

PAST, PRESENT AND FUTURE OF THE SMOKING EPIDEMIC

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INTRODUCTION

Tobacco was grown and used widely in North, Central and South America for two to three millennia before being introduced to Europe at the end of the fifteenth century. Two types of plant were grown, *Nicotiana tabacum*, itself a hybrid of two wild species, and *Nicotiana rustica*. The latter was grown in North America and had a slightly higher nicotine content, but the former has been, and continues to be, the principal type in tobacco products worldwide.

The use of tobacco was promoted initially for medicinal purposes, including the treatment of cough, asthma, headaches, stomach cramps, gout, diseases of women, intestinal worms, open wounds, and malignant tumours and was prescribed to be chewed, taken nasally as a powder, or applied locally. Its use for pleasure was frowned on by church and state, and it was not until the end of the sixteenth century that it came to be smoked widely, at first in pipes in Britain, where it was popularised by Sir Walter Raleigh. It became so common that by 1614 there are estimated to have been some 7,000 tobacco retail outlets in London alone.¹

Attempts to ban its use for recreational purposes were made in Russia, Switzerland, Turkey, parts of Austria and Germany, and in India and Japan, but the prohibition was invariably flouted and control by taxation came to be preferred. This eventually proved to be such an important source of revenue that in 1851 Cardinal Antonelli, secretary to the Papal States, ordered that the dissemination of anti-tobacco literature was to be punished by imprisonment.

Gradually, the way in which tobacco was most commonly used changed. By the end of the seventeenth century, its use as nasal snuff spread from France, largely replaced pipe smoking, and remained common until a century later when it, in turn, began to be replaced by the smoking of cigars, which had long been smoked in a primitive form in Spain and Portugal. By then cigarettes were being manufactured in South America and their use had spread to Spain, but it was not until after the Crimean War that they began to be widely adopted. They were made fashionable in Britain by officers returning from the Crimea and by the end of the nineteenth century cigarettes had begun to replace cigars. Smoking increased rapidly during the First World War and by the end of the Second World War they had largely replaced all other tobacco products in most developed countries.

By this time, smoking had become so much the norm for men that, in Britain, some 80% were regular smokers, and some doctors offered a cigarette to patients who came to consult them to put them at their ease. Women began to smoke in large numbers only much later, except for Maori women in New Zealand who were, by the end of the nineteenth century, commonly smoking pipes. In the 1920s, women began to smoke cigarettes, at first in the US and Britain, a process that was speeded up in Britain during the Second World War when an increasing proportion began to work outside the home and have an independent income. In many other countries, however, women have begun to smoke in large numbers only in the last few decades.

REASONS FOR THE SWING TO CIGARETTES

For its impact on health, the important change in the use of tobacco was the swing to cigarettes, which was brought about by two industrial developments. The first was a new method of curing tobacco. With the old method, the smoke that had come from the combustion of tobacco in pipes and cigars was alkaline, irritating and difficult to inhale. The nicotine in the smoke was predominantly in the form of a free base, and could be absorbed across the oral and pharyngeal mucosa. Blood levels of nicotine could consequently be high and addiction to nicotine was readily produced, but only small amounts of other constituents were absorbed. The new method, called flue-curing, was introduced in North Carolina in the mid-nineteenth century.² It exposed the leaf to high temperatures and increased its sugar content, and this caused the pH of the smoke to become acid. In this environment, the nicotine was predominantly in the form of salts and was dissolved in smoke droplets, and the smoke was less irritating and easier to inhale. With each inhalation, there was a rapid rise in the level of nicotine in the blood which was perceived in the brain and was particularly satisfying to the addict, but other constituents of the smoke were also unfortunately absorbed and were distributed throughout the body.

The second development was mechanical, namely, the introduction of cigarette making machines. One was patented in 1880 and was eventually adapted by the Duke family to work so efficiently that 120,000 cigarettes of good quality could be produced every ten hours by one machine, the equivalent of the production outlay of about 100 unassisted workers. As a result, the price fell and a mass market became feasible.

