

SPECIAL ARTICLE

Joseph Lister and Infection from the Air

In his book, *Floating Matter of the Air*, John Tyndall (Tyndall, p. 262) quotes from Robert Boyle's 'Essay on the Pathological Part of Physik' 'that he who thoroughly understands the nature of ferments and fermentations shall probably . . . give a fair account of divers phenomena of several diseases, which will perhaps be never properly understood without an insight into the doctrine of fermentations'. It was more than a century and a half before the first part of this suggestion was fulfilled, after which the unravelling of the causes of infective diseases proceeded rapidly. In 1836 de la Tour and, almost simultaneously, Schwann (Tyndall, p. 7) discovered, in yeast, the agent of fermentation as a living organism which reproduced itself in endless succession. Schwann also observed that putrefaction in meat broth did not set in if this was kept in contact, not with ordinary air, but with air which had been previously brought to a high temperature.

Not many years later Pasteur, exploring the reasons why the industrial fermentation of beet juice sometimes failed to yield alcohol, but instead an acid product, showed that living organisms from the air, multiplying and replacing the yeast, were the cause of this, as also of putrefaction. In an extensive series of experiments Pasteur then demonstrated that these 'Corpuscules organisées dans l'atmosphère' (1862) were discrete entities, numerous in localities where there was much activity but scarce in the air of undisturbed cellars or on the tops of mountains, and removed by filtration of the air or by its passage along a sinuous glass capillary (see also Lister II, 477).

THE DEVELOPMENT OF ANTISEPTIC SURGERY

These observations struck a chord in the mind of the surgeon Joseph Lister, much concerned by the appalling mortality following major surgery, largely attributable to gross sepsis. In his Glasgow hospital during the years 1864 and 1866 no fewer than 16 of 35 amputations ended fatally (Lister II, 123). In his paper to the *British Medical Journal* in 1867 (Lister II, 332) he wrote,

But when it had been shown by the researches of Pasteur that the septic property of the atmosphere depended not on the oxygen . . . but on minute organisms suspended in it . . . it occurred to me that decomposition in the injured part might be avoided . . . by some material capable of destroying the life of the floating particles. The material which I have employed is carbolic or phenic acid.

Following his use of this to treat and cover the wound the mortality after amputations fell for the years 1867, 1868 and 1869 to 6 out of 40 (Lister II, 123). His antiseptic treatment was thorough and included,

a silk thread steeped . . . two hours in strong fluid carbolic . . . fine catgut . . . soaked for four hours in a watery solution of carbolic acid . . . before operation the hair of the part was cut short and

a solution of carbolic acid well rubbed into the skin. the sponges were wrung out in a watery solution and all the instruments together with the finger of my left hand were treated with the same lotion some of which was poured into the wound after the last stitch (Lister II, 86 *et seq.*).

He was not, however, satisfied with this and devised a further attack on the airborne source of infection, the spray of carbolic acid, by which, though by no means justly, he is largely remembered,

two things are always to be attended to: first to leave the wound free from living putrefactive organisms, and, second to employ such an external dressing as shall securely prevent the entrance of such organisms at any subsequent period. The latter . . . satisfactorily accomplished; but the former, till we used the spray, was always a matter of more or less uncertainty. A floating germ might enter . . . into some cellular interstice . . . becoming surrounded by a clot of blood might escape the action of the antiseptic lotion (Lister II, 170).

He does not seem to have considered ventilation as a means of eliminating these floating germs although this idea was very much in the 'Air' at the time. In the Crimea in the 1850s Florence Nightingale flung open all the windows of her hospital and Brunel designed a 1500-bed prefabricated hospital for that campaign, erected within 7 months, which included positive-input mechanical ventilation to all the wards (Stone, 1965). In 1863 John Simon (Simon, 1864) in a very significant comment had distinguished between three agents of transmission of infective material in a hospital.

Contagions that will not spread except by . . . dirty bedding, towels or sponges, or by dirty fingers . . . or by pus or matters like pus floating in the air . . . in the air of a ward of St Thomas' Hospital . . . not only hairs, smoke, epidermic scales but also living forms . . . The ventilation must . . . flowing from inlet to outlet so that every unwholesomeness is at once removed . . . artificial wherein the currents would be determinately regulated.

Tyndall (p. 26) also comments, 'If, instead of using carbolic acid spray, he could surround his wounds with properly filtered air, the results would, he contends, be the same. In a room where germs not only float but cling to clothes and walls this would be difficult.'

