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Abstract
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Lessons from Medical History - Occupational and Environmental Diseases

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Two sorry stories.

In about 1990, two middle aged men died in Aberdeen Royal Infirmary from a fibrotic lung disease. I was asked to see the second of these men in his terminal illness and found that both had been working as stonemasons on Elgin cathedral, employed by Historic Buildings, Scotland. A visit to the workplace showed that they and their colleagues had been and were being exposed to very high concentrations of fine quartz dust from the use of powered tools on sandstone. There was no local exhaust ventilation to extract dust and the respirators provided were inadequate. Post mortem studies showed the two men to have died from acute silicosis, a condition not described in modern times in Britain. Fortunately, it was possible to prevent further serious illness in the remaining masons by appropriate action.

In 1995 a 40-year old stonemason presented to the rheumatology clinic at the Western General Hospital with painful, cold hands. He had been working for decades renewing Georgian houses in the New Town. I was asked to see him because his chest radiograph showed nodular and massive fibrosis; these changes were characteristic of advanced silicosis. His painful hands were a consequence of scleroderma. He had to leave his job and has subsequently retrained.

An interest in medical history is an indication of an inquisitive mind, the same sort of attitude that predicts success in clinical practice or scientific research. If, as you read a temperature chart or use your stethoscope, you ask yourself who first thought of taking a patient's temperature or of categorising the noises in the thorax and then take the trouble to find out, you are the sort of person who will do well in medicine. Diagnostic skill and the ability to find unsolved problems and perceive their solution both depend upon the child-like inquisitiveness that Rudyard Kipling described in the Just So Stories:

I keep six honest serving men
(They taught me all I knew);
Their names are What and Why and When
And How and Where and Who.

Environment and health: the original concepts.

Throughout history, there have been two rival concepts of disease causation, the imbalance of humours and attack by demons. The first refers to something innate in the body that determines personality, behaviour and susceptibility to disease, the vital spirit or "pneuma". To Aristotle and Galen in Greco-Roman times this came to mean too much blood, bile or phlegm and led, *inter alia*, to blood-letting as a cure. This concept persisted through the Middle Ages and held back understanding of illness until the Renaissance and the anatomical and physiological studies of Vesalius (1514-64) and William Harvey (1578-1657). The second probably arose in pre-history and animalistic times but received a boost from Christian belief, attributing disease to attack from without by malign spirits. Echoes of both these concepts are still heard today and the general ideas actually still hold true. Today's Galenists, unknowingly, are those geneticists who claim that my DNA determines my behaviour and predicts my future health. Today's demonists are people like me, who argue that the environment is the principal determinant of health and mortality. And, of course, both have hold on an element of truth.

De causis et sedibus morborum: how the body works and how it goes wrong.

The 18th century saw an extraordinary rise in scientific understanding that revolutionised medicine. Dissection of the body, pioneered by Vesalius, allowed doctors to learn anatomy and the experiments of Harvey led to an understanding of how it worked, physiology. The first great account of how disease affects normal structures, pathology, came from the work of Morgagni (1682-1771). The discovery by Priestley (1733-1804) of what was later called oxygen (which is as close as we have come to determining the character of the ancients' pneuma) allowed the possibility of understanding metabolism, and this in turn was built on by the great discoveries in chemistry of the 19th century. The experiments of the Abbé Mendel (1822-84) began to explain the mechanisms behind the theory of Darwin (1807-82) on evolution. This spirit of enquiry into the works of nature is the foundation of all the scientific and medical understanding that we now so easily take for granted.