IMPACT OF TOBACCO ON HEALTH

Until cigarette smoking became common very little evidence of harmful effects was detected – for the good reason that relatively few harmful effects were probably produced. One effect that was first suggested by Sömmering more than 200 years ago³ was the production of cancer of the lip, and to this was added cancers of the tongue and other parts of the mouth in the course of the nineteenth century, on the basis of clinical series in France,⁴ Germany⁵ and the UK⁶ – findings that are now simply explained because we know that these cancers can be produced at least as easily by the smoking of pipes and cigars as by the smoking of cigarettes. Little attention was, however, paid to them by clinicians and when, as a medical student in the mid-1930s, I asked the senior surgeon at my hospital whether he thought pipe smoking or syphilis was a cause of cancer of the tongue, he replied that he did not know, but that a wise man should certainly avoid the combination of the two.

One disease, however, was unequivocally attributed to tobacco, and was taught as being so: namely, tobacco amblyopia. It was described by Beer in 1817⁷ and was found in heavy pipe smokers in combination with malnutrition; it was probably caused by the cyanide in smoke not being detoxified because of a deficiency of vitamin B₁₂.⁸ The disease is no longer seen, at least in developed countries.

Early impact of cigarette smoking

With the advent of the twentieth century, several new diseases began to be associated with smoking: the first of these was intermittent claudication, described by Erb in 1904,⁹ and secondly, in 1908, a rare form of peripheral vascular disease affecting relatively young people, which Buerger described as thromboangiitis obliterans and which has subsequently been named after him.¹⁰ Both are now recognised to be greatly increased by smoking, the latter indeed being almost limited to smokers, but neither reached the epidemic proportions that two other relatively new diseases achieved in the next few decades.

One was coronary thrombosis or, as we would now prefer, in strict pathological terms, to call myocardial infarction. It was first described at autopsy in 1876,¹¹ though it had certainly occurred earlier, and it was not diagnosed in life until 1912 when it was diagnosed by Herrick.¹² Subsequently it was reported progressively more often every year for four or five decades. Hoffman, an American statistician, linked the increase with the increasing consumption of cigarettes as early as 1920.¹³ Several clinical studies of the relationship with smoking were subsequently published, but the findings were confused and no substantial evidence was obtained until 1940 when English, Willius and Berkson reported finding an association in the records of the Mayo Clinic.¹⁴ Their findings led them to conclude that the smoking of tobacco probably had 'a more profound effect on younger

individuals owing to the existence of relatively normal cardiovascular systems, influencing perhaps the earlier development of coronary disease'. They eschewed reference to causation, however, because the subject would be controversial, adding perceptively that 'Physicians are not yet ready to agree on this important subject.' That cigarette smoking played a part in the increasing incidence was eventually clearly demonstrated, but it cannot have been the only cause of the increase, or even probably the most important. Unlike the other disease that burst into medical prominence in the first half of the twentieth century, the full explanation of its rapid increase is still a matter for debate.¹⁵

The other disease was, of course, cancer of the lung. Until then it had been thought to be exceptionally rare. A small cluster of cases in tobacco workers in Leipzig had led Rottmann to suggest in 1898 that the disease might be caused by the inhalation of tobacco dust,¹⁶ but the first suggestion that it might be due to smoking was made by Adler 14 years later¹⁷ when he noted that, although the disease was still rare, it appeared to have become somewhat less so in the recent past. Many people were subsequently struck by the parallel increase in the consumption of cigarettes and the incidence of the disease, and by the frequency with which patients with lung cancer described themselves as heavy smokers, and they ventured to suggest that the two were related.¹⁸⁻²³ Few, however, believed it, for the occurrence of cases in non-smokers meant that Koch's postulates, which were taught to be the criteria for determining causality, could not be satisfied, and the idea that the increase was an artefact of improved diagnosis came to be widely believed, bolstered by the fact that pathologists failed to produce cancer experimentally by the application of tobacco tar to the skin of animals. Only Roffo succeeded in doing so in the Argentine in 1931,²⁴ and his results were discounted in the UK because he had produced the tar by burning the tobacco at unrealistically high temperatures.