We have seen that Lister's technique involved far more than trying to shoot down airborne germs with a spray, and incorporated procedures which developed those of Semmelweiss and Simon with regard to the hands of the operator and to fomites. Observations he made later seemed to him to indicate that these were the important things and that the directly airborne germs were irrelevant. Thus in 1881 (Lister II, 279) he wrote;

normal serum opposes an insuperable obstacle to the . . . individual bacterium . . . overcome by the association action of several of the organisms in close proximity: . . . suggests that putrefaction is due to septic matter in a concentrated form rather than to the diffused condition in air. . . . Is the spray necessary? . . . Concomitantly with the perfecting of the spray there has been improvement in other parts of our antiseptic arrangements and I am not prepared to say that our increased uniformity of good results may not be due to the latter rather than the former.

And in 1890 (Lister II, 336) he concludes:

As regards the spray, I feel ashamed that I should ever have recommended it for the purpose of destroying the microbes of the air . . . (which) cannot possibly have been deprived of their vitality . . . the floating particles of the air may be disregarded in our surgical work . . . (if) we can trust ourselves and our assistants to avoid the introduction into the wound of septic defilement from other than atmospheric sources (Lister II, 337).

These extracts from Lister's numerous publications, which can profitably be extended by reading them in full, illustrate vividly most of the crucial points in any consideration of the genesis and prevention of surgical wound infection. The immediate sources of the potentially infecting organism; the ubiquitous airborne particles, the hands, the sutures, the instruments and dressings, the clothes of the operators, all these can be the means; but what are their relative importance, and when the most effective is eliminated, will not infection then arise from those that remain? The conditions for organisms entering the wound to multiply and infect, the size of the inoculum, the 'inaccessible interstice', the blood clot (or foreign body), the effect of a disinfecting wash, the body's natural defences, the significance of each of these has by no means been resolved. Finally the clean environment; airborne particles can only very ineffectively be shot down by a rain of liquid droplets, it is surely better to exclude 'defilement from other than atmospheric sources' than to apply disinfectants. Surgical wound infection is still a reality, all the answers to the above propositions have not yet been fully found.

Lister's long life spanned the seminal years of microbiology; in 1870 he is still talking of putrefaction, of putrid exhalation and of being 'guided by the germ theory'. In 1891 he refers to *Staphylococcus aureus* as the most frequent cause of suppuration in man and as being more resistant to antiseptics than *Streptococcus pyogenes* and *Bacillus pyocyaneus* (Lister II, 342).

In 1881 at the international Congress at King's College in London, together with Pasteur, he watched Robert Koch demonstrate his new method of cultivating bacteria on solid media; which called out from Pasteur the encomium 'C'est un grand progrès monsieur'. Surely one of the most dramatically symbolic meetings in the history of medicine (Lister II, 332).

ASEPTIC SURGERY

With the general discrediting, or disbelief, in the airborne genesis of surgical infection the disadvantages of the reliance on antiseptics were more apparent, especially the harmful effect of phenol on the tissues of the patient and on the hands of the operator (the wearing of gloves seems to have arisen in the first place as a protection for the hands rather than to prevent infection of the patient). Alternative antiseptics were tried, and in the last years of the nineteenth century the use of boiling water and then steam became general. The development of the pressure autoclave provided a reliable method of destroying spores (Schimmelbusch, 1894; Walter, 1958). Antiseptics remained only for sensitive materials, e.g. catgut. Lister himself remained reluctant to change, being afraid of back-tracking into the wound through a dressing wetted through with blood or serum (Lister II, 338).

AIRBORNE MICROBES AND INFECTIVE DISEASE

While surgery was the first area where medical conclusions were drawn from the revelation of the bacterial content of the atmosphere other attempts were made to link this with disease. Towards the end of the century both Miquel in Paris

(1883) and Carnelly, Haldane & Anderson in Dundee (1887) collected extensive data in a variety of situations and at different times and attempted to relate these to the incidence of disease. No apparent connection could, however, be deduced, and such a general approach was implicitly criticized by Tyndall (p. 265), 'We have reached a phase when light should be thrown on the manner in which infective diseases take root and spread . . . the habitat of each specific disease and the mode by which its germs are spread abroad . . . it is only by such rigidly accurate inquiries . . . ' To this we may add the necessity that such inquiries should be quantitative. The demonstration that the agents of a particular disease can be and are distributed through the environment, including the air, and that infection can be initiated via a particular route are only preliminaries. The problem for epidemiology is the significance of the various possible pathways. The subsequent history of 'air hygiene' repeatedly illustrates this, with extreme oscillations of opinion as successive investigations revealed some of the relevant facts.

