the mortality from chronic airways disease is rather low in Japan. Genetic factors appear to contribute to the development of CAD.

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Chronic Airways Disease
The Smoking Component
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The first part of this article briefly summarizes some of the evidence linking smoking with chronic obstructive airways disease (COAD), also known as chronic obstructive pulmonary disease, chronic obstructive lung disease, chronic bronchitis, and/or emphysema. The second part provides background information and discusses general principles that apply to the prevention of smoking.

Tobacco and Causation of COAD

There is now a vast amount of evidence that cigarette smoking is by far the most important factor in the etiology of COAD. The evidence has been reviewed in many publications. The familiar components will be briefly summarized, with more elaboration of recent or less familiar information.

Mortality

Prospective studies: At least 8 prospective studies in 6 countries have shown a close relationship between previously recorded cigarette smoking habits and the subsequent mortality rate from COAD. The risk increased with the amount smoked. The mortality in heavier smokers (differently defined in different studies) was 2-25 times that in nonsmokers, varying according to the definition used and to the age and occupational group. Those who inhaled deeply had a higher mortality. The mortality decreased after stopping smoking, more impressively so if those who quit when already ill were excluded. Although the earlier studies were mostly in men, a 22-year follow-up on women doctors in Great Britain has shown results similar to those in men. Susceptibility is probably the same in both sexes. Mortality in pipe and cigar smokers is lower than that in cigarette smokers. For cigar smokers the ratio of excess mortality compared with nonsmokers has varied from 1 to 4 in different series; for pipe smokers from 1 to 9; in most studies the ratio has been about 2.

Retrospective studies: An elaborate retrospective “case-control” type of study was carried out in Northern Ireland on deaths from bronchitis over a 3-year period, 1960-62, using deaths from nonrespiratory diseases as controls. The results were consistent with those of the prospective studies, though smoking was thought to have accounted only for 55% of the deaths, possibly an underestimate in view of the accumulating evidence from other studies. Two other case control studies in northeast England confirmed the relationship to smoking.

Morbidity

The major importance of COAD as a component of chronic morbidity was recognized in the UK as early as the 1920s, as was its relationship to atmospheric pollution and dust. Numerous surveys have shown the much higher rates of cough and sputum in smokers than in nonsmokers. Indeed prevalence studies in many countries have confirmed this relationship. In some of these studies “chronic bronchitis” was almost confined to smokers. For instance, in a survey of rural and urban populations in Britain, in men aged 55-64, the prevalence was 17.6% among heavy smokers, 13.9% in light smokers, 4.4% in ex-smokers, and nil among lifetime nonsmokers.

Recent studies suggest that smoking lower-tar cigarettes does not necessarily reduce the prevalence of cough and sputum. However, smoking cessation usually leads to decrease in cough and sputum and may also reduce the number of exacerbations and decrease breathlessness, at least in the early stages of the disease.

Mortality figures from many developing countries are incomplete and may be misleading. Some data on prevalence are available from community surveys. There has been considerable variation in numbers and in the details of the surveys, though most have used the definition of “chronic bronchitis” of the British Medical Research Council.

There has been evidence of relatively high rates of chronic bronchitis in India, China (see Yans in these proceedings, p. 3395); Papua New Guinea, Nepal, Malaysia, rural Egypt, and the Caribbean. On the other hand, low rates have been recorded in Africa, admittedly 10 years ago, perhaps because of low smoking rates at the time.

