Source – P.D.O Davies. 1994, Clinical Tuberculosis, Chapman & Hall Medical, London

HISTORICAL BACKGROUND

1

C.C. Evans

Tuberculosis is at least as old as mankind, and the history of the disorder is intertwined inevitably with the history of civilization. Like no other illness, tuberculosis has taken its toll of human life over the millennia, and has spread literally world wide. It is thought to be the oldest of human diseases, which has waxed and waned in its incidence, but has remained a perpetual threat, often in the background without, at least until the present links with AIDS, producing the dramatic epidemics associated with smallpox, plague or cholera. Its worldwide incidence and prevalence has never really been established, but in Europe in the eighteenth century, John Bunyan[1] referred to tuberculosis as the 'Captain of all these Men of Death' and a century later, Oliver Wendell Holmes[2] described tuberculosis as the 'white plague'.

The disease has not only been inseparable from man's progress, but it has been impossible to disentangle the medical issues from the economic and social life of the community. Tuberculosis has been the natural meeting ground for many medical disciplines, including general practitioner, physician, community physician, surgeon, pathologist, microbiologist, radiologist, pharmacologist and medical officer of public health, all of whom with suitable cooperation have been able to benefit both the patient and the community. In the twentieth century, the disease has been the launching pad for the specialties of thoracic medicine and surgery and numerous thoracic societies, and the management and treatment of the disorder has demonstrated perhaps above all other conditions, the necessity for, and benefits of, clinical trials and structured research.

1.1 ORIGINS OF MYCOBACTERIA

Mycobacteria are believed to be amongst the oldest bacteria on earth, and are ubiquitous in the environment. They are free-living organisms to be found in soil, animal dung, salt and fresh water, mud flats and attached to algae and grasses. They are potentially pathogenic to many animals, including cattle and pigs as well as fish and reptiles.

It has been speculated that cattle were the source of human tuberculosis infection, and that *M. tuberculosis* was a mutant of *M. bovis*, which has a broad host range capable of infecting man and several other species, whereas *M. tuberculosis* is pathogenic only to man and not at all to cattle[3]. Interestingly, cattle first became domesticated in the Neolithic period[4], and studies of human skeletons from that time suggest that Pott's disease, showing collapse and anterior fusion of adjacent mid–thoracic vertebra, represents compelling evidence but not unequivocal proof, of such a hypothesis. The relatively recent finding of acid- and alcohol-fast bacilli in human remains comes from human skeletons in Heidelberg, Germany, dating back to 5000 BC (Fig. 1.1)[5]. Similar proof has been obtained from Egyptian mummies from around 3500 BC[6]. Other examples of prehis-

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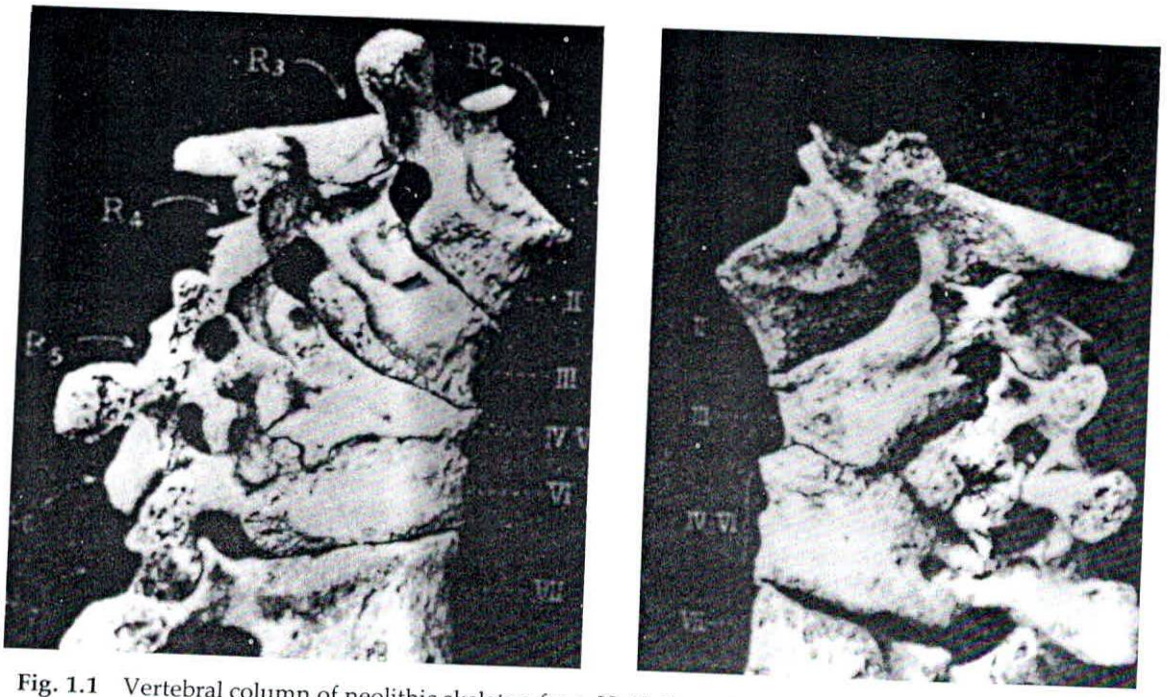

Fig. 1.1 Vertebral column of neolithic skeleton from Heidelberg demonstrating collapse of 4th thoracic vertebra and fusion with 5th. (Reproduced with kind permission from A.S. Lyons and R.J. Petrocelli, *Medicine: An Illustrated History*, Published by N. Abrams, 1987.)

toric skeletal tuberculosis include a Jordanian bronze age skeleton from 3000 BC[7] and a Nesperehan mummy from 1000 BC which revealed not only Pott's disease of the spine, but a psoas abscess[8]. Scandinavian skeletons illustrating Pott's disease have been found in Denmark from about 2000 BC[5] whereas the first UK skeletons are from 200–400 AD[4]. Similar proof of infection has been discovered in Southern Peru from about 700 AD[9], but the first descriptions in North America on skeletal remains were all after Columbus. Similarly, there has been no recorded evidence of tuberculosis in South Africa, Australia or New Zealand prior to colonization.

