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B2 Medical aspects of respiratory disease

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THE STRUCTURE OF THE RESPIRATORY SYSTEM

This year has seen the publication in Oxford of a comprehensive new British Textbook of Medicine. With this symposium in mind I turned up Agriculture in the index. The single entry refers to the following statement in the text: "Fungicides and pesticides carelessly used are frequent causes of dermatitis. This particularly occurs in isolated farms in developing countries." And that is the sole indexed reference to agriculture! I imply no criticism of this excellent text but seek only to highlight the apparent isolation between the disciplines of agriculture and medicine identified in the discussion document (Section A).

Today I want to consider respiratory disorders which may be linked with agriculture and the farming population. I approach from the standpoint of a hospital physician with a special interest in respiratory disease, serving a population of half a million in West Berkshire, an area not without farmers.

I hope that an initial brief consideration of lung structure and function and some of the factors influencing the inhalation of foreign materials will help later discussion, particularly for those without a biological background. The job of the respiratory system is to bring air into intimate contact with the blood to allow gas exchange. Oxygen is taken up and carbon dioxide is eliminated. The system is basically a bellows pump with an air conditioner at one end linked by conducting tubes to a gas exchanger at the other end.

Each day we breathe in and out about 10,000 litres of air which is warmed, humidified and filtered by the nose which is a remarkably efficient air conditioner. Inspired air passes from the nose into the conducting system beginning at the trachea and ending at respiratory

bronchioles from which the gas exchanging alveoli originate. Figure 1 is a photograph of a cast of the airways showing the complexity of this network from trachea to terminal bronchioles. From the trachea downwards each branch of the airways divides into two daughter branches smaller in calibre than the parent but, over the complete number of about 23 generations, the total cross-section and volume of the system increases, while the individual airways become smaller (Figure 2). Thus the maximum resistance to airflow is proximal in the trachea. With contraction of muscle in the walls of the smaller airways this situation can be reversed and this is essentially what happens in asthma.

The epithelium which lines the conducting airways is furnished with cilia (or minute hairs) covered by a thin layer of mucus. The cilia beat in a co-ordinated fashion moving the layer of mucus towards the trachea taking with it trapped foreign particles, somewhat like an escalator. Movement of as much as an inch a minute has been recorded. Cilial movement can be affected by certain inhaled substances, for example cigarette smoke is known to slow down their action. In the gas exchanging parts of the lung, which have no cilia, mobile scavenger cells engulf particles which are then either absorbed into the bloodstream or deposited on the mucus escalator.

Exchange of gases takes place across an enormous interface of about 80 m^2 in the adult, made up of some 300 million alveoli.

Here then is an arrangement of exquisite refinement which, despite its complex defences, is itself by its very nature vulnerable to insult from without, and provides rapid access to the bloodstream with consequent immense potential for harm.

REACTION TO INHALED SUBSTANCES

At this point I think it is worth considering briefly how potentially harmful substances may be brought into contact with the lungs. Materials of diverse nature and physical form once airborne may reach the airways and their physical properties are the main determinant of this. The more that a material is broken down, finely divided and dispersed, the more likely it is to become airborne. It is useful to distinguish between dusts and mists. Dusts can be defined as solid particles dispersed in air and mists as liquid droplets similarly suspended. The droplets may be formed by condensation of vapours or by "atomisation" of liquids around appropriate nuclei. The term aerosol may be used to describe airborne particles in all categories and thus include both dispersed particles and droplets. It is thus possible for potentially dangerous particles to vary in size between those just small enough to enter the upper respiratory tract down to actual gas molecules. Table 1 compares the size of some relevant particles.

How do our defences cope? Clearly gaseous poisons have virtually free access to the gas exchanging parts of the lung but against aerosols there is some defence. The nasal air conditioner is of great importance