Although a number of these studies show a strong correlation between smoking and COAD, in many there was
a higher proportion of nonsmokers with COAD than in most studies in developed countries. For instance, in the Chinese study quoted\textsuperscript{26} the prevalence of chronic bronchitis was 20.6\% among smokers, but still as much as 10.6\% among nonsmokers. In a recent smaller study in Bombay, India,\textsuperscript{30} the prevalence of cough, dyspnea, or both was 39\% in cigarette/bidi smokers but 13\% in nonsmokers (percentages recalculated from the original data). As discussed subsequently, childhood lower respiratory infection, domestic atmospheric pollution, or, certainly in Bombay,\textsuperscript{30} industrial pollution may have been factors in nonsmokers. However, if uncontrolled lower respiratory infection in childhood is important, it is surprising that COAD prevalence in the African study was so low.\textsuperscript{26}

**Lung Function**

Most surveys have shown evidence of decreased FEV or PEFR in smokers compared to nonsmokers\textsuperscript{1-3} and a steeper decline with age in smokers compared to exsmokers or nonsmokers\textsuperscript{4,5,31-38} (which may be further steepened by exposure to dust).\textsuperscript{39} Diffusing capacity is also decreased in smokers\textsuperscript{39-38} and pulmonary distensibility is increased.\textsuperscript{39} In the young, in whom function impairment is less advanced, significant improvement can be shown after stopping smoking.\textsuperscript{1,4,40} At older ages, cessation results in a less steep decline with age than in those who continue smoking.\textsuperscript{3,4,20} The rate of decline with age varies considerably among smokers and is not related to the amount of cough and sputum.\textsuperscript{3,20} Whether this is due to mode of smoking, to differences in individual susceptibility, or to an interrelationship between the two is still uncertain. There is probably some irritative effect of smoking on the larger bronchi and inflammation of larger and smaller bronchi, which may be the reversible elements, and a more important destructive, irreversible effect on the bronchioles and alveoli.\textsuperscript{7,44-46}

**Morbidity in the young:** There is evidence of ill effects from cigarette smoke at all ages. (See also section on passive smoking.) Infants of smoking parents have more respiratory illnesses than infants of nonsmokers.\textsuperscript{47,48} Smoking schoolchildren have more cough and more chest illnesses than nonsmokers.\textsuperscript{49-50} This has also been found at older age groups in 16-year-olds,\textsuperscript{51} in students,\textsuperscript{52} in student nurses,\textsuperscript{53} in soldiers,\textsuperscript{54} and in a British cohort followed from birth and assessed at ages 20,\textsuperscript{55} 25,\textsuperscript{56} and 36.\textsuperscript{57}

**Morbid anatomy:** The correlation is well established between smoking and the extent of emphysema found at autopsy.\textsuperscript{44-46} The extent of emphysema is less in exsmokers than in continuing smokers.\textsuperscript{38} There is also a close relationship with small airways pathology.\textsuperscript{44-46} The effect appears to be potentiated by atmospheric pollution.\textsuperscript{49,50}

**Pathogenesis**

There has been extensive research on how smoking damages the lung.\textsuperscript{7,49-48} Damage affects many elements in the respiratory tract, including mucus-secreting cells, cilia, bronchial muscle,\textsuperscript{7,51} small airways, and alveoli. The latter two forms of damage are mediated by inadequately antagonized enzymatic action by proteases (particularly elastase) derived from neutrophils, monocytes, macrophages, platelets, smooth muscle cells, fibroblasts, and perhaps mast cells.\textsuperscript{41} Some of these cells are recruited to the lungs by exposure to tobacco smoke.\textsuperscript{41} Antiproteases are inactivated by highly active oxidants in tobacco smoke,\textsuperscript{40} which may also directly damage connective tissue\textsuperscript{41} and by activated species of oxygen released from stimulated phagocytes.\textsuperscript{41} Repair mechanisms may also be inhibited.\textsuperscript{40} Smoking may decrease the maximal surface tension of surfactant,\textsuperscript{44} leading to overdistention of alveoli, and interfere with gas absorption through the surfactant layer.\textsuperscript{44}

It has always seemed possible that variations in disease outcome among individuals with similar smoking habits might depend, at least partly, on different modes of smoking. These variations might include differences between individuals in the bronchitic and emphysematous elements of COAD. There is increasing objective evidence to support this hypothesis.\textsuperscript{44,46} Additional variables might include differences in exposure to other people's smoke, to other forms of atmospheric pollution, and in number and severity of childhood and perhaps adult infections, as well as possible genetic differences in susceptibility.

