CHAPTER VIII
RESPIRATORY DISEASES

Professor Stephen Louw

INTRODUCTION

The respiratory system is affected by a number of habitual behaviours found in South African lifestyles. These include tobacco smoking (active or passive), dagga smoking, allergens (present mainly as preservatives) in highly processed food and environmental air pollution. These factors may singly or in combination damage the lungs by: *(a)* causing chronic inflammation of the airways, resulting in chronic hypersecretion of mucous, the clinical syndrome of *chronic bronchitis; (b)* causing chronic irritation at the alveolar level, inducing inflammatory reactions which result in digestion of the lung, leading to *emphysema;* and *(c)* causing the activation of allergic responses within the airways, resulting in airways hyperreactivity to non-specific stimuli, the clinical syndrome of *asthma*.

Clinical definitions

Chronic bronchitis is defined by the British MRC criteria, namely: "patients who have coughed up sputum on most days during at least three consecutive months in two successive years".[1]

Emphysema is a pathological enlargement of air spaces distal to the terminal bronchiole, accompanied by destruction of their walls, and without fibrosis.[2] Since a postmortem diagnosis is seldom obtained in relation to death certification or epidemiological surveys, the clinical diagnosis is usually dependent on features of hyperinflation and airflow obstruction; the epidemiological definition usually relies on some form of spirometry.

For clinical purposes, chronic bronchitis and emphysema are usually lumped together since they seldom occur singly. Their combined effect on the patient is respiratory discomfort, including coughing and breathlessness on exertion. Diagnosing the two conditions severally in life requires sophisticated lung function tests or radiological examinations. The combination of chronic bronchitis and emphysema are therefore often referred to as chronic obstructive airways disease (COAD) or chronic obstructive pulmonary disease (COPD). COPD generally manifests after 15 - 20 years of tobacco smoke exposure in susceptible individuals - it is thus a condition of middle aged and elderly people.

Asthma, a condition generally regarded as allergic in origin, is usually induced by an inhaled allergen, and less frequently induced by ingested substances. Asthma is characterised by intermittent airways obstruction due to spasm of the hypersensitive smooth muscle of the bronchi as well as oedema and inflammation of the airways submucosal tissues. Its diagnosis is dependent on demonstrating reversibility of airflow obstruction or hypersensitivity of the smooth muscle of the bronchi to specific chemical or cold air challenges. Patients with hypersensitive bronchi may have frequent attacks of wheeziness and breathlessness if they are exposed to cigarette smoke, ingested or inhaled allergens.

Professor Stephen Louw graduated M.B.Ch.B. from the University of Cape Town in 1974 and obtained the F.C.P. (S.A.) in 1980. A 2-year stint in Edinburgh, Scotland allowed him to perform epidemiological investigations of lung function and chest radiology, which formed the basis of his M.D. He spent 7 years as consultant in the Respiratory Clinic at Groote Schuur Hospital, Cape Town. During this time he pursued his interests in occupational lung diseases, asthma and the epidemiology of factors influencing pulmonary function. In December 1991 he changed his career direction by accepting an appointment as William Slater Chair of Geriatric Medicine at the University of Cape Town.

Overlaps occur: many patients with cigarette-induced emphysema may have an element of reversibility of airways obstruction, sometimes sufficient to warrant the co-diagnosis of emphysema and asthma. Chronic asthma (particularly if not adequately treated) may lead to an element of fixed airways obstruction, which may resemble emphysema.