Figure 1

A cast of the conducting airways of the respiratory system

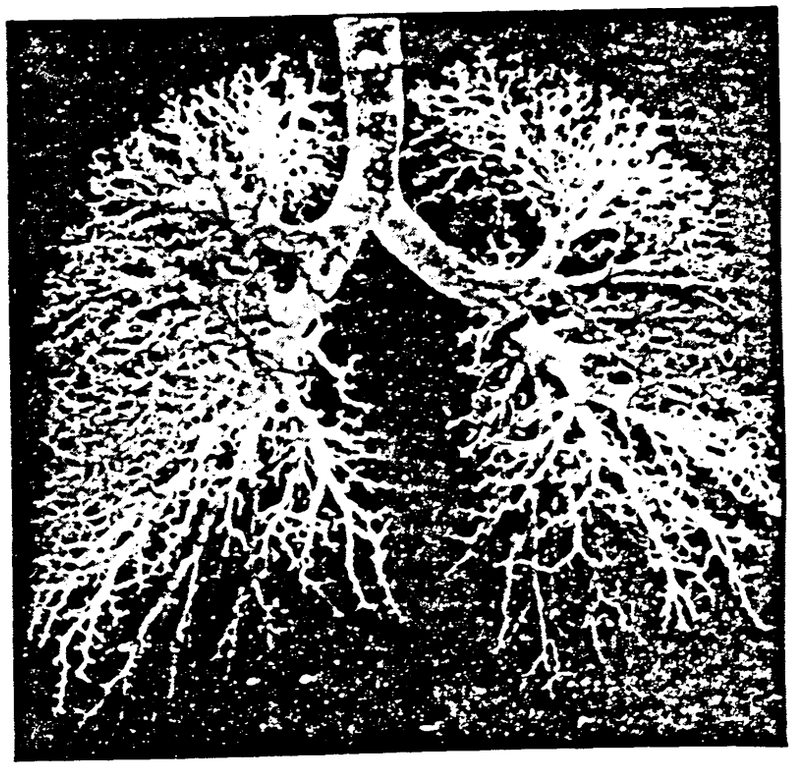

Figure 2

Generations of the conducting airways of the respiratory system

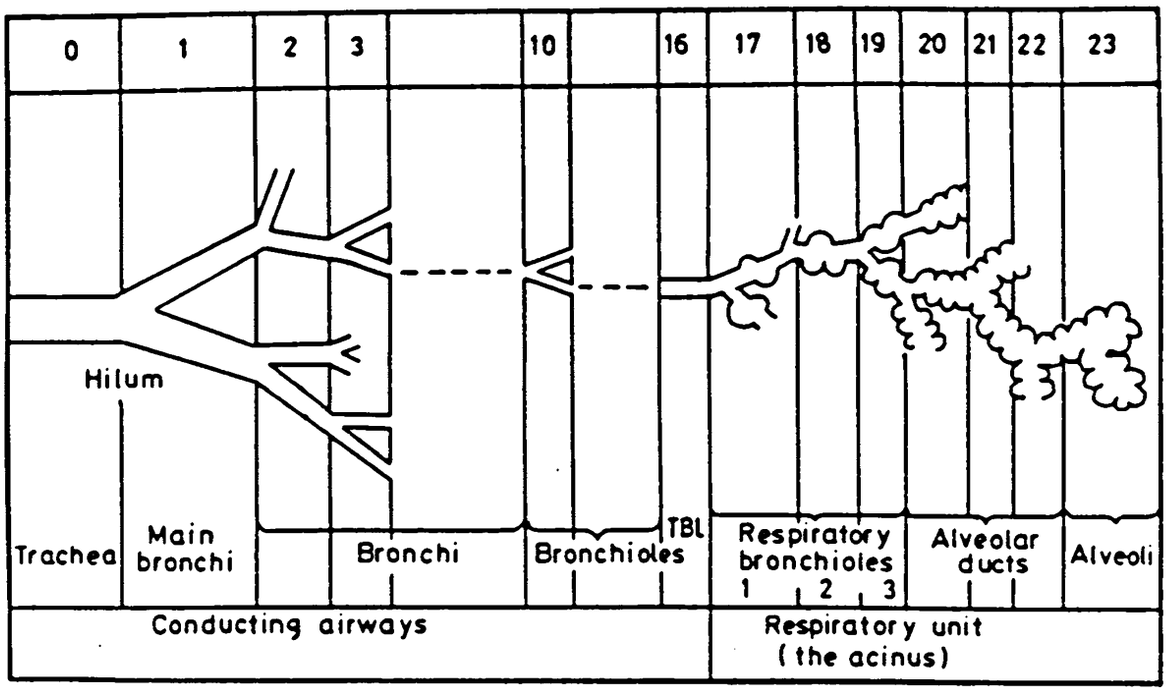

Table 1

Sizes of particles which may be inhaled

Sand grains	200 - 2000 μm diameter
Cement dusts	4 - 100 μm diameter
Pollens	10 - 100 μm diameter
Fungal spores	2 - 100 μm length
Actinomycete spores	0.6 - 2.5 μm length
Tobacco smoke	0.2 - 2.0 μm diameter

and removes most particles between 5 and 20 μm in diameter; in addition, deposition of many particles smaller than 5 μm is brought about by humidification which makes them grow in size. Within the air conducting tubes of the lung the factors governing deposition of particles are complex and not fully understood. It appears that particles between 2 and 5 μm in diameter are most likely to elude the defences and become deposited in the gas exchanging alveoli. Their subsequent fate during clearance is critical to the production of disease.