Three case control studies that were carried out in Germany and the Netherlands between 1939 and 1948 should have focused attention on smoking and all suggested, albeit on rather inadequate grounds, that smoking was a possible cause; but the war distracted attention from the German literature^{25, 26} and the Dutch paper²⁷ was published only in Dutch and thus not noticed widely for several years. Outside Germany, smoking was still commonly regarded as having only minor effects as late as 1950, while inside Germany, where chronic nicotine poisoning had been thought to produce effects in nearly every system, and propaganda against the use of tobacco had been a major plank in the public health policy of the Nazi government (because it damaged the national germ plasm and addiction to it distracted from obedience to the Führer), the reaction against the Nazis brought with it a reaction against their antagonism to tobacco.

The 1950 watershed

Then, in 1950, five case control studies were published in the UK and the US; much larger numbers of cases were reported on and, in some studies, far more refined techniques were used, so that Bradford Hill and I were able to conclude that 'cigarette smoking is a factor, and an important factor, in the production of carcinoma of the lung'.²⁸ The results were given wide publicity, but the tobacco industry presented them as controversial and they had little public impact. Scientific curiosity had, however, been aroused, a great deal of research was initiated, and government departments were forced to consider the implication of the findings for the practice of public health.

Acceptance of evidence of harm

Further evidence was, however, clearly needed if the scientific world was to accept that cigarette smoking was the cause of the epidemic of lung cancer, which was by

then spreading in all developed countries, and this was rapidly produced. Cohort studies were begun in which people who had provided information about their smoking habits were followed to see the extent to which their habits predicted mortality. One study obtained information from 34,000 male doctors in the UK and showed, within three years, that the mortality from lung cancer was proportional to the amount smoked, as predicted by the case control studies, and suggested that there might also be a similar, though less marked, relationship with coronary thrombosis.²⁹ Another study, based on larger numbers in the US, gave similar results and found that, under 65 years of age, the mortality from coronary thrombosis among men who smoked 20 or more cigarettes a day was twice that in non-smokers.³⁰ Laboratory workers, for their part, showed that tobacco tar, appropriately produced, contained polycyclic aromatic hydrocarbons that were known to be carcinogenic³¹ and that the tar could cause cancer on the skin of mice if

TABLE 1
Principal diseases caused in part by smoking.

Disease	Ratio of mortality rates in continuing cigarette smokers and lifelong non-smokers		
	British doctors 1951–91 ³⁷		US population 1984–91 ^a
	men	men	women
Cancers of mouth, pharynx & larynx	24.0	11.4	6.9
Cancer of oesophagus	7.5	5.6	9.8
Cancer of lung	14.9	23.9	14.0
Cancer of pancreas	2.2	2.0	2.3
Cancer of bladder	2.3	3.9	1.8
Ischaemic heart disease	1.6	1.9	2.0
Hypertension	1.4	2.4	2.6
Myocardial degeneration	2.0	} 2.1	2.1
Pulmonary heart disease	∞		
Other heart disease	–		
Aortic aneurysm	4.1	6.3	8.2
Peripheral vascular disease ^b	–	9.7	5.7
Arteriosclerosis	1.8	2.7	3.0
Cerebrovascular disease	1.5	1.9	2.2
Chronic bronchitis & emphysema	12.7	17.6	16.2
Pulmonary tuberculosis	2.8	–	–
Asthma ^c	2.2	1.3	1.4
Pneumonia	1.9	} 2.5	1.7
Other respiratory disease	1.6		
Peptic ulcer	3.0	4.6	4.0
All causes	1.8	2.5	2.1

^a C. Heath Jr and M. Thun, personal communication.

^b No death was reported in British doctors who were lifelong non-smokers.