Epidemiological definitions

The International Classification of Diseases - ninth revision (ICD-9) recognises an overlap of chronic bronchitis, emphysema and asthma. Section 490-496 is headed "Chronic obstructive pulmonary disease and allied conditions"; under 'Bronchitis' (490), there are the sub-entities "Obstructive chronic bronchitis; Bronchitis: asthmatic, chronic emphysematous/Bronchitis with: chronic airway obstruction, emphysema" (491.2); under 'Asthma' (493) there is the sub-entity "Chronic obstructive asthma: asthma with chronic obstructive pulmonary disease (COPD)" (493.2). Most epidemiological studies fail to distinguish the subtypes of COPD, and would therefore consider all conditions under 490-496. These include 'Bronchiectasis' (494) (a condition usually resulting from severe lung infections), 'Extrinsic allergic alveolitis' (495) (which mostly arises from exposure to moulds, etc. in agricultural occupational environments) and 'chronic airway obstruction, not elsewhere classified' (496).

In the light of these considerations, it is readily apparent that published data based on routinely gathered information are usually not capable of discriminating between emphysema, chronic bronchitis or asthma. By extension, conclusions regarding the aetiology of these clinical conditions are fraught with a large measure of uncertainty.

METHODS

Every effort was made to obtain all relevant publications of work done in South Africa since 1980; certain key references prior to this date were obtained and are included in this report. The following procedure was adopted: the Deans and/or Heads of the Departments of Medicine and/or Heads of the Departments of Pulmonology at the Universities of Cape Town, Stellenbosch, Pretoria, the Witwatersrand, MEDUNSA, the Orange Free State and Natal were contacted. They were requested to forward relevant sections of their Faculties' Annual Research Reports from 1980 to 1992. Reports were received from MEDUNSA (1987 - 1991), and the Universities of Pretoria (1986; 1989; 1990; 1991), Orange Free State (1980 - 1984; 1986 - 1991), Natal (1980 - 1991), Stellenbosch (1986 - 1991) and Cape Town (1980 - 1992). These reports were scrutinised using key words and the relevant references were obtained and photocopied for detailed scrutiny. Wherever the reference section of such publications contained references that appeared to be relevant to this report, they were followed up as well.

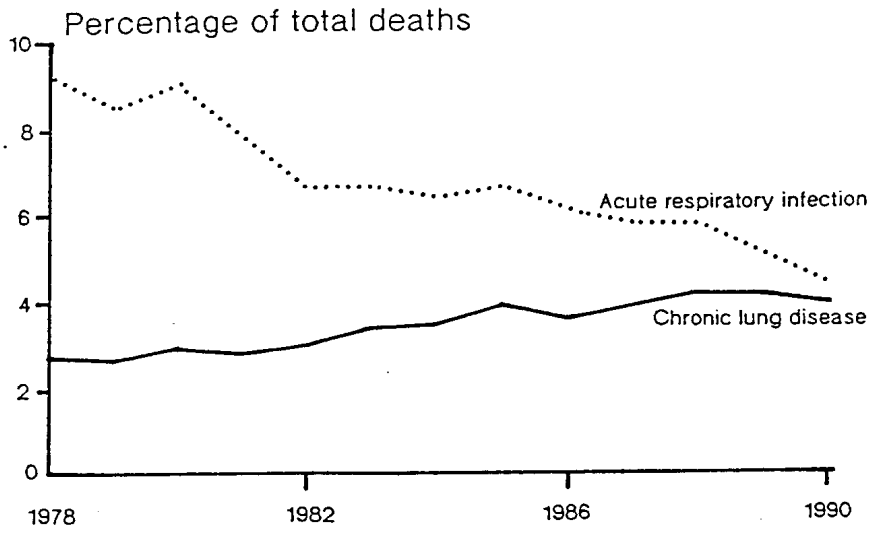
The MRC's publication *Review of South African Mortality, 1984* (Technical Report No. 1) was scrutinised and relevant references were obtained. The *South African Journal of Continuing Medical Education* (May 1993) was scrutinised in order to obtain relevant references. A Medline search was conducted, examining all cited publications of key South African researchers. In addition, a Medline search was conducted using a variety of combinations of subject key words. The MRC, HSRC and National Association for Clear Air were approached and advice and reference lists were obtained from these institutions. The abstracts of the South African Pulmonology Society's Congress Proceedings were scrutinised and relevant papers/posters were photocopied. Where appropriate, authors of such abstracts were contacted to obtain copies of publications. Dr Paul Potter (Editor of the *Journal of the Allergy Society of South Africa*) was asked to provide relevant publications in relation to food allergens. Dr Petro Terblanche (Manager: Environmental, Health and Safety Management Services of the CSIR Environmental Services) was approached and a list of over 100 references was obtained. Every effort was made to include theses and technical memoranda in the review.