Inhaled particles can be divided into those which are inert and do not stimulate a tissue response and those which by disturbing normal cellular behaviour trigger a chain of events which may lead to disease. In the conducting airways inert and insoluble toxic materials are virtually completely eliminated within a matter of hours by the mucus escalator. In the gas exchanging alveoli there is a distinct difference between the handling of inert and toxic particles. Elimination of inert particles is effected by scavenger cells which deposit them on the mucus escalator and this process may take a matter of years as exemplified by the continuing expectoration of coal dust by miners long after leaving the pits. Elimination of particles toxic to cells is quite different as they are lethal to the scavenger cells and are therefore denied transfer to the mucus escalator. They tend to remain in the zone of their deposition and can cause a scarring reaction with destruction of normal lung tissue or, if they are what is termed antigenic, may be capable of provoking an immune or allergic form of response. Soluble particles will dissolve and may pass into the blood or become bound to lung tissue thus mediating either widespread bodily or local lung reactions.

It can therefore be seen that the lungs are liable to occupational insult and it is against this general background that I would now like to consider some of the hazards relevant to agricultural workers.

AGRICULTURAL HAZARDS

I shall group diseases under three separate headings.

Farmer's lung (extrinsic allergic alveolitis)

Idiosyncratic (asthma)
Agrochemicals

Farmer's lung

There is much lay and indeed professional confusion about farmer's lung. I sometimes have the impression that virtually anything wrong with a farmer is automatically labelled as such. This is in fact a relatively rare disease, particularly so in this part of England and in more than five years in Berkshire, despite being on the lookout, I have not seen a single case. No exact figures are documented but the most reliable estimates suggest about 1000 cases annually in Britain. First recognised only fifty years ago in this country the condition was actually first described in 1700 by an Italian, Bernardino Ramazzini. It is now a prescribed occupational disease in the UK with entitlement to Industrial Injuries Benefit.

The cause is inhalation and subsequent immune sensitisation to the spores of a group of microorganisms which only grow at temperatures between 30-65°C. If hay with a water content of more than 30% is stored, considerable heat may be generated and these heat loving organisms will flourish. Subsequent handling of the hay, particularly in poorly ventilated enclosed surroundings, can lead to inhalation of massive doses of spores. The size of the spores, 1-3 μm in length, is such that they become deposited in the gas exchanging alveoli. A complex allergic form of reaction may then be triggered off due to the antigenic nature of the spores. On first sensitisation an acute illness develops which is characterised by shortness of breath, shivering, fever and cough, all coming on a few hours after exposure. X-ray of the chest may show widespread shadowing. With avoidance of spores the condition resolves spontaneously over a few weeks but re-exposure will cause rapid recurrence and repeated exposure can lead to progressive lung damage, eventually with death due to lung and heart failure.

Preventive measures are logical and obvious; adequate drying of hay before storage and forced ventilation in working areas. A farm worker who has had more than one acute attack should ideally change his occupation, as complete avoidance is virtually impossible and masks and respirators are not really effective in practice. Wider publicity drawing attention to the dangers of handling all mouldy vegetable produce is required to control what at the best can be disabling and at the worst life threatening.

Farmer's lung belongs to a group of diseases referred to technically as extrinsic allergic alveolitis. Many substances have been identified which are capable of causing similar diseases both at work and in the home. The most common in this group is budgerigar lung. Table 2 lists some of the exotic diseases now recognised and it will be noted that several of these occur in an agricultural setting.

Table 2

Forms of extrinsic allergic alveolitis other than farmer's lung

Animal food workers' lung
Animal handlers' lung
Bagassosis
Bird fanciers' lung
Blackfat tobacco smokers' lung
Cheese workers' lung
Coffee workers' lung
Dry rot lung
Furriers' lung
Humidifier fever
Malt workers' lung
Maple bark strippers' lung
Mushroom workers' lung
Paprika splitters' lung
Sauna-takers' disease
Sequoiosis
Sewage sludge disease
Suberosis
Wheat weevil disease
Wood pulp workers' disease

Asthma

Second on my list is asthma which can be defined as a disease characterised by an increase in resistance to airflow within the lungs. A proportion of individuals have an inherent "twitchiness" of their airways. Earlier I mentioned how contraction of muscle around the conducting airways by narrowing their calibre could increase airflow resistance. The temporal pattern of this response and degree of "twitchiness" vary greatly. The mechanisms behind this can have many other effects including stimulation of coughing and increase in mucus production and thus the presentation of asthma can be highly variable. Similar mechanisms are responsible for rhinitis or hay fever with increase in secretions, swelling of tissues and provocation of sneezing. Farm workers with this inherent tendency are exposed to many inhaled substances possessing the potential to trigger off these idiosyncratic responses. Whereas in farmer's lung anyone is at risk of being sensitised, in general only individuals with an inherent predisposition will develop asthma or rhinitis when exposed to appropriate inhaled substances. An increasing number of causes of occupational asthma has been recognised in recent years and it now appears that certain substances can cause asthma even in individuals without inherent predisposition. Recently occupational asthma has joined farmer's lung in being eligible for compensation.