1.2 TUBERCULOSIS IN ART AND LITERATURE

The Egyptians left many hunchbacks on Dynastic tomb inscriptions of about 3500 BC, but it cannot be proven whether these are evidence of skeletal tuberculosis or, in view of their abundant presence, mere stylistic art conventions of that culture (Fig. 1.2). It should be noted, however, that the hunchbacks of the early Egyptian Dynastic period are truly angular deformities, whereas the hunchbacked flute players of early prehistoric American art have smooth, rounded deformities, and cannot be accepted as proof of pre-Columbian American tuberculosis (Fig. 1.3)[8].

Early physicians diagnosed disorders on the basis of symptoms and superficial signs, and clearly lacked the precision of diagnosis afforded by modern techniques. Moreover, symptoms of tuberculosis are not always precise, nor confined to a single organ, so that the historian must be aware of the alternative terms used to describe various tuberculous organ disorders and their differential diagnosis that might be attributed to those symptoms and signs (Table 1.1).

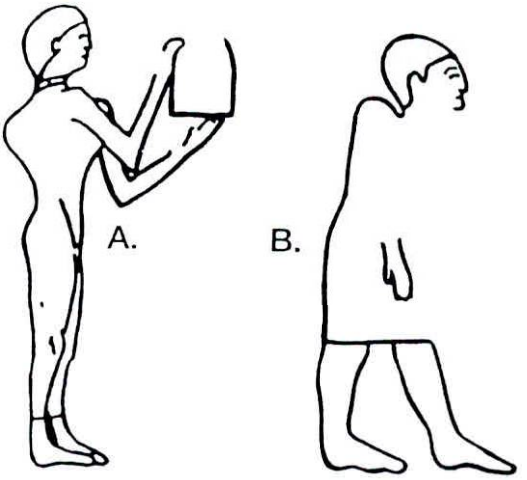

Fig. 1.2 Egyptian tomb inscriptions demonstrating hunchback figures: Dynastic period. (Reproduced with kind permission from D. Morse, D.R. Brothwell and P.J. Ucko, Tuberculosis in Ancient Egypt, *Am. Rev. Respir. Dis.*, 1964,1590, 528)

Fig. 1.3 Kokopelli – hunchbacked flute player shown on pottery bowl of Great Pueblo Period 1300 AD. (Reproduced with kind permission from K.F. Wellmann, Kokopelli of Indian Paleology, *J. Am. Med. Assoc.*, 1970, **212**, 1680.)

Egyptian medical papyri refer to cases of cervical lymphadenopathy in the Ebers papyri[10] and tuberculous scrofula might easily be the cause. Chinese writings of 2700 BC describe lung fever and lung cough, which, coupled with the expectoration of blood and sputum and generalized wasting, is strongly suggestive of pulmonary tuberculosis[11]. The Sanskrit writers of 1500 BC were clearly familiar with pulmonary tuberculosis, and the Rig-Veda is an original surviving record. Mesopotamian writings of 675 BC are more suggestive of pulmonary tuberculosis[12] and there are no descriptions to be found in the Old or New Testaments of the Bible.

Greek literature contains numerous references to conditions resembling consumption, including those by Homer (800 BC), Hippocrates (460–377 BC)[12], who probably introduced the term phthisis, Aristotle (384–322 BC), who recognized the contagious nature of the disorder[13], and Plato (430–347 BC), who recommended no treatment because caring for chronic tuberculotic patients was of no advantage to the patient or the state[13]. Galen (131–200 AD), practising in Rome, noticed how contagious phthisis was, and that bronchial obstruction could result in the expectoration of calcified bodies in the sputum[13]. Vegetius (420 AD) remarked that animals were victims of consumption, as well as man. Aretaeus, whose precise dates of living are not known, wrote a classical description of advanced tuberculosis in his book entitled 'On the causes and symptoms of chronic diseases'[14].

The Arabic physicians Rhazes (Al Razi 850–953) and Avicenna (Ibn Sina 980–1037) linked lung cavities with skin ulceration and wrote like the early Greeks, on the benefits to be had of dry air, good food and the potential curability of the disorder. These two Arabic physicians anticipated finding tuberculosis in young people aged 18–30 years with narrow chests and a thin body. At about the same time, Al-Majousi described clubbing of the finger and toe nails[15].

Table 1.1 Historical terms used to describe tuberculosis and other possible causes of that condition

Tuberculosis	*Historical synonym*	*Differential diagnosis*
1 Acute progressive	Galloping consumption	Neoplasms and diabetes mellitus
2 Pulmonary	Consumption	Bronchial neoplasm
	Phthisis	Rheumatic and congenital heart disease
	Tabes pulmonali	Pneumonia
	Tissic	Lung abscess
	Hectic fever	Empyema
	Gastric fever	Lymphoma
	Asthenia	Sarcoidosis
3 Cervical adenopathy	Scrofula	Malignancy
	Stroma	Syphilis
	King's Evil	Colonic neoplasm
4 Abdominal	Tabes mesenterica	Crohn's disease
		Appendix abscess
5 Skin	Lupus vulgaris	CDLE
6 Meningitis	Acute hydrocephalus	Bacterial meningitis
	Infantile encephalitis	Encephalitis
7 Vertebral	Pott's disease	Bacterial spinal abscess
		Hereditary degenerations

Source: H.M. Coovadia and S.R. Benatar, *A Century of Tuberculosis*, Oxford University Press, 1991, Tables 1.1 and 1.2.