Using these procedures, some 150 papers were obtained. All these papers were scrutinised and

classified into relevant/irrelevant; reclassified into tobacco, dagga, environmental air pollution and dietary allergens and under these headings subdivided into emphysema/bronchitis and asthma.

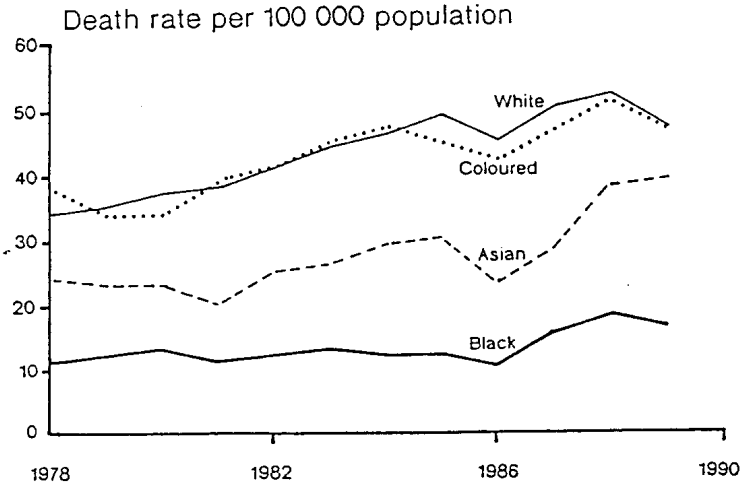
SCOPE OF THE PROBLEM OF COPD IN SOUTH AFRICA

The 1992 publication of the Department of National Health and Population Development (DNHPD), "*Health Trends in South Africa*" included the graph shown in Fig. 1. It can be seen that the percentage of total deaths attributable to chronic lung disease increased from 2,7% in 1978 to 4% in 1990.[1] The increasing mortality rates during the decade until 1990 by race group is reproduced in Fig. 2. This shows that the death rates due to chronic lung disease among the white and coloured population groups were similar (approximately 35/100 000 in 1980) and approximately 4 times higher than among the black population group; the Asian population group occupied an intermediate position.



Source: Central Statistical Service Reports on deaths

Figure 1. Comparative trends. Acute respiratory infection: Chronic lung disease Republic of South Africa



Source: Central Statistical Service Reports on deaths (Code 491-496. 500-515)

Figure 2. Chronic lung disease mortality - Republic of South Africa

Steyn, *et al.*[4] reported on their calculations of the proportions of deaths due to chronic diseases of lifestyle for all ages and for persons aged 35 - 64 years in South Africa in 1988. The ICD-9 code classifications 491 (bronchitis), 492 (emphysema), 496 ('other COAD') showed that 2,5% of all ages died of these diagnoses in 1988; for the age group 35 - 64 years, 2,6% died of these conditions.

These data, analysed by the above separate group of investigators,[4] are consistent with those reported by the DNHPD (if one bears in mind that the DNHPD report also included ICD classifications 500-515): pneumoconiosis and other lung diseases due to external agents (500-508); emphysema (510); pleurisy (511); pneumothorax (512); abscess of the lung and mediastinum (513); pulmonary congestion and hypostasis (514); and post-inflammatory fibrosis (515).

