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AIR-BORNE INFECTION*

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The conception of air-borne infection came thousands of years before the discovery of bacteria. As soon as man became an animal living in large settled communities epidemic disease was inevitable, and the most primitive intellect could grasp the significance of the unseen transmission of a fatal agent. The word " toxin " has carried on to the present day the Old Testament conception of an arrow flying in the darkness, and the mediaeval paintings of St. Sebastian continue the metaphor. Plague-stricken London anticipated Lister with fumes of brimstone ; the judge still carries his posy of flowers to ward off jail fever ; and the observations of Twort and his colleagues on the value of smokes as bactericidal agents must remind all who have visited Eastern bazaars of the itinerant incense carrier. Perhaps the use of incense in many religions had the neutralization of infection as one motive.

Eighteenth-century doctors, with their leisurely precision, made some guesses very near the mark. Sydenham wrote : " The matter so falls out that at this time or that time the air is furnished with particles that are adverse to the human body." Arbuthnot, in 1733, in *An Essay concerning the Effects of Air upon the Human Body*, said: " Nothing accounts so clearly for epidemical diseases seizing human creatures inhabiting the same tract of earth who have nothing in common that effects them except air " as that " air is the τὸ θεῖον in disease." Air is the mysterious something of the ancients. It was indeed through experiments on air, still recalled to bacteriologists by their daily use of the Pasteur pipette, that the whole of modern bacteriology evolved. In his first classic paper Lister wrote : " The air owes the property [of putrefaction] to minute parasites suspended in it, which are the germs of various forms of life " ; and Koch in one of his earliest papers wrote: " It is also highly probable that the tubercle bacilli are usually inhaled with the inspired air, clinging to particles of dust."

It is therefore not surprising to find that the early bacteriologists particularly studied the air. Flügge in 1897 put forward the conception of droplet infection, though it is only in comparatively recent years that the subject has again come to the forefront. Indeed, the early workers soon found that direct contact and contaminated instruments were in many cases far more important to the surgeons ; and they lacked equipment capable of controlled measurement of the bacterial content of the air.

* A lecture delivered at the Royal College of Surgeons of England.

Technical Methods

One of the oldest and simplest methods of culturing the air is to expose Petri dishes, and the method is still quite satisfactory. It is true that this gives no quantitative values, but the number of organisms falling on to a plate is proportional to the number in the air, and runs roughly parallel with more exact measurements. Quantitative estimates may be made by a simple technique devised by Elford: a piece of filter paper is placed in a Seitz filter, a known volume of air sucked through, and the disk dropped on to a semi-solid agar plate. For critical work, however, the air centrifuge of Wells or the slit sampler of Bourdillon must be used. It is possible to-day to give a reasonably exact estimate of the number of particles containing bacteria. The results of course vary according to conditions : probably the air is nowhere sterile, even at great heights. From personal observations it is found that a hospital ward normally has about fifty such particles per cubic foot, but when beds are made the number rises to 2,000–3,000. Bourdillon and Colebrook, using filtered air in a surgical dressing-room, found 0.005 particles per cubic foot ; this figure rose to more than 600 when dressings were done without ventilation. Canteens were found to have up to 250. In air-raid refuges the bacterial content gradually rose nearly tenfold over a period of hours.

Experiments on animals are not entirely satisfactory. Mice can be infected by mists of influenza virus and of pasteurella. Ferrets infected with influenza and virulent streptococci transmit the streptococci to ferrets, at the other end of an animal house, infected with influenza only ; rabbits infected with tuberculosis transmit the infection to others at a distance. On the whole, however, air-borne infection has not lent itself to experiments of this type.

General Principles

It is to be anticipated that certain forms of bacterial life would adapt themselves to aerial spread, as certain plants have winged seeds and as other bacteria adapt themselves, through their mobility, to aquatic life. The vast majority of air-borne organisms are non-pathogenic. The majority are resistant to desiccation owing to spore formation, and probably of low specific gravity. The universality of moulds is due to these factors. Moulds are of immense economic importance, and so versatile that they infest even cold-storage plants. Indeed, the control of mould infection offers great scope to the technique used in the control of infection, and appears to be neglected.