I shall not attempt to list all possible causes but rather consider a

few important illustrative examples. Firstly, grain dusts, which have been associated with asthma since Ramazzini's time in the 18th century. Variation in grain dusts and associated moulds is wide according to whether they are encountered during harvest, storage, handling or milling. Our present knowledge indicates that predisposition to asthma is important and that smokers are more likely to develop trouble. Prevention lies in dust control measures, selection of regular handlers from the ranks of the non-smoking non-predisposed and appropriate medical treatment.

Secondly, barn allergy, which presents as rhinitis and asthma and is caused by inhalation of the droppings of a range of storage mites which infest stored vegetable produce. This condition may easily be confused with farmer's lung wherein lies its importance because barn allergy does not cause destructive lung change and is susceptible to simple medical measures.

Finally, hay fever sufferers are only too well aware of the importance of grass pollens which can also cause asthma. Hay fever is at present one of the very few allergic responses for which specific treatment may produce lasting beneficial effects.

Prevention of asthma and rhinitis caused by extrinsic assault logically involves measures to reduce the dose of the offending inhaled substance. However, each case should be considered on its merits as there is a tendency to over-reaction with resulting recommendations for quite impractical avoidance measures. In industry it may be necessary to identify susceptible workers and exclude them from certain processes but, apart from farmer's lung, I see little application of this in agriculture. Both increasing understanding of asthma and our modern drugs have made it possible for the majority of susceptible individuals to remain well despite exposure.

Agrochemicals

Finally, let us consider the dangers from inhalation of agrochemicals. A vast range of potentially toxic substances is used in agriculture today and it seems reasonable to speculate that their inhalation in various forms will be responsible for significant harm to man. Epidemiological study however suggests that this is not the case and it appears in fact that the incidence of poisoning from inhaled chemicals is remarkably low.

DDT for example has been condemned for its biological persistence and extrapolation from animal experiments has fostered worries about congenital malformations and malignancy, but there is no evidence in man to confirm this. Organophosphorus insecticides, which have largely replaced DDT, owe their origin to nerve gases developed during the last war but the chemical derivatives for agricultural use are much modified in action. They can be absorbed via the skin, gut or lungs. Problems normally only arise from swallowing concentrates although farm workers can be at risk during crop spraying. Significant exposure

causes excessive sweating, salivation, vomiting and colicky abdominal pains and in severe cases hospital treatment is a matter of urgency. There is a specific blood test which can be used to monitor workers repeatedly handling these chemicals.

The chlorphenoxyacetate herbicides are the so-called hormonal weedkillers. 2, 4, 5-T which belongs to this group has been the subject of much controversy but, despite allegations of association with malignancy, no confirmatory evidence exists for this in man. Occupational poisoning with this group of herbicides is virtually unknown.

The bipyridilium herbicides are total weedkillers and one of these is paraquat or gramoxone which has attracted a certain notoriety. By mouth as little as two teaspoonfuls of the concentrated solution can be lethal. As doctors we are familiar with this in attempted suicide. Direct inhalation into the lungs from sprays is unlikely as the particle size is too large. Only one case of lung disease due to inhalation is reported in the medical literature and this was non-fatal and thought to be due to inhalation of a mist of paraquat drifting from a field into a nearby garden. Absorption of concentrated solutions through the skin is the main occupational risk and several deaths caused by careless handling have been reported. Poisoning by this chemical is of particular interest to respiratory physicians as even in the absence of inhalation a delayed and progressive form of lung fibrosis results. Prevention lies in education of workers in correct usage with respect for concentrates and the use of protective clothing with impervious footwear during spraying.

CONCLUSION

I have not set out to present an all embracing review and I have left unmentioned topics such as silo-filler's disease and infections such as brucellosis, anthrax, psittacosis and Q fever.

The potential for harm by inhalation presented by substances encountered in modern agriculture is clearly substantial but the observed results in terms of disease do not support the concern which is expressed in some quarters. Certainly I do not countenance complacency, constant vigilance and acute awareness of potential dangers are greatly to be applauded, but a measure of common sense must be encouraged. Camels in the desert do not develop silicosis; household bleach is known to be harmful and we do not swallow it and if the kitchen is too hot we get out of it! I suggest that little has changed since the time of Ramazzini.