An article by Bradshaw, *et al.*[5] draws attention to the fact that trauma, poverty-related diseases and chronic diseases related to lifestyle all contribute to high levels of adult mortality, particularly affecting the black population of South Africa. Using a summary index of adult mortality, the 45Q15 (the probability, expressed as a percentage, of a 15-year-old dying before the age of 60 if the mortality rates remain at the same level) it was found that this figure was 42,8% for black males, 29,4% for black females but 21,8% and 11,5% for their respective white counterparts. The four leading causes of death in the black population for age 15 to 64 years (total 60 723 deaths in 1988) were trauma (32%), ill-defined (18%), circulatory (14%), neoplasm (20%); for the 65 to 84 year age group (25 480 deaths) ill-defined (36%), circulatory (23%), neoplasm (11%) and respiratory (11%). Thus, in the black population respiratory deaths form a substantial component in the elderly population, but less so as compared to the other causes of death in the younger age groups. In the white population 8% of the 13 423 deaths for the ages 15 to 64 years were due to respiratory diseases - this was the fourth most common cause in this age group after circulatory (32%), trauma (23%), neoplasia (21%). For the older age group (over 65 years), respiratory diseases (±14%) was the third most important cause of death for the white, coloured and Asian population groups, after circulatory (±42%) and neoplasm (±17%). It should be pointed out, however, that in this paper death due to acute illnesses was combined with deaths due to chronic illnesses. The authors assert that in developing countries health workers have tended to focus on "the causes of infant morbidity and mortality (mainly infectious diseases) without due regard for the causes of adult ill health... The assumption implicit in this approach is that once newborns are helped through their first 5 years ... their mortality experience will be the same as that observed in developing countries." Bradshaw, *et al.* highlight the impact of trauma and poverty-related diseases among the poorer sectors of our society and the high proportion of deaths related to circulatory, neoplastic and respiratory disorders which may relate more to diseases of lifestyle among the higher socio-economic sectors of our society.

Three papers by Wyndham published in 1981, 1982 and 1985[6-8] examined the economic impact of 'destructive lifestyles' among the potentially economically active population (aged 15 - 64 years) of South Africa. Looking at the *'Loss from premature deaths of economically active manpower in the various populations of the RSA'* (in 1970), Wyndham noted marked differences in the age-adjusted mortality rates for the four principal ethnic groups of South Africa.[6] "At the one extreme were the whites in whom the five leading causes of death (in rank order) were ischaemic heart disease, motor vehicle accidents, cerebrovascular accidents (CVA), cancer of the digestive system and *bronchitis and associated respiratory diseases* - a mortality pattern which is characteristic of a developed Western community. The black population was at the other extreme, in whom the five leading causes of death (in rank order) were 'ill-defined' diseases, the pneumonias, tuberculosis, CVA and homicide and unspecified violence - a mortality pattern commonly seen in less developed communities." It is noteworthy that at the time of publication Wyndham suggested that "quite different health strategies are needed to reduce mortality in the whites and Asians on the one hand and the coloureds and blacks on the other."[6] In the former populations changes in lifestyle were required whereas in the latter groups "elementary public health measures" were necessary. In 1970 bronchitis and allied conditions ranked as the fifth most important cause of death, accounting for 4% of total deaths; the fifth most important cause among Asians (accounting for 6% of all deaths),

the ninth most important cause among coloureds (accounting for 4% of deaths) and for the black population it did not rank in the top ten but accounted for 2% of all deaths.