Morgagni called his great book "De causis et sedibus morborum" – on the causes and seats of disease. This demonstration that the cause of disease lay within one was a stimulus to the humoral imbalance theory, and pursuit of this idea has now led to the dramatic discoveries of molecular and cell biology, DNA and the genomes of an increasing number of organisms including human beings. But also, in the 18th and 19th centuries, came the demonstration of the value of scientific study of the relationships between the environment and health. James Lind (1716-94), an Edinburgh surgeon, showed the importance of fresh fruit in preventing scurvy, doing the first controlled trial in the process. Edward Jenner (1749-1823) built on the empirical observations of others by experimentally developing an effective vaccine for smallpox from cowpox pustules. John Snow (1813-58) showed the relationship between contaminated drinking water and risk of cholera, and demonstrated the practical relevance of epidemiology by removing the pump handle to cut short the epidemic in Broad Street, London. Louis Pasteur (1822-96), originally a chemist, developed the science of microbiology and laid the scientific basis for producing effective vaccines, without which some of you might well not have survived childhood to read this article or I to write it. But long before such scientific methods were applied to the study of environmental effects on health, empirical observations had begun to support the demonic theory. Indeed, Hippocrates (c400BC), the father of medicine, had written of the occurrence of epidemics and promoted ideas of preventive public health. In the Middle Ages, some doctors had noticed that certain jobs were particularly unhealthy – Georg Bauer or Agricola (1494-1555) had drawn attention to the short life span of Bohemian metal miners, for example. The flowering of scientific understanding in Renaissance Italy, where Harvey went to study, included systematic observations by Bernardino Ramazzini (1633-1714), professor of medicine in Padua, on the diseases of different trades, and this was a theme taken up by Charles Thackrah (1795-1833), one of the founders of the Leeds School of Medicine, in the early 19th century. He even mentioned diseases of students in his book, including, "...A highly excitable state of the nervous system,...irritability of temper, vain fear and anxiety about trifles..." that he attributed to long periods of study without adequate exercise. We now call it "stress".

The 18/19th centuries saw a revolution in industry, great national prosperity, and increasing longevity but, paradoxically, a rise in epidemic diseases as cities grew and overcrowding and poor sanitation became a huge problem. Awareness of this imbalance gave rise to the concept of professional idealism, that the well educated and fortunate in society owed a debt that could be repaid by devoting themselves to amelioration of the lot of those less fortunate, a concept enunciated by Priestley as the pursuit of "the greatest happiness of the greatest number" and formulated as the Utilitarian Philosophy of Jeremy Bentham (1748-1832). This intellectual climate, in which the Scottish Enlightenment and Edinburgh

University played an important role, led to control of these diseases by public health measures (including the great Victorian water engineering works that have lasted up to the present time and are only now needing replacement). The classical occupational diseases, lead and mercury poisoning, silicosis and coalworkers' pneumoconiosis, were well described, and the first causes of cancer were discovered; interestingly, these were all occupational. First, Percivall Pott (1714-88), a London surgeon, described scrotal cancer in chimney sweeps' apprentices in 1766. Then, late in the 19th century, scrotal cancer was described in west Lothian oil shale workers by Joseph Bell (1837-1911), an Edinburgh surgeon and the model for Conan Doyle's Sherlock Holmes, while in Germany Härting and Hesse described lung cancer in metal miners (now known to be due to radon gas exposure) and Rehn described bladder cancer in chemical dye workers (now known to be due to absorption of aromatic amines). Ironically, it was these dyes that formed the basis of the studies by Paul Ehrlich (1854-1915) into chemotherapy and led to the development of the first effective antibacterial agents. And all these discoveries led in due course to the enactment of public health measures, legislation and regulation intended to prevent them; this is the objective of research into environmental and occupational disease.

A rolling road, a reeling road: from observation to prevention

The author GK Chesterton wrote a poem about the winding English road, made by the rolling English drunkard, and I have often thought of this as I have considered the many pitfalls between observation of an association of disease with an environmental cause and implementation of effective preventive action. Three such associations are worth considering before I return to the unfortunate patients I briefly described in my introduction.