On general principles, again, we should expect organisms which infect the respiratory tract to travel via the air. This, however, does not imply that they do so travel. It is exceedingly difficult to isolate pathogens from the air by the most refined technique. In tests with which I was concerned large barrack-rooms with very poor ventilation were tested. Nearly all the inhabitants were found to be carriers of meningococcus, but no meningococci were isolated from the air. For the greater part of a year I tested the air of crowded air-raid refuges without isolating haemolytic streptococci or pneumococci. The only haemolytic streptococci which I have isolated from the air came from the neighbourhood of patients with infected wounds. Such organisms have been isolated from scarlet-fever wards by many observers, but even the most crowded room occupied by healthy persons yields amazingly few pathogenic forms.

Flügge's original conception of droplet spread was criticized because the majority of droplets fall quickly to the ground. However, W. F. and M. W. Wells found that some were so minute—nuclei, as they named them—as to remain suspended for long periods. In this way infective agents might theoretically remain and build up in unventilated rooms. However, it appears certain that it is the organisms which fall to the ground or on to clothing or bedclothes which are the most important. Dust is undoubtedly rich in pathogenic bacteria and viruses. The varieties so isolated, even by the simplest technique, are most significant. Diphtheria bacilli can usually be found in fever hospital dust and tubercle bacilli in sanatoria, and the poliomyelitis virus has been identified in the dust of a room occupied by a case. I have rarely failed to isolate *Cl. tetani* and *Cl. welchii* from London dust, and infection with tetanus has been ascribed to air-borne spread. Streptococci are of particular importance, as they remain viable on blankets and clothing for a month or more. Smallpox virus remains infective on crusts for many years, and influenza virus in dust can survive for long periods. It is practically certain that under epidemic conditions plague and typhus, normally spread by insect vectors, can be spread by dust.

It is obvious, too, that organisms from the respiratory tract infect wounds ; indeed, the early infections of wounds are largely from that source, the later infections being of faecal origin. Haemolytic streptococci, staphylococci, and diphtheria bacilli reach wounds from the respiratory tract either direct as droplets or indirectly on dust particles.

General Principles of Control

It is necessary to do some clear thinking on the objectives and limitations of aerial disinfection. The provision of a pure water supply, though difficult, is possible and most desirable, since we can treat all the water drunk. But we cannot sterilize all the air breathed. The open air is always safe, but the maximum risk of air-borne infection, especially through droplets, is present where human beings are grossly crowded together as they are under modern transport conditions. Even if we could ensure safe air during the rest of a city worker's life he would be exposed at least twice a day to conditions where no known method of air sterilization could possibly operate. It was seriously suggested, at the outset of the recent war, that under epidemic conditions masks might be worn by all, and masks were in fact ready in store. But even if it were possible to induce people to wear them, would it really be beneficial? The medical history of the war was most instructive. Ventilation was very poor in the black-out. Air-raid refuges and tube stations were crowded, all the conditions for epidemics appeared to be present, and I was one of those who formed a team to combat them. But apart from German measles, which did not appear to be related to overcrowding, no epidemics broke out. Again, the number of carriers of meningococci increased alarmingly, so that nearly all soldiers in certain barracks were affected ; but the rise in the incidence of meningitis, though significant, was never a serious problem. Transports going to Egypt were grossly overcrowded : during the first week of the journey respiratory infection was universal, but the rest of the two-months journey was healthy. This was not true, however, of native troops from Africa, who suffered severely from pneumonia, chicken-pox, and meningitis. Is it not a fact that immunity from the common respiratory infections is closely related to constant exposure to infection? Herd immunity is a real thing ; and we are all aware that a holiday from urban conditions is bought at the price of an acute "cold" on returning to town. If it is not possible to deal with crowded transport conditions, what merit is there in dealing with offices, places of amusement, restaurants, and churches ?

There are two exceptions to this rule: the first, that times of pandemics with a new or rare infection deserve special consideration ; the second, that children are analogous with the native troops in transports, as they represent a group with little or no acquired immunity and spend much of their time in homogeneous groups. There is a lot to be said in favour of air sterilization in schools, and still more in favour of keeping children away from crowded places. The cinema is probably a greater danger to child health than to child morals, and the special matinées for children are ideally devised to spread infections. Moreover, if we are again faced with a dangerous pandemic of influenza, doubtless every method of limiting the dose of infective agent would be logically employed. Whether any known method of air control would help is, in my opinion, doubtful.