In his paper,[7] Wyndham compared the trends over time among South Africa whites, the USA, Australia, England and Wales and Scotland for the same period. The percentage of deaths due to chronic lung disease for white South African males aged 15 to 64 years in 1968 was 3,7% and in 1977 was 3,2% (range 1,8% to 3,8%). Comparisons with the other countries showed that the proportion of deaths due to chronic respiratory disease was slightly higher among men in England and Wales, Scotland and Australia (range 3 to 6%). Deaths due to chronic respiratory diseases among USA females was ±1%, 3 to 4% among South African females, 4 to 7% among females in England and Wales; whereas over the period under investigation there was no change in trends in South Africa, there was a substantial decrease in the USA (by 29%) and England and Wales (by 30%) and a substantial increase in Australia (by 53%). For these comparisons Wyndham included under 'chronic respiratory diseases' the entities bronchitis, emphysema and asthma. Wyndham points out that there appears to be a paradox that during the period under investigation the mortality rates for lung cancer were rising in certain of the countries under review, whereas the mortality rates for chronic respiratory diseases declined markedly. He speculates that this might be due to the fact that "during this period vigorous steps were being taken to reduce atmospheric pollution in the UK and the USA. The decline in mortality rates for chronic respiratory diseases would seem to indicate that cigarette smoking plays a less important role in chronic respiratory diseases than it does in lung cancer."

In 1985, Wyndham compared the death rates in 1970 and 1980.[8] It was found that deaths of white males and females due to chronic lung diseases fell from 22,0 (N = 526) to 18,6 (N = 495) per 100 000 in 1980 for ages 15 to 64 years (standardised to the population age profile of 1970). Thus, despite an increase in the white population in this age group from 2,39 million in 1970 to 2,93 million in 1980, no increase in the mortality rates due to chronic lung diseases had occurred. This finding may reflect a plateau in response to the beneficial effects of the anti-smoking campaign. It is noteworthy that Wyndham's analysis of the data is possibly at variance with the DNHPD data referred to above, which included ICD codes 500-515.

A paper by Epstein, *et al.*[9] examined the 5-year mortality rates in coloureds, whites and Asians for: (1) pneumonia and influenza; (2) chronic obstructive lung disease and allied conditions (ICD 490-496); (3) pulmonary tuberculosis; and, (4) carcinoma of the lung and bronchus by age, sex and ethnic group-specific rates. Changes in the respiratory disease mortality rates over the 5-year period were examined by calculating the age-standardised mortality rates for each condition in each of the 5 years. The mortality rate for chronic obstructive pulmonary disease rose in all groups, except Asian females. The authors acknowledged that the ICD 490-496 category of classification includes several diseases that have different frequencies at various age brackets. COPD accounted for between one fifth and one third of respiratory deaths in the various ethnic groups. The age-standardised mortality rates per 100 000 for COPD as compared with carcinoma of the lung and bronchus in 1980 are shown in Table I.

The value calculated for white males differs from Wyndham's[8] because it was calculated for all ages and the population has been age-adjusted to 1980. It is noteworthy that for Asian males and Asian and Coloured females the mortality rate due to COPD was higher than that of carcinoma of the lung and bronchus; at any rate one must conclude that cigarette smoking contributes to a very high respiratory death rate among South Africans.

Further references dealing with the general impact of COPD on the SA population include Wyndham,[10] some descriptions of tobacco-smoking behaviour,[11-13] the economic impact of smoking,[14] small studies of disease patterns in hospitals[15-17] and general practice[18] and a report on the respiratory health effects of passive smoking.[19]

Table I. Age-standardised mortality rates per 100 000 for COPD compared with carcinoma of the lung and bronchus in 1980

	Males	Females
COPD		
Whites	19,64	8,35
Asians	27,36	11,40
Coloureds	36,66	14,55
CA Lung and Bronchus		
Whites	38,14	11,51
Asians	18,51	4,41
Coloureds	52,67	10,32

TOBACCO SMOKE AND CHRONIC LUNG DISEASES

The trends and social impact of tobacco smoking in South Africa is dealt with in chapter III by Derek Yach. This section describes the South African research publications that have examined the impact of tobacco smoking on the respiratory system. The section is divided into studies on COPD and those on asthma.