Asbestos. Although asbestos has been used for fireproof materials since ancient times, it became a major industrial material right at the end of the 19th century and was used in Britain and most other industrial countries until very recently. It found many applications in strengthening other materials such as cement and plastics, in fire prevention and in sound-proofing. Up until the 1970s it was very widely used in buildings and ships, and it is still present in many buildings of that era and before. The first evidence that it was harmful came from reports of a progressive lung fibrosis in asbestos millers at the very end of the 19th century. By 1930 this was well established as the disease asbestosis and regulation to reduce exposure in factories was enacted. But also by this time, the industry was receiving alarming indications that some of its workers were dying of cancer and in 1950 the high risk of lung cancer in people with asbestosis was established by Sir Richard Doll (born 1912, and still working every day at the age of 92 – an example to all students who turn up late for lectures) and his colleagues. This was not all, since the industry was also aware of another fatal malignant condition of the pleura and peritoneum, mesothelioma, occurring in workers, early examples of which had been noted in Glasgow shipyard workers in the 1940s. There is evidence that the industry took the ostrich approach to this alarming suspicion, but in 1960 a pathologist in South Africa, Chris Wagner (1923-2000), described a high risk of mesothelioma among workers mining and milling blue asbestos. The hope of industry was that this disease only occurred in highly exposed workers, but sadly this proved not to be the case. By the time effective legislation was first introduced in the UK in 1969, many tens of thousands of industrial workers in shipyards, construction, engineering and countless other occupations had been exposed to sufficient to imply a real risk of development of the disease. Indeed, a man born in the 1940s has a 1% overall lifetime risk of mesothelioma; if he has been a shipyard worker that risk is about 7%. Today some 2000 people each year die of mesothelioma and this number is likely to rise for another 10 or 15 years until the effects of the cessation of asbestos use in 1980 has taken effect, since the disease has a latent period from first exposure to tumour development of many decades.

The lesson from asbestos is that a powerful industry is able to prevent effective legislation if it fears that its interests will be harmed. One way it does this is by diverting research from epidemiology (to quantify exposure-disease relationships) towards understanding mechanisms by animal experiment, and there is evidence that this is what the asbestos industry did. In the long run the consequence was, apart from tens of thousands of deaths, the demise of the industry and many of their insurers.

Smoking. It is difficult to believe that there was a time when the link between smoking and lung cancer was not obvious, but such is the case. In fact, lung cancer was relatively uncommon before the 1939/45 War, since smoking of manufactured cigarettes began in a big way in the trenches of the 1914/18 War (incidentally, women started smoking seriously in the Second World War when they went to work in the factories). In the early 1950s, Richard Doll started to investigate the rise in lung cancer, thinking it might be due to industrial pollution. His famous paper published in 1956, the year I went to medical school, showed its very strong relationship with smoking, and our governments have had no excuse not to legislate against the tobacco industry ever since. However, the tax derived from tobacco and the sponsorship of politicians, arts and sports by the industry have provided an object lesson in how altruistic legislation may be prevented. We now know that smoking makes an important contribution to the cause of many different cancers, from leukaemia to bladder cancer, and of heart attack, peripheral vascular disease and stroke. And yet Bernie Ecclestone, of motor racing wealth, was easily able to persuade our current Government that his 200mph cigarette advertising boards are perfectly acceptable on our TV screens. And have you noticed number of film and TV actors smoking on camera recently? You can bet that someone is paying them to do so, to influence the young.

Although men in general have now begun to get the message about smoking, this is unfortunately not true of women, and the lung is now the main site of cancer among them. We know how to prevent it, we know why people keep smoking (nicotine is seriously addictive), but we have been very slow to take effective action. We are up against an industry that is richer than many countries and more ruthless and less moral than the worst African republic. Let us hope that Scotland will soon follow Ireland and California in banning smoking in public places.