1.3 RENAISSANCE PATHOLOGY

During the Middle Ages, there was no record of the incidence of tuberculosis, although the Montpellier physician Arnold of Villanova (1235–1312) noted that scrofulous patients always had alternative sources of infection within them, and recommended that there was no purpose in operating externally[16]. The healing touch of the monarch was restricted to tuberculosis of the neck glands, and records show that Edward I touched 533 victims in one month, and Philip of Valois (1328–50) put the king's hand on 1500 scrofula cases at a single ceremony[17]. These achievements were insignificant when compared with the 92 102 scrofulous patients on whom Charles II bestowed the royal touch[18].

By 1650, consumption was a leading cause of mortality recorded in London's Bills of Mortality, and there were references in Shakespeare's plays, such as 'the consumptive lover' in *Much Ado About Nothing* and scrofula in *Macbeth*.

Paracelcus (1490–1541) wrote of miners' phthisis[19] and Frascatorius (1483–1553) postulated the existence of imperceptible particles as the cause of the disease some 300 years ahead of the microbiological discovery[17]. By now, pathological dissection was contributing to physicians' understanding of the 'great killer', and Sylvius in Leyden (1614–72) correlated the development of tubercles with various symptoms[20], and at roughly the same time Thomas Willis (1621–75) appreciated that systemic manifestations attributable to consumption must result from internal lung ulceration[21]. Richard Morton (1637–98) described many pathological tuberculous features and gave sound advice about

the prevention of phthisis, including the enjoyment of 'an open fresh and kindly air'[22].

Morgagni (1682–1771) believed that there were many potential causes for phthisis[18], but Desault in Bordeaux (1675–1737) believed that the disease was spread by infected sputum[23] – an opinion to be shared by Stark (1741–70)[24].

1.4 FRENCH CLINICAL EXAMINATION

It was Auenbrugger (1722–1809) who originally described the technique of clinical percussion in Austria[25], but it required Corvisart (1775–1821) in Paris to rediscover the technique during the golden age of French medicine[26]. It was he who taught Laennec (1781–1826) who subsequently invented the stethoscope, thereby permitting him to correlate physical findings with pathological dissected states, which had been taught to him by Bayle (1774–1816)[27]. There were opponents to the infective concept of tuberculosis however, and Virchow (1821–1902) asserted in the nineteenth century that phthisis was hereditary[28], whereas Southern Europeans in Italy, Spain and the South of France, centred around Montpellier, came to regard tuberculosis as infectious. Indeed, in the Italian Republic of Lucca in 1699, physicians were instructed to give notice to the Council of the names of patients suspected as suffering from tuberculosis, and Ferdinand VI in Spain introduced tuberculosis notification[29]. In Naples in 1782 it was mandatory to destroy the clothing of a patient dying of tuberculosis, but such foresight into prophylaxis was not sustained, and was lost until Koch's wonderful discoveries in 1882[30].

1.5 BACTERIOLOGY

In Northern Europe, in Britain, France and Germany, the notion existed that tuberculosis was indeed hereditary, and that one inherited the tuberculous diathesis. This so-called eugenic theory was smashed by Villemin (1827–92) who, in 1865, transmitted tuberculosis from man to rabbit by inoculation of tuberculous material, and subsequently from cow to rabbit, when the transmitted disease was much more severe[16].

In Berlin in 1882 Robert Koch (1843–1910) described the tubercle bacillus. Earlier, in his country practice in Wolstein, he had discovered the anthrax bacillus, and laid down his bacteriological postulates. Using aniline dyes and an oil immersion microscope, he was able to identify the tubercle bacillus in every lesion in the human or animal victim, he was able to culture the bacillus outside the body, and when he inoculated the bacillus into an experimental animal, it produced tuberculous lesions. Henceforth, searching for the bacillus in the sputum of suspected cases quickly became standard clinical practice[30].

Koch considered initially that there was no difference between human and bovine tubercle bacilli, but in 1898 Theobald Smith in Harvard showed that there were microscopic, morphological and toxic differences between the various bacilli[31]. In all, five varieties of tubercle bacilli have been distinguished, and these are human, bovine, avian, murine and piscine. The human bacillus is now thought to account for 98% of cases of pulmonary tuberculosis spread by droplet infection by coughing and sneezing, and 70% of non-pulmonary forms. Bovine infection was commonly acquired by drinking infected milk or, rarely, by eating infected beef. Bovine infection is related to the non-pulmonary forms of the condition such as cervical lymphadenopathy, intestinal and abdominal tuberculosis, bone and joint disease, skin infections and tuberculous meningitis, especially seen in children.

1.6 RADIOGRAPHIC DISCOVERY

In 1896 Röntgen (1845–1923) announced the discovery of X-rays, which technique was

quickly applied to disorders of the chest and tuberculosis in particular. In time, but sadly not immediately, this advance in diagnostic achievement was to revolutionize the management of tuberculosis.

1.7 PUBLIC ATTITUDES

In the early nineteenth century, during the time of these pivotal pioneering and scientific discoveries, the incidence of tuberculosis was increasing in Europe and the United States, although precise figures are lacking. It has been estimated that 30% of all deaths under 50 years of age in Europe could have been attributed to tuberculosis. Death certification became mandatory in the UK in 1838, although tuberculosis mortality was probably underestimated because of the reluctance of relatives and friends to have the death so registered because of the stigma attached to the disease. Such a stigma reflected the public notion that tuberculosis was an inherited weakness, and as such might interfere with potential marriage and employment of other relatives.