Chronic Obstructive Pulmonary Disease

Mechanisms

Although there is no reason to believe that the mechanisms by which tobacco smoking cause COPD in South Africans differ from those in other countries, there are a number of publications of work conducted by South African authors. The Medical Research Council Unit for the Study of Phagocyte Function at the Department of Immunology, Institute for Pathology at the University of Pretoria and the Respiratory Unit, Department of Medicine, Coronation Hospital and University of Witwatersrand, has published papers dealing with cigarette smoke-mediated oxygen stress and its effect on phagocytes, anti-oxidant effects of vitamins C, E and beta-carotene.[20-23] They have also shown that passive smoking by humans sensitise their circulating neutrophils.[24] The same group (no longer an MRC unit) subsequently showed that spirometric abnormalities in young smokers correlate with activation of blood phagocytes.[25] A series of papers with Anderson as the first author, from the same group comprised: studies on the anti-oxidants ascorbate, cystine and dapsone as being capable of regulating degeneration of reactive oxidants from activated phagocytes from cigarette smokers;[26] on ascorbic acid in the same role;[27] on vitamin C, E and beta-carotene in the modulation of oxidant stress mediated by cigarette smoke-activated phagocytes;[28] and an overview paper of the role of phagocytes in oxidant stress mediated by tobacco smoke.[29]

Papers published, mainly with Maritz as the first author from the Department of Physiological Sciences (University of the Western Cape), have tended to focus on the impact of maternal nicotine exposure on neonatal lung tissue in rats.[30-35]

Social Impact

One South African study has examined the relationship between smoking and respiratory symptoms in children. A questionnaire study among 1 716 white high school children in Cape Town by Prout

and Benatar[36] showed that 21% were current smokers, smoking an average of 170 cigarettes per month. Peer influence was found to be the single most important determinant of the smoking habit. Chronic cough and sputum production, symptoms suggesting asthma, dyspnoea on exertion were all more common in ex-smokers and current smokers than in children who had never smoked. Of current smokers 8,2% gave a history of chronic cough, 12,2% a history of chronic sputum production, and 28,3% a history of dyspnoea on exertion. Chest illness resulting in absenteeism from school was found in 19,8% of current smokers, 3,5% of ex-smokers and 11,7% of those who had never smoked. The study did not include lung function tests.

A study by Coetzee[37] reported on the findings of successive questionnaires sent to graduates from Pretoria Medical School. The study was commenced in 1978 and covered the period 1947 (when the first class qualified) to the end of 1975. Of 2 636 doctors who were approached, 2 080 (79%) replied. Of these, 1 878 were men. The male study group comprised 656 smokers, 554 ex-smokers and 668 non-smokers. Replies to the question "do you suffer from obstructive airways disease?" indicated that, after correcting for age this condition occurred significantly more often in male smokers (3,51%) and ex-smokers (2,53%) as compared to never smokers (0,60%).

A study by Wicht and Kotze examined the impact of cigarette smoking on symptoms of COPD.[38] This study was a randomised sample of the Bellville population in which 272 men and 237 women were recruited. The prevalence of current smokers was 71% for men and 38% for women. An inverse relationship between social class and smoking was 'partly shown'. A distinct relationship between smoking in men and symptoms of cough and sputum production was shown. Of men who smoked 30,6% had grade 2 dyspnoea as compared to 10,4% of non-smokers ($P<0,001$). In women a significantly higher prevalence of morning cough and morning sputum production was found among smokers. No significant relationship linking smoking to grade 2 or higher dyspnoea in women could be shown. This study spanned the age range 20 - 79 with approximately a quarter of participants over the age of 50. Wicht, *et al.*[39] published the precursor report on the above study data. The data from the British MRC (1966) questionnaire were examined by item and correlations with smoking history explored; the lung function data were similarly examined. The term diffuse obstructive pulmonary syndrome was held to include atopic asthma, chronic bronchitis and emphysema. Patients were classified as having DOPS if the FEV_1/FVC ratio was below 70% or if the patient was found to have features of chronic bronchitis or intermittent wheeziness or a previous history of bronchial asthma or emphysema on the questionnaire. It was found that 11,4% of the men and 9,3% of the women had an FEV_1/FVC ratio of less than 70%, 22,4% of men and 25,7% of women qualified for the diagnosis of DOPS under the symptom questionnaire only, and 10,7% of men and 8% of women satisfied both the symptoms criteria and the lung function criteria. Among men there was no statistically significant difference in the prevalence of DOPS in smokers (46%) and in non-smokers (41%). Similarly no difference could be demonstrated among the women. The authors comment that this lack of an association between smoking and DOPS may be due to the fact that the FEV_1/FVC ratio criterion and the diagnosis of asthma in the questionnaire were not very strict. It would appear that the subsequent publication by Wicht and Kotze[38] arose from the recognition that a more detailed analysis of individual respiratory symptoms may "provide an answer regarding the finding that cigarette smoking apparently had no influence on the total prevalence of DOPS" in the former study.