There has recently been renewed interest in the Dutch hypothesis\textsuperscript{44} that there is an atopic element in susceptibility to tobacco smoke. The earlier evidence has been summarized by Burrows.\textsuperscript{58} Recent community studies suggest that the prevalence of bronchial hyperresponsiveness is related both to atopy and to smoking and is correlated with symptoms.\textsuperscript{20,73} Mode of smoking may affect the degree of bronchial hyperresponsiveness,\textsuperscript{44} and even IgE levels.\textsuperscript{73} Like others, our own group found intermittent sputum eosinophilia in COAD patients.\textsuperscript{74} We also found in longitudinal studies, a highly significant inverse relationship in the individual patient between FEFR and variation in sputum levels of IgE, histamine, and SRS-A.\textsuperscript{75} Even if the atopic element is confirmed by further work, it is probably relatively small compared with the overwhelming and potentially lethal long-term effect of tobacco smoke in inducing emphysema.

**Russie Smoking**

The 1984 Surgeon-General's report\textsuperscript{4} reviews 7 reports from 4 countries that showed a significant correlation between parental smoking and bronchitis or pneumonia in young children. In older children some studies have shown a correlation and others have not. A number of studies have also found small but significant decreases of lung function in children of smoking mothers, especially in young children. Smoking in the household has been found to be strongly associated with continuing asthmatic symptoms in young children.\textsuperscript{76,77} Continuing symptoms 3½ years after an attack of acute bronchiolitis in children was significantly associated with maternal smoking.\textsuperscript{78} Some but not all studies have demonstrated minor changes in adults. The significance of these findings for the later development of COAD is uncertain. In the absence of smoking in adult life, the effects of passive smoking are probably of little importance. Among children who later do take up smoking, any effect is likely to be small compared with that of active smoking. The possible effect on later COAD of pneumonia in infancy, more frequent in children of smokers, is reviewed subsequently.
OTHER CAUSATIVE FACTORS

Atmospheric Pollution

This may occur (a) in the atmosphere of cities and towns, the pollution derived from industrial or domestic sources; (b) within chimneyless homes in developing countries, the pollution derived from cooking or heating fires or cooking oils; and (c) within the workplace, the pollution derived from industrial dust or fumes. All of these are discussed in separate articles in this symposium.

There is, of course, an interrelation with tobacco smoking; the effects are at least additive and may in some circumstances be synergistic. Atmospheric pollution was formerly a very important factor in developed countries where it is now much better controlled; control may be poorer in developing countries in the early stages of industrialization. In some developing countries, domestic pollution may be very important; especially for women exposed in the course of cooking, and for both sexes where the weather is cold and there is exposure to smoky indoor fires. Atopic subjects may be especially susceptible (see Aoki, p 343S).

Alcohol

It is difficult to differentiate an alcohol effect from that linked to smoking. Two recent studies come to opposite conclusions. If there is an effect, it must be minor.

Infection

There is increasing evidence that respiratory illness in infancy predisposes to later chronic or recurrent cough or wheeze. Studies in the UK of a cohort, followed from birth and reassessed at ages 20, 25, and 36 showed that chronic winter cough was more common, both in smokers and in nonsmokers, in those who had had recorded childhood lower respiratory infections. Nevertheless, chronic cough was much more common in the smokers. Surveys in the UK and USA have shown an association with lower FEV1 in adult life, especially in smokers. A recent study has shown a strong geographic correlation in England and Wales between death rates from chronic bronchitis and emphysema during 1959-78 and infant mortality from bronchitis and pneumonia in 1921-25.