1.8 COLONIZATION

The hereditary theory of tuberculosis historically gained credence because of the apparent increased susceptibility of various ethnic groups consequent upon their first exposure to infected people as a result of colonization, mainly from Europe. The so-called virgin population concept has been seen in the native populations of North America (American Indians)[32], South Africa (Africans)[33], Australia (Aborigines)[34], New Zealand (Maoris)[34] and Papua New Guinea[34], in which the natives developed a higher incidence and more severe form of consumption than the colonizers. Such a concept permitted the colonizers to explain the increased mortality due to tuberculosis in the natives rather than to admit that the changes they had induced in the natives' environment played any role in the development of the fatal scourge. It was the colonizers who brought the disease to the native population, not only in the nineteenth century, but as early as the Mayflower pilgrims in 1620[32] (Chapter 10, p. 191).

1.9 MIGRATION

European migration in the nineteenth century was also responsible for an increased incidence of tuberculosis. As a result of the Irish potato famine, many Irish immigrants settled in Boston, Massachusetts[35], and Liverpool, England, but smaller epidemics brought about by immigration were described, such as the Outer Hebrideans entering the city of Glasgow. Migration not only occurred for economic reasons, but tuberculous victims were deliberately encouraged to migrate and move to regions where their chances of recovery would be enhanced by allegedly favourable environmental circumstances. Thus, many Europeans with tuberculosis were tempted to travel to the fashionable, sunny, Alpine resorts of Davos and Leysin in Switzerland, Cape Town in South Africa[36], Melbourne in Australia[34], and Colorado in the USA[37].

1.10 SOCIOECONOMIC DEPRIVATION

It is now believed that the common explanation for the increased incidence of tuberculosis both in the colonized and the immigrants is the socioeconomic decline suffered by these groups. Loss of land by natives in colonized countries not only led to overcrowding, but also to loss of valuable food sources. Severe overcrowding during the European industrial revolution in the seventeenth and eighteenth centuries, caused many people to be living in appalling conditions that were dark, damp and congested. Such people were invariably underfed. Whole families lived in rooms no more than 3 m^2 in urban squalor, where they would also be exposed to high doses

Table 1.2 Famous victims of tuberculosis

Henry Purcell	1659–1695	Composer
Voltaire	1694–1778	Philosopher
Sir Walter Scott	1776–1832	Romantic poet and novelist
Niccolo Paganini	1782–1840	Violinist
Percy Bysshe Shelley	1792–1822	Poet
John Keats	1795–1821	Poet
Elizabeth Barrett Browning	1806–1861	Poet
Edgar Allan Poe	1809–1841	Writer
Frederic Chopin	1810–1849	Composer
Charlotte Brontë	1816–1855	Writers
Emily Brontë	1818–1848	
Anne Brontë	1820–1849	
Fyodor Mehailovich Dostoevsky	1821–1881	Writer
Edvard Grieg	1843–1907	Composer
Robert Louis Stevenson	1850–1894	Writer
Anton Chekhov	1860–1904	Playwright
Amadeo Modigliani	1884–1920	Painter
D.H. Lawrence	1885–1930	Writer
Katherine Mansfield	1888–1922	Writer
Joseph Boynton Priestley	1894–1984	Writer
George Orwell	1903–1950	Writer

Source: H.M. Coovadia and S.R. Benatar, A Century of Tuberculosis, Oxford University Press, 1991, Table 1.3.

of infective and infected sputum. In the USA, Trudeau (1848–1915) demonstrated in rabbits the significance of such deprivation. He inoculated ten rabbits with a similar dose of tubercle bacilli setting five free and confining the other five to a damp, sunless existence, and given a poor diet. When those who had been set free were subsequently captured and sacrificed, their bodies showed features of healing from their inoculation, but those confined all died of tuberculosis[38]. A similar intriguing observation linking social deprivation with an increased incidence of tuberculosis was seen in European Jews during the Second World War. Ashkenazim and Sephardim European Jews have been thought traditionally to have a large racial resistance to tuberculosis, but during Jewish persecution, their tuberculosis mortality exceeded that of Gentiles, having hitherto been substantially less[29]. The increase in tuberculosis during the Second World War in Northern Europe has been attributed more to nutritional shortages than overcrowding and housing loss.

1.11 FAMOUS VICTIMS

Many doctors, physicians and pathologists died of tuberculosis, including notably Laennec and Trudeau. Many doctors who survived the disease were to work in sanatoria, and to take up thoracic medicine and surgery as a career. Many famous people suffered and died from tuberculosis, and until this century, the disease was thought to confer a creative energy and skill termed by the Greeks as 'spes phthisica'. No such real association is now thought to exist, and it is not surprising that a disorder accounting for up to one-third of deaths should have affected so many people; millions of less famous people were also victims, but for completeness a list of known creative tuberculotic patients is shown in the Table 1.2.

1.12 CATTLE AS A SOURCE OF INFECTION

At the start of the twentieth century, the elimination of infected milk at source was inaugurated, but not until Koch had acknowledged that there was indeed a difference in

the bacilli. Such public health measures were shown to very good effect in the USA from 1917 when there was a dramatic decline in non-pulmonary causes of tuberculosis[35]. In Europe, however, where most forms of the disease were, and are, due to pulmonary tuberculosis, the elimination of infected cattle was not associated with any significant reduction in overall tuberculous mortality.

1.13 MEDICAL MANAGEMENT

Reference has been made already to Hippocratic teaching in which the humoral inbalance of blood, phlegm, yellow bile and black bile required to be corrected for the restoration of health. This was thought to be achieved by venesection or the application of leeches, emetics and aperients, and induction of skin ulceration by blistering agents.