Sluis-Cremer, *et al.*[40] examined the respiratory symptoms and spirometry in black and white mining and non-mining industrial workers in South Africa. A previous data set of the prevalence of respiratory symptoms and lung function in white gold miners over the age of 35 (reported in 1967) comprised a male population in Carletonville comparing 562 miners and 265 controls. These data were compared with another previously published study (1970) comparing 825 black gold miners with 165 black non-miners over the age of 35. The participants were selected by excluding all cases with cardio-respiratory disease and chest radiograph abnormalities. A third study, carried out by the National Research Institute for Occupational Diseases compared the findings of 1 185 black factory workers with 326 white factory workers, the majority of whom were over the age of 35. Spirometry tests were conducted, sputum samples were collected and tobacco smoking history was

obtained. Among the industrial workers a significantly lower FEV_1/FVC ratio was demonstrable among the white men who smoked >25 g per day as compared to the other groups; no such difference was demonstrable among the black industrial workers. Although a wealth of other data is supplied in this paper none of the other comparisons showed statistically significant differences. The authors state that "it does appear that blacks suffer a negligible rate of respiratory symptoms while they restrict themselves to pipe smoking and live in relatively unpolluted areas". The authors warn that "it is probable that as black miners increasingly take to cigarette smoking their respiratory symptoms and lung functional loss will approach those of white miners, as has occurred in the case of black industrial workers."

Yach and Joubert[41] examined deaths related to smoking in South Africa in 1984 and made projections for deaths among coloureds and blacks in the year 2000. Chronic obstructive lung disease was defined as ICD codes 490-496. In 1984 the percentage of total deaths for whites due to COPD was 5,3%, Asians 4,4%, coloureds 4,4% and blacks 1,6%. The comparable figure for England and Wales (1983) was 4,0%. It is noteworthy that the percentage of deaths due to carcinoma of the lung was roughly half that due to COPD and that among the white and Asian groups, deaths due to ischaemic heart disease were roughly four times higher than those due to COPD.

Current Concepts

In their revision of the prestigious respiratory text *Crofton and Douglas' Respiratory Diseases*, Seaton, *et al.*[1] make the following comments: "The most important evidence associating smoking and mortality from chronic bronchitis is that of Doll and Peter. In a study mainly aimed at determining the aetiology of lung cancer, 40 000 medical practitioners in Britain recorded their smoking habits, the cause of death being determined later in those who died during the follow-up period. It was found that the death rate for chronic bronchitis was significantly higher in cigarette smokers than in non-smokers and increased with the amount smoked."

"Sample surveys of respiratory symptoms in the population have shown a much higher prevalence of cough and sputum among smokers than among non-smokers. In such surveys, chronic bronchitis, whatever the definition used, has been almost confined to smokers."

"A number of surveys have included simple tests of respiratory function such as FEV_1 or PEFR. On the whole these tests indicated poorer function in smokers than in non-smokers. Follow-up studies have shown a steeper decline in FEV_1 among smokers than among ex-smokers and rapid deceleration of the rate of decline following smoking cessation." In this regard, the follow-up study by Fletcher and Peto[42] produced the graph (Fig. 3), which is a classic reference in the respiratory literature.