We are left with hospitals, particularly with fever and children's hospitals. Here there is a clear case for control of air-borne infection. Sick and devitalized patients are grouped together, many of them with wounds actually or potentially infected, and all that we know of the bacteriology of air and dust teaches us that every known method of control is most desirable. In America this problem has long been seriously tackled ; here in England in spite of much pioneer work we lag sadly.

Methods

The methods available fall into several headings—control of droplet infection, ventilation, control of dust, and sterilization of air. Droplet infection must mainly be controlled by adequate masking : poorly designed masks merely collect organisms, which are then expelled in large doses. All nurses in infants' wards should be masked, and nurses with even minor respiratory infections should not remain on duty. The Spartan traditions of nursing are altogether bad. Since on speaking 300 organisms per word are emitted, operations should be silent. Sneezing expels 100,000 organisms per sneeze. The use of handkerchiefs is most desirable, but it would probably be far better if these were of paper, and used only once or twice. Proper ventilation is also essential. It is usually said that a poorly ventilated room has ten or less turnovers of air per hour ; the best air-conditioning increases this to twenty-five turnovers. But in certain circumstances, as in operation theatres and surgical dressing-rooms, which at least for septic cases should be separate from main wards, a positive pressure of filtered air over the patient, as suggested and adopted by Bourdillon, is most effective, preventing banking-up of infected particles, and blowing away particles emitted by attendants. There is no substitute for good ventilation in the control of all forms of infection. In one hospital during the war an outbreak of cross-infection in casualties ceased only when the windows were blown in during an air-raid. But we cannot always rely on bombs.

Dust control, again, is a paramount concern. By air-borne infection we usually mean infection by contaminated dust. This has long been known, and the rounded corners of well-designed hospitals and operation theatres follow on this principle. It has been placed on a firm basis by the classic work of van den Ende and his colleagues, one of the most important contributions ever made to this subject. The majority of hospitals, however, still have dangerously polished floors, and blankets are only rarely washed; indeed, dark-coloured blankets are used to make the need for washing less obvious. Treatment of floors by spindle oil and of blankets by a special oiling method will control dust to a remarkable degree and entirely prevent the phenomenal rise of air bacteria during bed-making. It is true that tests of this method of preventing cross-infection have not always been conclusive; there are a great many other loop-holes in aseptic technique, as Spooner and others have shown. But, whatever other methods may eventually prove necessary in this matter, it is certain that dust control will remain a first essential. The removal of infected plaster casts from suppurating wounds is a further source of dangerous dust formation, and oil should be used along saw cuts.

Air Sterilization

We now approach a more vexed question, the sterilization of air by antiseptic mists and smokes and by ultra-violet light. At the outset it must be stressed that both these methods are effective only or at least mainly against droplets and droplet nuclei. This is often overlooked, for the greater part of the experimental work has been with organisms sprayed from fluid suspensions into the air. It is with this type of work that I have personally had most acquaintance, and I have satisfied myself that, while both methods are entirely effective against droplets, they break down with dust. Since dust is the most dangerous infecting agent their use is severely limited.

The method of antiseptic mist spraying dates from the time of Lister. Lister's phenolic mists were in fact not effective, since phenol used in his way is a poor aerial antiseptic. The last lair of Listerian technique is the cinema, where entirely useless spraying with odoriferous fluids is still practised. The originator of this technique on an efficient basis was Trillat, in France. Becholt developed the method in Germany, though neither author attracted much attention, and their names are rarely heard. In this country these antiseptics were developed largely through the laudable enterprise of commercial interests. There is an unreasonable and unfair prejudice in the medical profession against such activities, and it is only right to commemorate the work of firms such as the makers of "milton," the makers of "phantomyst," and the Portslade laboratories. The most important work is that of Twort and his colleagues at Portslade. Before and during the late war I had some personal contact with the method. Later it crossed the Atlantic, gaining, as is customary, much momentum and some amnesia in the transit. Of recent years most of the work on the subject, other than that of Twort and his colleagues, has been done there.