While no fresh air was recommended as a treatment in the Middle Ages, Sydenham extolled the virtues of fresh air taken while riding on horseback or travelling in an open-air carriage. The antiphlogistic therapy of venesection, emetics and purgation continued. All sorts and manners of dietary manipulations were attempted without any proven success. These consisted of the consumption in excess or avoidance of, milk, beef, tea, coffee, cocoa, alcohol and even tobacco: the application locally of ham fat was recommended by some. Laennec surrounded his patients with seaweed from the Brittany coasts. Drugs such as laudanum, digitalis, antimonicals, cod liver oil and astringents were all fashionable at one time or another[16].

1.14 SANATORIA AND NAPT

The sanatorium era lasted almost 100 years. The concept of such an institution was originated by George Bodington of Sutton Coldfield, who, in 1840, with remarkable perspicacity, urged that the tuberculous patient should be in an airy house in the country, which, if on an eminence, so much the better[39]. The neighbourhood should be dry and high, the soil of a light loam, the atmosphere free of damp and fogs, and the cold never too severe to breathe in from the open air. Exercise was encouraged, and the physical well-being sustained with a good diet and generous wine. Bodington's principles of treatment were not favoured in the UK initially however, but were taken up in Germany in particular. The first sanatorium was opened there by Brehmer in Silesia in 1859[40], and this was to be followed by his former patient Dettweiler in Falkenstein. It was here that rest periods in the open air gained popularity, and the Black Forest Institution of Walther at Nordrach became famous[41]. At the same time, sanatoria were being developed in the USA by Trudeau at Lake Saranac and in Denmark at Vejlefjord.

Many British physicians visited Nordrach and set up sanatoria in Wales, England and Scotland, all carrying the Nordrach prefix: Nordrach in Wales, Nordrach upon Mendip, and Nordrach on Dee at Banchory, Scotland[41]. Alexander Spengler founded the famous private sanatorium in Davos in 1866, which was to be the setting for Thomas Mann's novel *The Magic Mountain* ('Der Zauberberg') in which he gives an insight into the sanatorium concept where patients become dependent on the protected environment of the mountain and pine forests, and become disabled not only by the disease, but by the cure[42].

Koch's discovery of the tubercle bacillus in 1882 gave fresh impetus to the sanatoria movement. Some cures were achieved, and it became clear that if oxygen was indeed harmful to the tuberculous organism, open-air treatment would have some scientific basis.

In the UK in the second half of the nineteenth century, many consumptive patients were nursed and died in Poor Law Institutions, since there were attempts to keep them out of the voluntary hospitals to protect the

beds there for patients suffering from potentially curable diseases. Some of these voluntary hospitals however were specializing as chest hospitals for tuberculosis, such as the Brompton hospital, which opened in London in 1841. In 1898 the National Association for the Prevention of consumption and other forms of Tuberculosis (NAPT) was set up[43]. This was inspired by Sir William Broadbent who informed the Prince of Wales, later King Edward VII, together with Lord Salisbury the Prime Minister, as well as leading physicians that 'this terrible waste of life is preventable', to which his Royal Highness uttered the now famous comment, 'if preventable, why not prevented?'

Nearly 20 years after Koch's discovery, the realization of its importance became apparent, not only to the medical fraternity but to informed members of national associations against tuberculosis. They appreciated not only the scientific achievement of isolating the tubercle bacillus, but also recognized that the former unseen killer was now a visible target against which blows could, and must, be struck. NAPT was part of an international movement already flourishing elsewhere. In the USA, the National Tuberculous Association in 1889 fully realized that tuberculosis was distinctly preventable, that it was not directly inherited, and that it was acquired by direct transmission of the tubercule bacillus in sputum from the sick to the healthy [44]. Such education needed to be made available to the community at large, and similar propaganda was put out by the League against Tuberculosis, which had been inaugurated in France in 1892, its German equivalent established in 1895, and the Dutch association initiated in 1897. The three areas in which NAPT concentrated on prevention were education, the provision of institutional treatment and the elimination of tuberculosis from cattle. NAPT advertised, provided pamphlets and books, and their lecturers travelled all over the country educating people about bad food, bad air and bad drink as well as overcrowding, overwork and overstrain. It was recognized that there was a higher incidence of tuberculosis in those who were less prosperous, but NAPT did not have the power to improve the lot of city dwellers living in industrialized poverty and squalor. NAPT attempted to educate individuals to be personally responsible for not contracting tuberculosis by improving their lifestyle, but such advice could be neither understood nor taken by poor people. Sanatoria were constructed by public subscription in the UK and were a colossal investment at a time when institutions were an international panacea. They were certainly attractive objects of philanthropy, as the donors could see the results of their charity in a most substantial way.

Patients were admitted to sanatoria for an indefinite period. Discipline was stern, complaints were not tolerated, and the physician superintendent sought a submissive attitude of compliance at his initial interview. The atmosphere in many was like a school, and the attainment of good health was the teaching. Drinking, originally encouraged by Bodington, often resulted in dismissal, but smoking was permitted. Men and women were separated, gathering only for meal times, and the mail was censored in order to avoid mental agitation. Many sanatoria were in the countryside, making access difficult for visitors while at the same time isolating the sputum-positive victims from the community. Most sanatoria faced south, south-east and south-west, with radial pavilions leaving no part in the shade (Fig. 1.4). Design was spartan to resist the notion that luxury led to survival, lest return home might lead to relapse. Sunbathing was encouraged, and ingenious rotating summer houses were installed to maximize sun exposure in the UK (Fig. 1.5). The health-giving properties of the sun were the *raison d'être* for the Swiss clinics of Rollier at Leysin, which specialized in actinotherapy (Fig. 1.6).