^c Continuing cigarette smokers and ex-cigarette smokers combined, as asthma may cause smokers to stop smoking.

applied regularly for months on end.³² By 1957, the Medical Research Council was consequently able to advise the British government that cigarette smoking was the cause of the increased incidence of lung cancer,³³ and similar conclusions were reached over the next three years by specially appointed committees in the Netherlands, Sweden and the US and by the World Health Organisation.³⁴

Impact on total mortality

When, a few years later, the Royal College of Physicians in London³⁵ and the Surgeon General in the US³⁶ issued reports on smoking, it had become clear that its total impact was greater than had at first been conceived and that the incidence of more diseases might be affected. With the passage of time, the total number now believed to be caused in part by smoking is at least 35, 22 of which can be recognised in the cohort study of British doctors and in the massive study of a million men and women undertaken by the American Cancer Society, as shown in Table 1. Other conditions caused in part by smoking are listed in Table 2. For these, evidence has often had to be obtained from case control studies or surveys or, occasionally, from cohort studies in which special enquiries have been made about the condition of interest. That so many should be affected is not necessarily surprising as the smoke contains some 4,000 different chemicals.

TABLE 2
Other conditions caused in part by smoking.

• Cancer of lip	• Crohn's disease
• Cancer of nose	• Osteoporosis
• Cancer of stomach	• Periodontitis
• Cancer of kidney (pelvis)	• Tobacco amblyopia
• Cancer of kidney (body)	• Reduced fecundity
• Myeloid leukaemia	• Reduced growth of fetus
• Age-related macular degeneration	

Some of the excess mortality from all causes is, of course, due to confounding, but detailed investigation has shown that this effect is relatively small. The excess has, moreover, increased with time, as the smoking epidemic has matured and old people have come to be smoking cigarettes throughout their smoking lives. This is shown by the data in Table 3 from both the British doctors' study, which has continued for over 40 years with periodic updates on changes in smoking habit, and the studies of the American public, carried out by the American Cancer Society over different periods. It is now clear that regular cigarette smoking doubles mortality, on average, throughout middle and old age, so that one in four smokers die prematurely, as a result of their habit, in middle age (now defined as 35–74 years), and one in four similarly die later.

TABLE 3
Cigarette smokers compared with lifelong non-smokers: change in all cause mortality in men.

British doctors ³⁷	Period	1951–71	1971–91
	Relative risk	1.6	2.1
American public ³⁸	Period	1959–65	1982–6
	Relative risk	1.8	2.3

The epidemic that the world is now facing is not, in truth, a smoking epidemic so much as a cigarette epidemic, for the small effect of smoking pipes and cigars that gave rise to so little concern in the nineteenth century has continued to be of the same order. In our study of British doctors, for example, the mortality of pipe and cigar smokers who had never smoked cigarettes was only nine per cent greater than that of lifelong non-smokers³⁹ – a material increase in all cause mortality, certainly, but qualitatively different from that of cigarette smoking, and it is only the effect of the latter that I shall consider further.

SPREAD OF EPIDEMIC

Two matters about it are clear. Firstly, the number of manufactured cigarettes consumed has increased astronomically from near zero in 1880 to some 5,700 billion a year worldwide in the mid-1990s, since when there has been a very slight decrease.⁴⁰ Secondly, the increase in cigarette smoking occurred at different rates at different periods in different countries. Even within developed countries, to which the increase was initially confined, the differences were substantial.

TABLE 4
Manufactured cigarette consumption in 1920 and lung cancer mortality in 1955.

Country	Mean no. of cigarettes smoked daily by adults 1920–9	Lung cancer mortality in 1955
Finland	3.6	89
Greece	3.4	57
UK	3.0	109
Sweden	0.8	16
Norway	0.7	11
Portugal	<0.7	11