There is an impression, and indeed a likelihood, that childhood respiratory infection may be an important component of COAD in developing countries, where uncontrolled respiratory infections in infants are both more common and more serious than in developed countries. Nevertheless, one must be cautious in assuming a causal relationship with COAD, because the common factor could be poor social conditions or genetic predisposition. Recurrent chest infection frequently complicates COAD and is often a terminal event, but, surprisingly, it has proved impossible to correlate frequency or severity of these episodes with deterioration of lung function.

Socioeconomic factors

The higher rate of COAD in persons of poorer socioeconomic status has long been noted in Britain. As the differential also applied to wives, general industrial atmospheric pollution was formerly deemed the most important factor. With the dramatic decrease in atmospheric pollution in Britain, this factor has diminished but has been replaced by the increased differential in smoking rates, the upper socioeconomic groups having decreased their smoking more than the lower (see Holland p 318S). Domestic overcrowding facilitates infection, both primary lower respiratory infection in infants, which may be a predisposing factor, and secondary infection in patients with COAD leading to exacerbations and sometimes to death. There is recent evidence that damp housing predisposes to respiratory infection in infants. In Britain there is also some evidence that downward social migration may contribute to the higher rates in poorer groups.

Genetic factors

Alpha,-antitrypsin deficiency: This genetic deficiency was found to predispose to the early onset of emphysema, and to be associated with a particular susceptibility to damage by tobacco smoke. The clear-cut clinical picture is seen only in homozygotes. Because of the confusing effects of smoking, it is still uncertain whether heterozygotes are more than normally susceptible to damage. The discovery of this condition led to the extensive and rewarding research on the pathogenesis of smoking-induced emphysema. Apart from genetic counseling, the most important preventive action is to convince susceptible persons of the overwhelming importance of not smoking.

Other factors: Other possible genetic factors in susceptibility to smoking are suggested by twin studies and some evidence of family clustering. Although there may be individual susceptibility to more rapid loss of lung function with smoking, and much effort has been made to develop laboratory techniques to identify susceptible persons, these efforts have so far been unsuccessful. Although it is likely that there is the usual biologic variability, as indicated previously, most of the variance is probably due to the amount, duration, and mode of smoking as well as to other environmental factors. However, there is renewed interest in "the Dutch hypothesis" that an important atopic component contributes to susceptibility. If correct, atopy probably has a genetic basis (see Macklem p 361S).

PREVENTION OF SMOKING

The aims of antismoking activities are to encourage children not to start smoking and adults to quit. The prevention of COAD through the prevention of smoking will, of course, also prevent other smoking-related diseases. Action must be based on relevant information, summarized below, and certain well-recognized principles of smoking control.

Background

Smoking behavior complex: Factors influencing smoking behavior are summarized in Figure 1, in which each factor is given an arbitrary rating based on research and experience. Family habits and attitudes and peer pressure are among the highest ratings, with peer pressure becoming steadily more important as the child matures. School programs, advice from professionals, etc, are likely to have little effect if they run counter to pressure from family and peers. A continuous favorable background from general public
health education, both official and unofficial (through media and word of mouth), will facilitate specific action and help to create a positive climate of opinion among family and peers. Single health education campaigns, which are not continually followed up, have very temporary effects. With its enormous economic resources, commercial tobacco promotion through advertising, radio, television, and sports and arts promotion has a powerful and continuous counter effect, especially on the young.

Age of starting smoking: In most developed countries smoking begins in childhood, often between the ages of 11 and 13. In the UK the smoking rates by age 16 have become similar to the overall rates in adults. It is rare to start smoking after the age of 21. This general statement may be less true in countries in which the spread of smoking is more recent. For instance, present evidence suggests that children's smoking rates are low, relative to adults, in Japan and China. This difference from Western industrialized countries may be due to strong cultural disapproval of children smoking, though it is possible that this disapproval leads, in surveys, to children underreporting their habit. In countries in which the habit is relatively new, it is, of course, first adopted by adults and only later spread to children as they seek to emulate adult habits.