The culture in the sanatorium was for a

Fig. 1.4 Leasowe Sanatorium, Merseyside, showing south-facing pavillions, all directed towards the sun.

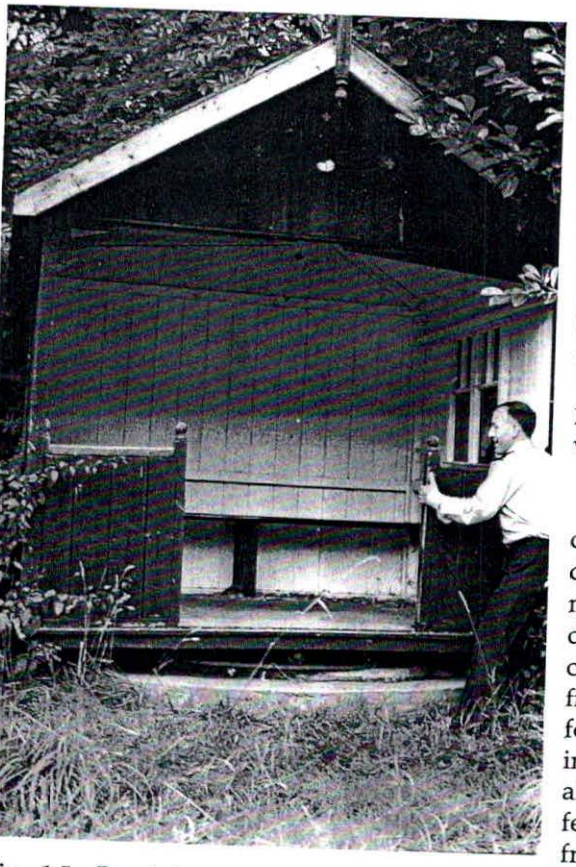

Fig. 1.5 Revolving summer house at Crossley Sanatorium, Cheshire.

Fig. 1.6 Children taking sunlight on a pavillion ward with the Swiss Alps in the background.

conscientious sustained performance of self-denial, self-restraint and endurance. The medical issues centred around rest, and disease activity was judged by the fever chart. Graded exercises such as receiving the first visitors were only permitted after a fortnight without fever, and washing, feeding and going to the lavatory were then allowed provided that there was no return of fever or haemoptysis. Good food and lots of fresh open air were followed by graded exercises, all carefully supervised with compulsory rest periods every day. With further

health improvement and weight gain, patients were encouraged to indulge in gardening, road making, carpentry and poultry keeping, and this formed the basis of the so-called 'pick-axe cure' for consumptives, which was to be the forerunner of the village colonies developed after the First World War in the UK. On discharge, patients were provided with home manuals which contained strict advice as to how to sustain good health[43]. These were to set patterns of public behaviour for years, and indeed generations. Medical follow-up was often carried out in the UK at the dispensaries, and additional drug therapy from a vast pharmacopoeia was tried. These included iron salts, calcium salts, cod liver oil, arsenic, antimony, gold, quinine, salicylates, iodine, creosote, turpentine, carbolic and tuberculin, none of which was demonstrated to be of any practical therapeutic value. Tuberculin, which is a glycerine extract of pure culture of the tubercle bacillus, had been developed by Koch in 1891, and when given subcutaneously in various strengths, showed positive skin reactions in all tuberculous patients. Koch considered that this potential remedy would form an indispensable aid to diagnosis. Unfortunately, tuberculin was introduced internationally prematurely, amid wild enthusiasm and without critical challenge, so that it quickly fell into disrepute as a treatment[45]. It has, of course, remained as a diagnostic tool.

Although sanatorium treatment remained one of the main weapons in the fight against tuberculosis for almost a century, there is no scientifically acceptable evidence that it reduced the toll of the disease. Sanatoria did make some patients feel better, and in others death was delayed. For some, especially children diagnosed as pre-tuberculous but without the disease, sanatorium treatment must have been harmful, as Thomas Mann suspected in *The Magic Mountain*. Comparative results from Saranac, Davos, Brompton and Norway were all similar, demonstrating that about 50% of sputum-positive patients survived for 5 years.

1.15 PUBLIC HEALTH

The International Union against Tuberculosis, with its double-barred cross emblem, was founded in 1902, with offices in Berlin. These were closed down during the First World War but reopened in 1920 in Geneva. The International Union was to encourage a system of tuberculosis control throughout Europe, consisting of notification of all cases, contact tracing and the provision of dedicated dispensaries and institutions, which were usually sanatoria. The prototype for these recommendations had come from Robert Philip in Edinburgh, who founded the Royal Victoria Hospital supported by public subscription; this was to become a model to be emulated world wide for the administrative liasions between the dispensary in the community, the sanatoria and the colonies, the hospital and the Medical Officer of Health, whereby contact tracing and home assessments by Health Visitors were introduced and coordinated[46].

In 1913, national legislation was passed in the UK to verify the notification of all forms of tuberculosis, and this was soon followed by the compulsory isolation of tuberculotics. The 1921 Public Health Tuberculosis Act made local authorities responsible for these aspects of tuberculosis care, and the cost was met from the local rates supplemented by an Exechequer Grant.