Developed countries

Detailed consumption rates of different tobacco products in 22 developed countries have been brought together by Nicolaides-Bouman *et al.*⁴¹ from the time of the earliest record to 1985. The three highest and three lowest rates of consumption of manufactured cigarettes by adults, averaged over the decade 1920–9, are shown in Table 4 together with the corresponding age standardised mortality rates for lung cancer in 1955, some 30 years later, to allow for a sufficiently long period of exposure

to produce an appreciable effect. That lung cancer was more common when manufactured cigarettes were taken up early is clear, but the correlation is not close. This, however, is hardly surprising, for so many factors affect the incidence of the disease other than the one cited in Table 4: the changes in consumption over the intervening period; the distribution of consumption by sex and age; the characteristics of the cigarettes; the way in which they are smoked; the amount of tobacco consumed in hand-rolled cigarettes and in other tobacco products, which are not without hazard; and, it appears, the local diet which may modify the quantitative effect of a given number of cigarettes.⁴²

A method for estimating the mortality attributable to cigarette smoking that is not dependent on statistics for tobacco consumption was, therefore, suggested by Peto and his colleagues.⁴³ This is worth describing in some detail as so much depends on it. In brief, they used the excess mortality from lung cancer over that observed in non-smokers in the American Cancer Society's massive second cancer prevention study as an indication of the extent to which the population had been exposed to tobacco products in the past. This is justified for developed countries, for whenever data are available, the mortality from lung cancer in lifelong non-smokers has been found to be low and approximately the same in

each country and not to have changed over time. These rates cannot, however, be used directly to estimate the effects of smoking on mortality from other diseases, as the rates for other diseases in non-smokers vary considerably and smoking interacts with other causes in a multiplicative rather than in an additive manner. Peto and his colleagues consequently divided other causes into eight broad categories (Table 5) and used the second cancer prevention study's data as an indication of the *proportional* excess mortality to be associated with the corresponding *absolute* excess of lung cancer in each five year age group. To be on the safe side, however (that is, to under- rather than over-estimate the mortality attributable to smoking), they excluded all deaths in two categories (cirrhosis and non-medical causes) and all deaths under 35 years of age in all categories, even though some in both groups were attributable to smoking, and then *halved* the estimated excess proportion for each of the remaining six categories. This last statistical device, it should be noted, is not as extreme as halving the number of deaths attributable to smoking, for it has little effect on the number of deaths attributable to tobacco when the relative risks are high; reducing it, for example, by only ten per cent if the relative risk is nine-fold.

The trends in the proportions of mortality consequently attributed to smoking between 1955 and 1995* are shown in Table 6, separately for men and women, and for the UK, the US and all developed countries, the last divided into the Organization for Economic Collaboration & Development (OECD) countries and former socialist economies. The highest percentage was in men in the UK in 1975, since when the proportion has dropped by a quarter and is now less than that in the US. The OECD countries as a group had slightly lower proportions than the US and the proportion stabilised in 1985. In the former socialist economy countries the percentage has increased progressively and in 1995 was approaching

TABLE 5
Categories of disease used by Peto *et al.*⁴³

• Lung cancer	• Vascular diseases
• Upper aerodigestive cancers	• Cirrhosis of liver
• Other cancers	• Other medical causes
• Chronic obstructive pulmonary disease	• Non-medical causes
• Other respiratory diseases	

TABLE 6
Trends in per cent mortality attributed to smoking: selected populations.*

Sex	Country	Year				
		1955	1965	1975	1985	1995
M	UK	27	35	36	34	27
	US	14	20	26	28	29
	OECD	12	19	23	25	25
	Former socialist	15	22	24	29	32
F	UK	3.0	5.9	9.8	14	17
	US	0.3	2.0	7.1	14	22
	OECD	0.5	1.7	3.9	7.4	12
	Former socialist	1.3	2.0	3.0	3.7	5.2

* The data for 1995 were projected from the trend between 1985 and 1990, but have been found to be generally reliable.

the maximum previously recorded in the UK. In women, the proportions have generally been much lower, but in 1995 were approaching the figures for men in both the UK and, most notably, the US. In all four categories the increase in women was progressive and the highest figures were in the latest period.