Vinyl chloride monomer. It is perhaps worth telling one tale about things going right, since this does happen occasionally. Polyvinyl chloride, or PVC, became a ubiquitous material in the 1950s and 1960s. It is made by polymerising vinyl chloride, a narcotic chemical that was once suggested as an anaesthetic. Such a simple chemical was not initially considered particularly harmful, but in the 1970s a few workers at a factory in the US developed a rare liver tumour, angiosarcoma. The factory doctor was alarmed and persuaded the industry to commission research on rats; this demonstrated that vinyl chloride caused the same tumour in them. The message rapidly went round all the PVC-producing industry that exposure to the monomer was potentially fatal, and steps were taken to enclose processes and prevent exposure. Happily, this was possible (although at some capital expense) without destroying the industry, and very few further cases of angiosarcoma have occurred since the initial outbreak.

To return to the beginning.

The disease silicosis was described as the cause of lung disease in stone-cutters and grinders in the 18th century, and lung disease was known in miners centuries before that. It was a particular risk to the knife manufacturers of Sheffield, who were known to die early as a result and, because it was common in many trades such as mining and tunnelling, it was one of the first diseases in Britain that allowed the sufferer to claim Industrial Injuries Benefit. We have known how to prevent it (stop people inhaling quartz dust by enclosure of processes, exhaust ventilation and if necessary respiratory protection) since the 19th century. And yet cases still occur, always through neglect of simple precautions. In the case of the Elgin stonemasons, the men were aware that the dust was dangerous and had asked for steps to be taken to reduce concentrations, but their managers had deferred doing so on the grounds, apparently, of cost. These managers were presumably unaware of the risks, silicosis being a disease that has largely been prevented and had thus become rare; legally they didn't have a leg to stand on.

The case of the man with scleroderma was particularly interesting, since in 1914 an Edinburgh physician, Byrom Bramwell, described for the first time an association between scleroderma and exposure to stone, among masons working on the New Town. His case reports of workers he had seen in the late 19th and early 20th centuries, which you can read in the Edinburgh Medical Journal of that year (1914;12:387), recount almost exactly the occupational history that I obtained from my patient. It is

even quite possible that they had worked on some of the same buildings. In over 100 years, nothing had changed.

So, what's in it for you?

We have evolved within our environment, and it is reasonable to suppose that, wherever we live, our internal milieu is somehow matched to our external. Things begin to go wrong with radical environmental change; this is most obvious of course with floods, war, famine and so on. More subtly, changes to diet from the efforts of the food industry or changes to the structure of work and play may influence our health. For me, interest is aroused when I hear of a disease being on the increase or decrease. Such changes occur when populations move, as in times of war or revolution, or over time with natural or induced changes to the environment. Think for example of the rise in skin cancers associated with the increased ability of UK citizens to afford holidays in the sun. Think of the current increase in cirrhosis in young women associated with the ready availability of cheap alcohol and relaxing of the taboo on female drunkenness in public. The recent rise in asthma and allergies seemed to me to be related to very substantial changes in the population's diet, perhaps by modifying susceptibility; could these be connected? Our current research in Aberdeen suggests strongly that some components of maternal diet in pregnancy and of early childhood diet do indeed modify the risks of these diseases. The occurrence of Parkinson's disease in certain drug abusers suggested that similar neurotoxic substances used as pesticides might have similar effects; our recent study in five European countries has shown exposure to them to be a significant risk factor for the disease.

The story of the gradual elucidation of the relationships between the environment and health is an unfinished one. From my own perspective, I should like to continue to disentangle the relationships between asthma, vitamin E and selenium. Do these nutrients influence immune development and expression of asthma genes? Can we find evidence that improving diet prevents asthma? I should like to know what environmental factors are responsible for the increase in Alzheimer's disease. I should like to know whether infecting organisms cause rheumatoid arthritis and other collagen or arteritic diseases. In these and all other unsolved mysteries in medicine, the cause is an interaction between genes and the environment, between the humours and the demons. Therein lie the opportunities for you, the next generation. Do not forget the demons!

A book to ask for, for your birthday.

Roy Porter. *The Greatest Benefit to Mankind: a medical history of humanity from antiquity to the present.* London, Harper Collins, **1997**.
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