The facts are most fascinating and still largely unexplained. A limited number of antiseptics of low vapour pressure, when dissolved in low-vapour-pressure solvents and sprayed into the form of fine mists, can kill all droplet bacteria in five minutes or less. The amounts used are homoeopathic in their values: 5 ml. of 1% sodium hypochlorite will sterilize 1,000 cubic feet of air in less than five minutes, and less than 0.00025 g. of hexyl-resorcinol in propylene glycol will sterilize 1 cubic metre in a similar time. Robertson, in America, has claimed good results with propylene glycol alone; under the conditions of my experiments I did not find it valuable. Except in the possible case of sodium hypochlorite the question of volatilization—that is, solution of antiseptic in air—does not arise, for the amount of antiseptic sprayed is wildly outside the effective concentrations in fluids, and the effective agents are poorly volatile. I have suggested a species of balloon-barrage effect, through collision of particles, but mathematicians suggest that the rate of kill found is more rapid than collision would explain. It is possible that there may be attraction by an electric charge on the particles. Whatever the value of this method, from a bacteriological standpoint the results are of great interest.

More recently Twort has studied the effects of certain smokes (of which tobacco is not one) and has introduced heat volatilization of resorcinol, which greatly simplifies the technique.

All mists suffer from certain inevitable disadvantages. As mists are constantly being removed by ventilation, and also as all mists have a limited life, they must be constantly renewed; the better the ventilation the greater the volume of mist needed. Except with Twort's heat volatilization, this requires a constantly running mechanism, or at least one operating at frequent intervals. The occupants of rooms so treated are constantly breathing minute amounts of antiseptic. Some of these, such as sodium hypochlorite, are almost certainly harmless, and none have been shown to be harmful. Indeed, we probably inhale a great many phenolic substances every day without trouble. The most elaborate experiments on animals have failed to show any dangerous results. However, drugs and allergic individuals being what they are, sooner or later someone is sure to prove susceptible; with hypochlorites, also, some fading of textiles and corrosion of metals over a long period is possible. Most, though not all, have characteristic odours. Finally, although the volumes of antiseptic used are small, over long periods the expense would not be negligible.

Bacteria suspended in air can be as readily killed by ultra-violet light as by bactericidal mists. Indeed, from the point of view of speed and efficiency of kill there is little difference between the methods. The shortest period elapsing between the introduction of an organism and the production of practically sterile air was, in my experiments, about five minutes by both methods. The killing effect of light on bacteria has been known since 1899. The discovery that the bactericidal effect is mainly in the ultra-violet spectrum was due to the Klemperers in 1922. Here, again, transatlantic migration has proved a revitalizing process, and nearly all the work has been done in America. The names of Wells and Hart will always be closely associated with it.

Ultra-violet light with a wavelength of approximately 2,537 A.U. is used. It is produced by quartz low-pressure mercury discharge tubes provided with filters to control the rather objectionable ozone emission. There are no moving parts, upkeep is minimal, and the amount of electricity used insignificant.

The lamps may be used in many ways. For the sterilization of wards and living-rooms it is convenient for them to be above eye-level, and they must be mounted so that no rays are directed below this level. For operating theatres they have been directed on to the operation area, but the operators and attendants must wear goggles and all skin must be protected against burns. It has been suggested that there is a risk of adversely affecting viscera by exposure to the rays. I think that there are better methods of keeping bacteria out of wounds.

The Americans have been using ultra-violet rays for air sterilization for many years. It is a standard equipment in many schools and hospitals. Wells calculates that it is equivalent to 500 turnovers of air per hour, compared with the 25 turnovers by the best ventilation. In groups of schools the incidence of susceptibility to measles in an epidemic was from 9 to 15.5% in irradiated schools, and 55.3% and 51.8% in two unirradiated schools. Similar results have been found with chicken-pox. Experimentally, rabbits have been protected against air-borne tuberculosis. In my opinion ultra-violet light is the simplest and most efficient technique of this kind, and has no objectionable features if the eyes and skin are not irradiated.

Respiratory disorders, from tuberculosis and pneumonia, through sinusitis to the common cold, are far the most frequent of the diseases of mankind, and they are spread mainly through the air. The common infectious and virus diseases of childhood cause a high mortality and lifelong respiratory tract disease, and the air is again the commonest vehicle. Air-borne sepsis and cross-infection are common, particularly in wartime. There is still a tendency to laugh away the protagonists of the control of air-borne infection as faddists I heard a gynaecologist quite recently become vastly humorous at the suggestion that a nurse with a cold was a menace. But there is far too much hospital-bred infection, and far too many "sterile" operations go wrong. I feel quite sure that the time will come when the methods of controlling air-borne sepsis discovered in Europe and developed in America will return fully fledged to roost in their parent country.