Developing countries

For the developing countries there are few substantial data, apart from those for China, where cigarette consumption increased from about one a day per adult in 1952 to ten a day in 1992. Two studies are particularly revealing. A case control study of a million deaths in men and women in 98 parts of China, both urban and rural, obtained information about the deceased persons' smoking habits, and compared those of men and women who died of cancer, respiratory disease, and vascular disease with those of men and women who died of other diseases,⁴⁴ while a cohort study of a quarter of a million men aged over 40 in 45 selected representative areas provided mortality rates by smoking habit over a five to six year period.⁴⁵ Both led to the conclusion that about 12% of deaths in middle-aged and elderly men were attributable to smoking, while the case-control study provided the much lower figure of two to three per cent in women, few of whom had been smoking outside the big towns. The pattern of mortality was, however, different from that in the developed world, with a much smaller proportion of attributable deaths due to ischaemic heart disease and lung cancer and a greater one due to stroke, chronic obstructive pulmonary disease and cancers of the oesophagus, stomach and liver.

FUTURE EXPECTATIONS

What then of the future? For China, it is relatively easy to predict: for the prevalence of smoking and attributable mortality are reproducing the data observed in the US 40 years previously, where cigarette consumption per adult had been one a day in 1910 and ten a day in 1950, and the risk of premature death in smokers attributable to smoking increased from one in four in the early 1960s to one in two in the 1980s. For men who began smoking before they were 20 years old, the risk is already one in four in China and must be expected to become one in two in 20 years' time. Two-thirds of men now become smokers before 25 years of age and, if present patterns continue, about 100 million of the 300 million Chinese males now under 30 years of age will be killed by tobacco. The number of women may, however, be relatively few as, contrary to what has happened in the West, progressively fewer have been starting to smoke and the prevalence for those born in 1950–64 is now only one to two per cent.

For the developing world as a whole, Peto and Lopez estimated that there were already in the 1990s likely to have been one million deaths a year attributable to tobacco in contrast to approximately two million in the

developed world.⁴⁶ In many parts, however, the prevalence of smoking in men, like that in China, already exceeds 50%, although again the female prevalence is relatively low. It is also well established that in, for example, India, where tuberculosis has become a major cause of death, the impact of smoking on that disease, as it was in the developed world 40 years ago, is to increase the incidence of clinical cases and double the fatality. In many countries, however, there is still a major mortality from causes unrelated to tobacco, such as most other infectious diseases and trauma, so that the proportion of persistent smokers eventually killed by the habit may be only a third rather than the half suggested by the North American, British, and indeed also the Chinese data. Perhaps, therefore, only about 250 million of the 800 million young people who, on current patterns, will be smokers in early adult life, will be killed by the habit. Of course, the majority of the deaths will not occur for some decades when smoking has been prolonged and the chronic diseases of middle age become common, but in two or three decades the total toll must be expected to be about ten million deaths a year worldwide, of which some seven million will be in what are now the developing countries.⁴⁷

The benefit of stopping smoking

If the prevalence of smoking stays as it is, the toll of tobacco in the first half of the century will be tremendous, but there is no reason why it should; the prevalence can be reduced and, with it, some years later, the mortality from lung cancer⁴⁸ and from all other tobacco related diseases.⁴³ Moreover, it is never too late to stop, for the risk is reduced by stopping at any age, though naturally it is reduced progressively less the later the age, as we found in our recent study of lung cancer in Devon and Cornwall.⁴⁸ Nor is the benefit limited to the reduction in the risk of developing cancer of the lung. In our study of British doctors we found that survival was improved whatever the age at which smoking was stopped. It was indistinguishable from that of lifelong non-smokers with the numbers we had when smoking was stopped under 35 years of age, and longer than that of continuing smokers even if smoking was stopped after 65 years of age.³⁷

I believe, therefore, that with adequate education of the public, for which doctors must take the prime responsibility, with the support of the media, and with the help of the government in prohibiting promotion of the habit, we may see the current predictions materially reduced. But whether it will be possible to reduce the prevalence rates of smoking by young people to much below their present level, I take leave to doubt, unless we are prepared to undertake a major all round attack on the habit like that undertaken in Massachusetts and California.

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