1.16 COLLAPSE THERAPY

In addition to first controlling the pulmonary disease by physical rest in the holistic sense in sanatoria, physicians adopted the idea of resting the lung itself by collapsing it with a pneumothorax. James Carson, an Edinburgh graduate, practising in Liverpool, induced artificial pneumothorax in experimental rabbits with beneficial results. When he tried to induce an artificial pneumothorax in man in 1822, in two cases of pulmonary tuberculo-

sis pleural adhesions and loculated empyema prevented a successful outcome[47]. Forlanini 60 years later in Italy induced artificial pneumothorax using nitrogen introduced via a needle with 200 ml instalments on a daily basis[48]. Forlanini's method of repeated small fill-ups was adapted and modified by Murphy in the USA, who gave a 1–3 l large-volume induction of nitrogen under radiographic control[49]. It became apparent that some of Forlanini's patients may have suffered gas embolism, which he termed 'pleural eclampsia' when the needle attached to the nitrogen cylinder was introduced. In Denmark, Christian Saugman added a water manometer to the needle and nitrogen source so that the operator was now able to identify where the tip of the needle was in the pleural space, and thus the safety of the procedure was improved[41]. During the early years of collapse therapy induced by artificial pneumothorax, benefit was thought to accrue only after a long period, but this view was challenged by Ascoli in 1912 who not only obtained effective healing using only a small artificial pneumothorax without significant lung collapse, but he was able to induce bilateral artificial pneumothoraces, further extending the application of the technique to subjects with bilateral pulmonary tuberculosis[50].

It is surprising how few sanatoria were capable of performing radiographs in the UK. In 1914, only 5 of 17 local authority dispensaries and 7 of 96 sanatoria in England and Wales provided facilites for radiography[41]. A notable exception had been Lawson, who installed an X-ray suite in his new sanatorium in Nordrach on Dee in 1900[51]. Morriston Davies had indicated that radiology was of extreme importance in the diagnosis of phthisis, and that it was essential before laying down a rational scheme of treatment[52].

1.17 THORACIC SURGERY

With the wider use of radiology, it was apparent that after induction of the pneumothorax, collapse of the diseased part of the lung frequently did not occur due to pleural adhesions. The idea of severing these adhesions was that of Friedrich in 1908, and this was brilliantly developed by Jacaboaeus of Stockholm using a thoracoscope in 1922. This enabled him to dissect and divide the adhesions under direct vision. This technique quickly spread throughout sanatoria in the Western world, and was known as intrapleural pneumonolysis. Impressed with the results of lung collapse achieved by artificial pneumothoraces, surgeons began to deliberately cause lung collapse by other physical methods in which the ribs were removed in part or in whole, and there were some heroic assaults on the thoracic cage and the patient (Fig. 1.7). The early surgical experience of this type caused an unacceptibly high mortality, but thoracoplasty as it was called became modified and refined, being performed in two stages. The first stage involved resection of the paravertebral portions of the lower ribs as proposed by Wilms[53], and this was followed by the second procedure in which the upper ribs were resected as proposed by Sauerbruch[54].

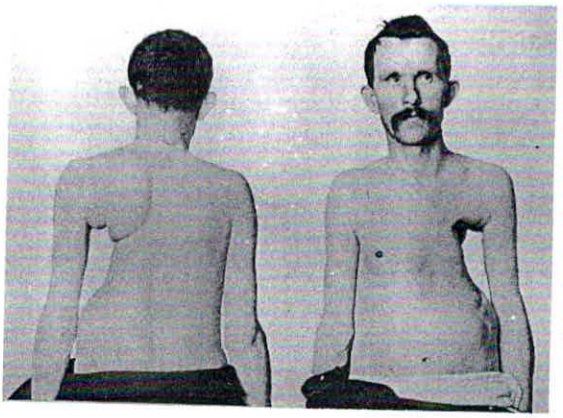

Fig. 1.7 Rib and pulmonary resection. Germany c. 1930.

Other forms of surgical collapse therapy, particularly directed to the upper lobe, were invented, and these included extrapleural

pneumonolysis, during which various substances were inserted into the extrapleural space in order to maintain lung collapse. In particular, surgeons used abdominal fat and moulded paraffin wax, producing a so-called extrapleural plombage. Collapse of the lung was also achieved by instilling oil rather than air into the pleural space, when an oleothorax was created. These latter procedures were never adopted universally, but phrenic nerve damage causing diaphragmatic paralysis proved very popular. Resection, division and evulsion of the nerve caused permanent injury, but phrenic nerve crush induced a temporary paralysis lasting about 6 months. Phrenic nerve crush was used in conjunction with other simple forms of collapse therapy, but was rarely successful when used on its own. In the 1930s phrenic crush was often used in conjunction with pneumoperitoneum when a 2–3 l insufflation of air was introduced into the peritoneal cavity to elevate both diaphragms and cause some lower lobe collapse.

Thoracic surgical prowess was advancing, and Carl Semb in Oslo combined a modified thoracoplasty with dissection of the apical extrafascial plane, so as to cause collapse of the upper lobe cavity[55]. This issue had been unsuccessfully addressed previously in pulmonary tuberculosis by Monaldi when he introduced the technique of cavity drainage. At the Massachusetts General Hospital, Churchill and Klopstock introduced upper lobectomy[56], and thanks to the further elucidation of bronchopulmonary anatomy by Brock in London, it became possible to perform pulmonary segmentectomy in tuberculous areas[57]. This was usually performed in the apicoposterior segments of the upper lobes and the apical segments of the lower lobes after a technique developed by Chamberlain.

1.18 THORACIC RESEARCH

The scientific role of surgery in pulmonary tuberculosis was considerable, but it is difficult, if not impossible, to estimate its value in reducing mortality and the transmission of the disease. There was neither controlled trial nor rigorous testing of any of the techniques, and such was the faith in collapse therapy and sanatorium treatment that such a trial would have been considered unethical. The close co-operation between physician and surgeon, however, was to strengthen the specialty and led to a much more critical and rational approach to therapy thereafter than in any other branch of medicine. This co-operation led to the inauguration of medical societies composed not only of physicians and surgeons, but of radiologists and pathologists and epidemiologists, and in Britain the current British Thoracic Society and the Society of Thoracic Surgeons of Great Britain and Ireland have in their origins the Society of Medical Superintendents of Tuberculosis Institutions, the joint Tuberculosis Council and the British Tuberculosis Association.

