. Had any work been done on the nature of the surface of the filtering material?

MR. G. SYKES, in reply, pointed out that to increase the air flow rate through the filter did not necessarily produce a gale, but there was an optimum rate of flow. Also it did not necessarily follow that every particle impinging on the filter carried bacteria. It had to be borne in mind in designing sterile rooms that the points of ingress of the air and extraction were both important, and that infection could come from various sources, particularly from personnel inside the room. Adequate treatment of the air was only one of the factors in the design of a sterile room. He had recently seen published the statement that particles in the atmosphere of London average 0·6 μ whereas in the provinces the particle size was 1 μ or greater. There was no doubt that resin-treated filters were more effective than glass wool and similar filters. The device described by Mr. Oakley was useful, and appeared to be in effect another impingement apparatus. There was no doubt that the surface of an impingement unit played a very important part. Further information on the effect of different oils in filters would be desirable. The problem of high humidities was scheduled for investigation. He did not think that an ultra-violet lamp was of any use in sterilisation.

The CHAIRMAN, in closing the science sessions, thanked the authors and those who had contributed to the discussions. He thanked particularly the Editor of the *Journal of Pharmacy and Pharmacology* for having made preprints of the papers available.

BRITISH PHARMACEUTICAL CONFERENCE LONDON, 1953

(*continued from page* 955)

REPORT OF A SYMPOSIUM ON CONTAINERS AND CLOSURES

AT the Symposium Session the Chairman, Dr. G. R. Boyes, presided, and introductory papers were read, in abstract, by Miss Violet Dimbleby, Mr. James Haworth, Mr. D. Stephenson, and Professor H. Berry.

For Miss Dimbleby's address see *Review Article, pages* 969 to 989. The other papers are printed below in abridged form.

THE TECHNOLOGY OF RUBBER

BY JAMES HAWORTH, B.SC., A.R.I.C., A.Inst.P.
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INTRODUCTION

IN spite of continuous contact between rubber users and the manufacturer since 1822, when Thomas Hancock was covering corks with rubber to improve their sealing properties, many misunderstandings have existed between the two parties. The causes of these appear to be twofold. In the first place, while rubber has found a wide range of application owing to its remarkable properties, little is really known of the basic physics and chemistry of its structure and properties. Empiric methods rather than scientific techniques play the major part in dealing with problems arising in the use of rubber. Secondly, owing to the fact that rubber technology is more an art than a systematised science, much of its terminology lacks the precision of more scientific techniques. The use of the word "rubber" for a wide assortment of materials including raw rubber of many botanical species, the infinite number of vulcanised rubbers of varying composition and the newer synthetic rubbers, illustrates how even the key word of the industry can confuse.

The basic raw materials of rubber technology are materials possessing properties intermediate between solid and liquid whose behaviour cannot be explained by laws appropriate for either ideal solids or liquids. Since the properties of the materials can be moved over the range between the ideal states, showing under some conditions properties akin to a liquid and under others more characteristic of a solid, it is perhaps not suprising that many perplexing results are obtained in service.

WHAT RUBBER IS

Natural Rubber.

Raw rubber is obtained as an aqueous dispersion (rubber latex) which exudes from the trunk of the tree when shallow cuts are made in the bark. Rubber latex contains 30 to 45 per cent. dry rubber and is subject to some considerable variation as is usual with materials of botanical origin.