Tuberculosis

Among the many specific organisms responsible for infectious diseases characterized by Robert Koch in the 1880s was the tubercle bacillus (Reid 1974). Following this discovery there was strong controversy between those who attributed infection to the inhalation of dried sputum ground into dust, demonstrated where possible by animal experiments, and those who favoured the direct airborne route through the dispersal of droplets from the mouth in talking, coughing and sneezing (Flugge, 1897; Flugge *et al.* 1899). The controversy next developed into an argument as to the role of bovine tuberculosis, spread by milk, which it was claimed remained dormant, breaking out in the lung many years later. Flugge's experiments had indicated that the droplets expelled from the mouth were only carried a short distance before deposition on the slides he used for their detection. This seemed at variance with the epidemiological picture, although Gordon, commenting on Flugge's work, had pointed out that guinea-pigs kept in a ventilating shaft in the Brompton Hospital acquired the disease, although remote from any patient. It was Gordon also (1904) who suggested a refinement of the general approach to the relationship between airborne bacteria and disease, by suggesting that the numbers of salivary streptococci in the air might serve as an index of the hygienic quality of the air much as *Escherichia coli* is used in relation to water.

Droplet nuclei

In the early 1930s Wells (1934, 1936) realized the implications of the evaporation of small liquid droplets (Langmuir, 1918) and devised apparatus (Wells, 1933) for collecting and culturing the residual 'droplet nuclei'. Any aqueous drop smaller than about 0.1–0.2 mm in diameter expelled from the mouth evaporated down to a particle no more than about one-fifth of this size, small enough to be carried long distances on air currents and including some small enough to penetrate into the depths of the lung. Although Wells himself was well aware that such particles did in fact settle, and indeed used the ratio between the numbers in the air and those settling as a measure of their size, subsequent writers have often appeared unaware of this and talked as if the 'projectiles' of Flugge and the 'droplet nuclei' of Wells were totally distinct entities, the latter all so small as not to settle at all.

On the basis of his studies Wells proposed the revival of Gordon's suggestion for the use of the numbers of salivary streptococci in the air as an index of its hygienic quality. This work of Wells led to a rapid development in the elucidation of the transmission of pulmonary tuberculosis. Animal experiments (Wells & Lurie, 1941; Ratcliffe, 1952) showed that the disease was effectively produced by those particles carrying the tubercle bacillus that were small enough (less than about $5\ \mu\text{m}$ in diameter) to penetrate into the depths of the lung and that, in a susceptible host, a single bacterium was sufficient to produce a tubercle. Wells and his colleagues (Wells & Lurie loc. cit.) also showed that these airborne organisms were killed by exposure to ultraviolet irradiation. There followed one of the most elegant and convincing demonstrations of the airborne transmission of disease (Sultan *et al.* 1960; Riley *et al.* 1961, 1962). Air from a six-bed ward of a tuberculosis hospital was extracted and passed over batches of guinea-pigs (shades of Gordon and the Brompton Hospital!). From analysis of the tuberculous lesions produced in the lungs of these animals and by consideration of their breathing rate they could estimate the numbers of infective particles in the air; this averaged no more than one in $400\ \text{m}^3$ of air. The numbers, however, varied greatly from time to time, and most derived from only a limited number of the patients, two-thirds of the infectious particles derived from only 3 patients out of 77 involved. Although the average patient dispersed only 30 infectious particles a day the most prolific generated 50 times as many. The effect of this on the nurses corresponded quantitatively, it could be estimated that during her time on duty the average nurse inhaled around $750\ \text{m}^3$ of air in a year. From the guinea-pig data this would have carried rather less than two infectious particles. The average time for tuberculin conversion among susceptible nurses was about 1 year. It is of great interest to note that in the immunologically simple situation such small numbers of airborne organisms could exert a significant effect, a matter of considerable relevance when, as sometimes, the possibility of infectious transfer is denied on the grounds that the numbers of organisms passing by a given route can only be very few.