It must be admitted that treatment of pulmonary tuberculosis up to the Second World War was more of an art than a science. The exact size and duration of the artificial pneumothorax was a matter of clinical experience not easily transmitted to others by rational explanation, and other therapeutic or physical manoeuvres were matters of preference and prejudice rather than reason. No major research work was carried out during this time, and monies for any research were directed to NAPT. Nevertheless, the UK figures for tuberculosis mortality from 1850 to 1950 show an astonishing and gratifying reduction, with the notable exceptions of the two great World Wars (Fig. 1.8). It is clear that socioeconomic features as well as medical factors were in operation.

1.19 BCG

In 1924 Calmette, working in the Pasteur Institute in Lille, successfully developed an attenuated strain of tubercle bacillus that was incapable of producing tuberculosis in

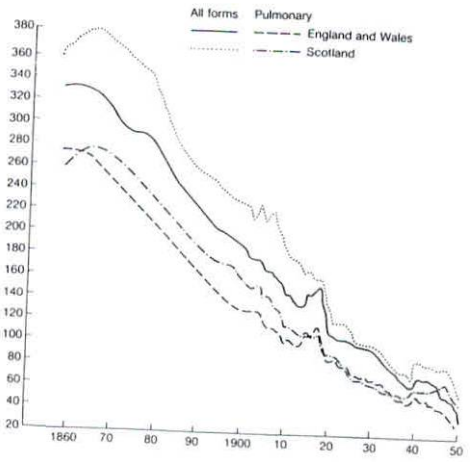

Fig. 1.8 Standardized death rates from tuberculosis per 100 000 population, England and Wales, and Scotland: 1850–1950. (Source: Lynda Bryden, *Below the Magic Mountain*, Clarendon Press, 1988, Fig. 1.)

any laboratory animals[58]. In France, many infants received the oral vaccine of the Bacillus Calmette–Guerin (BCG), but for a variety of reasons, it was not taken up in the rest of Europe. Tragically, in 1930 in Lubeck, Germany, 67 of 249 babies given the vaccine died of acute tuberculosis subsequently shown to be due to the inadvertent administration of virulent tubercle bacilli stored in the same fridge as the BCG[59]. The Scandinavian countries pioneered the use of BCG and administered it intradermally; by 1950 this was being offered throughout Europe in a mass vaccination campaign to all children. From 1954, most health authorities in the UK began voluntary vaccination of 13-year-olds. BCG has never been taken up enthusiastically in the USA. Throughout Europe and the USA, mass miniature radiography was introduced during the Second World War, and this was to play an integral part in identifying unsuspected cases of tuberculosis.

1.20 CHEMOTHERAPY

In 1944 Waksman in the USA discovered streptomycin and found that it was bacteriostatic against *M. tuberculosis*[60]. Clinical trials were set up in the USA and in Britain, where they were supervised by the MRC who set the standard for the scientific assessment of antibiotic efficacy in tuberculosis. Of patients treated with streptomycin, 51% showed radiological improvement of their disease, whereas only 8% of controls did so. Streptomycin was shown to be potentially life-saving in tuberculous meningitis and miliary tuberculosis, but to give rise to adverse effects, most frequently disturbances of balance and hearing. It was appreciated from the onset that resistance to the antibiotic by the tubercle bacillus occurred after 2–3 months continuous therapy, and that special rhythms of treatment or additional therapy would be required to overcome this problem. In fact, this was rapidly realized by Lehmann in Sweden who detected bacteriostatic activity of para-aminosalicylic acid (PAS) against *M. tuberculosis*[61]. The MRC again supervised a trial using streptomycin alone, PAS alone and a combination of both drugs. Unequivocal proof of the action of PAS was established, but a much greater consequence was that combination therapy could be used for prolonged periods without the development of drug resistance[62]. The adverse gastrointestinal effects of high-dose PAS frequently demanded fortitude and endurance by patient and physician, so that the discovery by Robitzek and Selikoff in New York in 1952 of the effectiveness of the relatively inexpensive isonicotinicacid hydrazide (isoniazid) was again welcomed with uncritical enthusiasm[63]. However, the MRC demonstrated that bacterial resistance developed when isoniazid was used singly[64], but in combination with daily streptomycin it was shown to be the most effective remedy available[65]. The use of prolonged combination chemotherapy extended for upwards of 2 years

was pioneered in Edinburgh by Crofton and colleagues, and it was possible at long last to envisage cure of pulmonary tuberculosis in all cases[66].

Such chemotherapeutic success challenged the role of traditional management of tuberculosis of bedrest, sanatorium treatment, surgery and rehabilitation, all of which were to become quickly superfluous. Sanatoria have been found a new role as institutions for the elderly, collapse therapy is unnecessary, surgery is hardly ever required unless concurrent lung cancer is suspected, and dispensaries and chest hospitals have been closed down in the Western world. With modern drug therapy, including pyrazinamide introduced in 1954, ethambutol discovered in 1962, and rifampicin discovered in 1969, all that is now necessary is to take the correct drugs in the correct dosage for the correct duration, which nowadays may be as short as 6 months. The tragedy today is that this great potential has not been achieved universally, because tuberculotic patients remain undiscovered, while others remain ill and infectious because money cannot be made available for effective chemotherapy. Most disturbingly, immunosuppression induced by AIDS is permitting a Third World epidemic of proportions akin to those experienced in the sixteenth and seventeenth centuries not with tuberculosis, but with plague, cholera and smallpox.

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