**Principles of Smoking Control**

These are now well-recognized and there are a number of useful guides to action. The basic components are generally accepted. They include: (1) the setting up of a government smoking control program; (2) the prohibition of all forms of tobacco promotion; (3) progressive increases in tobacco tax (the resultant percentage decrease in consumption is always less than the percentage increase in price, so that a government both increases its tax receipts and improves the nation's health) (Fig 2); (4) increasing nonsmoking in public places, transport, and workplaces; (5) government health warnings on cigarette packets (and on tobacco advertisements and promotion material, pending abolition of these); (6) intensive health education in schools, among opinion leaders, and in the media; (7) making tobacco sales to children illegal; and (8) monitoring of trends in national consumption and tobacco-related mortality and morbidity. Details will be found in the handbooks quoted. There is space here only to comment on certain aspects.

Developing the climate of public opinion against smoking is the main aim and is the basis for achieving the above measures. This is a complex of many factors, including the influence of health professionals, public figures and other opinion formers, voluntary bodies, the media, politicians, and government, all of these mutually interacting. Commercial tobacco promotion may be a powerful countereffect, especially on the young. A powerful negative influence is the commercial lobbying of politicians and others.

Much research has been done on discouraging children from smoking. School programs should be merged with other health themes, involve children in discussion and development of "life skills" to resist tobacco promotion and peer pressure, and if possible to involve parents. A promising new initiative in the UK is the launch of "Smoke Busters," children's clubs providing exciting alternatives for the relevant age groups. Best et al. and Swan et al. have provided valuable critical reviews in this area.

Evidence in industrialized countries indicates that, as the measures outlined previously develop, large numbers of adults quit spontaneously and that the majority of smokers wish to do so. There are already nearly 10 million successful quitters in the UK and 35 million in the USA. The great majority quit without specific help, but pamphlets of counseling for those with particular difficulties are symbols of a desire to help.

A national campaign should be as comprehensive and continuous as possible, with the message coming to the public from as many directions as possible and adapted to the local culture, eg, strong support from influential religious leaders is very valuable in some countries. Success in other countries can also be used to influence politicians and administrators.

**Conclusions**

Cigarette smoking is undoubtedly the most important causative factor in COAD and is largely responsible for the characteristic decline in lung function observed in smokers.
Atmospheric pollution, industrial or domestic, and inhaled dusts, act at least additively with cigarette smoking and clinically tend to show their major effects in smokers. Childhood lower respiratory infections probably play a part in the bronchitic element of airways obstruction and may be particularly important in developing countries where such infections are more common and less well controlled, but the evidence suggests that infection is not an important cause of emphysema. Apart from the clear evidence of enhanced susceptibility to tobacco smoke, and consequent premature emphysema, in those with homozygous alpha-antitrypsin deficiency, genetic predisposition is of doubtful importance, though a possible atopic component is again under examination.

Multiple factors determine whether or not a person, often a child, will start smoking and, similarly, whether or not someone who already smokes will quit. Knowledge of the factors that contribute to the "smoking behavior complex" have led to some well-established principles of smoking control that, when applied on a national level in a comprehensive and continuous manner, are effective in reducing the number of people who smoke.

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Acute Respiratory Infections

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The role of acute respiratory infections (ARI) in the natural history of chronic airways disease (CAD) is not clear. It seems probable that severe acute lower respiratory infections can cause irreparable damage to the delicate epithelium of the bronchi and bronchioles in infants and young children. They may thereby also render the small airways more susceptible to other harmful agents or to repeated infections in later life, thus initiating a process of progressive damage and deterioration of respiratory function. It is also possible that acute infections, at any stage of life, may accelerate declining respiratory function by their effects on airways already damaged by other pathologic conditions.

ARIs are usually regarded as a trivial problem except in countries where mortality rates are high. But if, by whatever mechanism, they also contribute to the development of CAD, their prevention is worthwhile even where they are rarely fatal.

We describe the magnitude of the problem of ARI and examine the evidence that ARIs in early life cause permanent...