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At a meeting of the North of England Obstetrical and Gynaecological Society held in Liverpool on July 4 Prof. T. N. A. Jeffcoate described a simple method of replacing the retroverted uterus by manipulating it with a Hodge pessary. This method made the usual bimanual replacement unnecessary before inserting the pessary. With the patient in the left lateral position the Hodge pessary was inserted and allowed to take up its own position. The upper rim came to lie in the anterior fornix and the lower bar projected beyond the introitus. One finger was then inserted behind the lower bar, through the pessary, and in front of the upper rim, which was pushed against the anterior aspect of the cervix. The cervix was thus deflected backwards and the body began to rotate forwards. Ultimately the upper rim slipped past the cervix into the posterior fornix. By this time the retroversion was nearly always corrected but sometimes only partially, the uterus lying with its axis vertical. In such cases the upper end of the pessary was pushed firmly against the posterior vaginal wall and the posterior fornix repeatedly "stroked" backwards and slightly downwards with the pessary. At the same time the lower end of the pessary came to lie at a higher level. Thus the cervix was levered backwards and the fundus came forwards and the pessary was automatically left in its correct position. Prof. Jeffcoate also read a paper on pyrexia as a sign of endometriosis. He had found no reference to this sign in the literature but did not claim it as original. He said it had been established that temperature varied with the menstrual cycle, but the peak occurred premenstrually and the onset of the flow was characterized by a fall. In endometriosis he had several records of cases where a temperature up to 101° or 102° F. (38.3°-38.9° C.) appeared cyclically during menstruation and gradually disappeared one or two days after the flow ceased.

BRITISH ANTI-LEWISITE

A Report on its Use and Therapeutic Value in Arsenical Intoxications, from the BAL Conference, Medical Research Council

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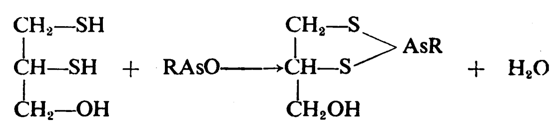
British anti-lewisite (BAL) is the name given to a compound, 2,3-dimercaptopropanol, discovered early in the war as a result of a planned research for the Ministry of Supply and developed as an antidote to the local and systemic damage caused by contamination of the skin or eyes with arsenical vesicant gases.

In the pure state it is a colourless oil, readily soluble in fat solvents, and soluble to the extent of about 6% in water. During 1941–2 its value in counteracting the effects produced by contamination with lewisite was exhaustively studied, and it was finally adopted officially as a suitable agent for the treatment of the effects of lewisite and the other arsenical vesicants. Its efficacy as an arsenical antidote and its power to reverse the tissue damage caused by arsenicals depend on its ability to form relatively stable ring compounds with arsenoxides, thereby diminishing the reaction of the arsenical with the tissues and increasing its urinary excretion from the system:



A review of the original work with lewisite has already appeared (Peters, Stocken, and Thompson, 1945), together with an account of the early developments of this work in the U.S.A. (Waters and Stock, 1945).

The application of BAL to the treatment of dermatitis and other complications arising in the course of arsenotherapy has also been extensively studied both in this country and in the U.S.A. The present short report summarizes the findings of a clinical trial of the therapeutic value of the compound carried out recently under the auspices of the Medical Research Council, a full account of which will shortly be published (Carleton, Peters, and Thompson: in the press).

Trial in Arsenical Dermatitis

The trial was based on the results obtained in 44 cases of arsenical dermatitis collected with the assistance of the Service Departments and the Ministry of Health. To facilitate the interpretation of any effects noted, the cases were selected so that the dermatitis was in each instance severe and widespread, 41 of them being of the acute exfoliative type.

Treatment was carried out by the clinicians in charge of the cases according to a scheme prepared by the BAL Conference, which was intended for initial guidance as to dosage. The ampoules of BAL used in this work were prepared by a modification of the method described by Eagle in the U.S.A., and contained 5% BAL in arachis oil