Air disinfection

If the air is a medium for the transmission of disease it may be possible to prevent or limit this by some means of supplying uncontaminated air, or of air disinfection. Already Simon had suggested the supply of filtered air, Lister had tried a chemical spray which he realized must have been ineffectual and now Wells proposed the use of ultraviolet irradiation. He pursued this first in relation to a disease easily recognized and where the susceptible population could be clearly defined, namely measles among school children (Wells, Wells & Wilder, 1942). This study was followed by a long series of investigations, of which the latest was that in the schools of Southall in West London (UK) (Report, 1954). Without going into these in detail the results can be relatively simply summarized. The rate of acquisition of the disease was slower in the irradiated classrooms, it was also slower in those unirradiated classrooms where the numbers of salivary streptococci in the air were fewer. This did not, however, result in any reduction in the incidence of the disease in the population. The reduced exposure to infection merely resulted in more prolonged outbreaks with, effectively, almost all the susceptibles ultimately succumbing. This is again an important point in

considering the possibility of controlling disease – reduction in exposure does not necessarily, or even usually, result in a proportionate decrease in incidence, especially if other exposure takes place outside the treated environment.

Ultraviolet irradiation was also applied to the surgical operating room, and a very large reduction in the incidence of post-operative wound infection was claimed (Hart, 1960); a later report from the same source (Hart, 1968) suggested a two- to threefold reduction, for comparable operations, compared with an adjacent unirradiated hospital. A very extensive multihospital study, however, recorded only a very modest reduction of about 25%, confined to 'clean' operations (Report, 1964).

Chemical agents

Since a variety of chemical substances are capable of killing bacteria their use to destroy the life of the 'floating particles' was also proposed. Many potential substances were suggested, and references to these can be found in Wells (1944) and Williams (1949), and a discussion of the physical factors involved in the transfer of the agent into the particle is to be found in *Studies in Air Hygiene* (1948). Useful reduction in the numbers of airborne bacteria in occupied places was, however, found to be more difficult to achieve than laboratory experiments had indicated. In the first place, natural loss by settling is substantial, the average particle settling at about 30 cm per min (Noble *et al.* 1963), so that killing rates as high as 60/h are necessary to reduce the contamination to 10%. Secondly, naturally dispersed bacteria (and viruses) are embedded in the dried residue of the menstruum in which they originally multiplied, and this has a considerable protective effect. Killing rates are, therefore, much lower than for small droplets produced experimentally from cultures or bacterial suspensions. Both of these qualifications also apply to the use of ultraviolet irradiation, and the first one to the employment of normal ventilation, where the clean air mixes with the contaminated so that removal of this is an asymptotic exponential process. An extended study in office populations in England (Kingston *et al.* 1962) compared the effects of increased ventilation, ultraviolet irradiation and two chemical agents on the bacterial content of the air and the respiratory infections experienced by the staff. Although there were reductions in the numbers of bacteria in the air these were not very great, no more than 40% for the general flora, mainly 'micrococci' of various types, and up to 67% for salivary streptococci. There was no effect whatsoever on the incidence of respiratory infection.

Dispersal of bacteria from the skin

Although Simon had noted the presence of 'epidermic scales' in the air of hospital wards it was not till 100 years later that these were recognized as the major source of the bacteria found in the air of occupied rooms (Davies & Noble, 1962). Skin squames are shed continuously at a rate of some 10^9 per day, but the proportion of these which are dispersed into the air and which carry bacteria varies widely between individuals (Mackintosh *et al.* 1978). The size range of the fragments that carry bacteria is comparable to that of the 'droplet nuclei', i.e. with a median settling rate of about 30 cm per min, and they appear to be even more resistant to the action of ultraviolet and chemical disinfectants in the air. Unexpectedly, *Staphylococcus aureus*, which is normally found in the nose, appears

to be little dispersed directly from the respiratory tract but more often on skin squames to which it has been mechanically transferred, presumably via the fingers. When this organism does colonize the skin, e.g. in the perineal area, less often the axillae and in skin lesions, it may then be dispersed in large numbers. Since normal fabrics offer little, if any, obstacle to the penetration of skin squames – the apertures in the weave are commonly up to 100 μm while the squames are no more than 20–30 μm – ordinary clothing, whether sterilized or not, including that generally worn in the operating room, has a negligible effect on the dispersal of skin-carried organisms.

The 'sterile' operating room

Although the successes of antiseptic and aseptic surgery had very greatly reduced the incidence of post-operative wound infection an obstinate amount remained, and attention was once more directed to the air as a possible source (Meleney, 1933). Ventilation of the operating room was often provided as a means of removing escaping steam from the autoclaves, but as this was usually an extract system air was drawn in to the operating room from other parts of the hospital and carried with it bacteria from these (Report, 1948). Even in the absence of definite suction, temperature differences between the operating rooms and the passage outside led to substantial air exchange between them (Wolf, Harris & Hall, 1961). To counter this intrusion the concept of positive-pressure ventilation of the operating room became accepted as a standard provision (Report, 1972).

The extreme development of the idea of a sterile room isolated from the rest of the hospital was, perhaps, the design of Jean Walter in 1937 for Lille Hospital (Report, 1955). The rooms in the sterile block were to be sterilized before use by formaldehyde vapour, followed by ammonia. The patient was to be completely stripped and slid through a hatch into a preparation room where skin disinfection was carried out. He/she was then to be placed on a sterile stretcher hanging from a monorail and transported, through further hatches, into the anaesthetic room and then into the operating room. It is clear that such an elaborate system is entirely frustrated if the operating staff shed bacteria throughout the subsequent operation. Contamination of the air within the operating room can be reduced, first, by reducing bacterial dispersal from the staff, i.e. by eliminating unnecessary numbers and activity. As said, normal clothing has little effect in this respect and face masks have, at most, a limited significance since the organisms responsible for surgical sepsis, with the exception of β -haemolytic streptococci, are not found or not dispersed from the upper respiratory tract.

The possibility of occlusive clothing to prevent the shedding of skin squames was demonstrated in 1948 (Duguid & Wallace, 1948; Blowers & McCluskey, 1965), but was too uncomfortable to come into general use in the absence of convincing evidence that the wearing of it was of clinical significance. The second approach, by removing the bacteria dispersed more effectively through improvements in ventilation was accepted, in spite of the lack of unequivocal evidence for its benefit, since it, on the whole, improved comfort conditions in the operating room (Report, 1972). During the 1960s a class of operation much more sensitive to infection from small inocula and from organisms common on the skin came into widespread application, namely the replacement of the arthritic joint with an

artificial prosthesis. Sepsis rates were high. Was clean air, at least in part, the answer? In a long series of studies which reduced the bacterial contamination levels in the proximity of the wound by more than 100-fold and which was accompanied by a better than 10-fold reduction in sepsis, it seemed that this might indeed be so. The reduction in airborne contamination was achieved by the wearing of occlusive clothing, which reduced dispersal by nearly 10-fold, and the use of directed-flow ventilation systems (essentially as proposed by Simon 100 years earlier), which produced a further fall of more than 10-fold again (Charnley & Eftekhari, 1969). Finally, a fully controlled study confirmed that in these operations the reductions in joint sepsis were, indeed, due to the reduction in air contamination at the time of operation (Lidwell *et al.* 1987).

CONCLUSION

A lot of water has flowed under the bridge since Lister revolutionized the practice of surgery on the initial assumption that it was 'les corpuscules organisées dans l'atmosphère' (Pasteur, 1862) that were the agents of surgical sepsis. Although he was ultimately persuaded that other routes predominated it is perhaps fitting in this year, the 75th anniversary of his death, that surgery should be a part of medicine where control of bacterial air contamination has not only been achieved but also shown to prevent infection.

Although airborne transmission of pulmonary tuberculosis does still occur (Rao *et al.* 1980) it is antibacterial treatment which controls its spread, not only by treating the disease but also by the rapid elimination of bacterial dispersal by the patient.

Airborne spread of animal and plant pathogens is undoubtedly a considerable problem with intensive husbandry but, once recognized, is susceptible of attack by methods not applicable to human populations.

The controversial area concerns the whole range of upper respiratory infections which, from their characteristics, would be supposed most plausibly to spread by the airborne route. The possibility, but not the demonstration of the primary importance, of this route has been shown. Direct control by means of measures to limit airborne transport does not at this time seem likely. The immunological complexities, coupled with the multiple possible places for transfer of infection to take place, must mean that any reduction in incidence will be very much less than proportionate to the reduction of airborne contamination with the aetiological agents in any one place (see e.g. Kingston *et al.* 1962). As with tuberculosis, it may be that control of dispersal is the more plausible.

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