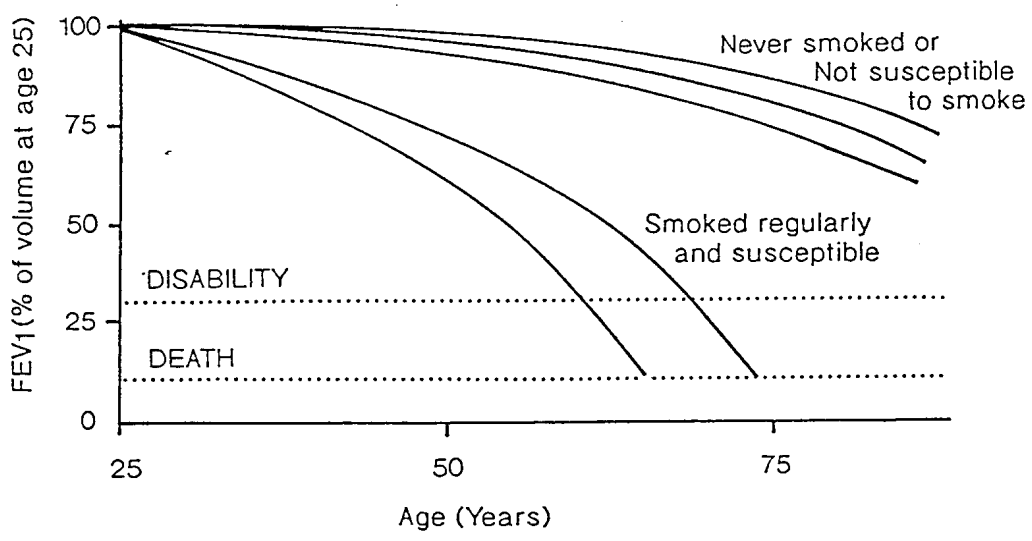


Figure 3. Decline in FEV_1 with age[42] (modified)

"The method of smoking is important. Chronic bronchitis has been predominantly related to the inhalation of cigarette smoke. Pipe and cigar smokers have a much lower prevalence of the disease and less impairment of function. Children who smoke have more cough and more chest illnesses than non-smokers. Even the infants of smoking parents have more respiratory illnesses than infants of non-smokers."

Asthma

Mechanisms

Although no original research has been conducted in South Africa exploring tobacco smoking as a cause or precipitating agent for asthma, one editorial in the *South African Medical Journal* by Ehrlich[43] provides a fair summary of the information linking parental smoking and childhood asthma. He quotes nine studies in the general population which showed a relationship between maternal smoking and wheezing or asthma in childhood. In three of these studies an exposure response relationship was found between the number of cigarettes smoked daily and the occurrence of wheezing or asthma. The mechanism of this association with maternal smoking is unknown. Ehrlich quotes data that have shown that maternal smoking enhances IGE levels and skin-prick test for allergen reactivity in children. Also, the children of mothers who smoke have an increased risk of more severe lower respiratory infections in childhood. Ehrlich concludes "there is now enough evidence for public health purposes to add childhood asthma or persistent wheezing to the list of smoking-related diseases."

Social Impact

A paper by Joubert, *et al.*[44] reports a study on patients who attended an allergy clinic. The group comprised 55 white and 63 coloured patients aged 12 - 40 years. It was found that repeated acute bronchitis episodes occurred in 22% of the white male and 44% of the white female patients. In the coloured patient group 53% of the males and 61% of the females manifest this factor. Cigarette smoking was thought to be a 'possible contributory factor' in 86% of the coloured as opposed to 56% of the white patients ($P<0,01$). Passive smoking was a more significant factor in the coloured population and in this group 14,3% were still active smokers (as compared to 4% of the white population - $P<0,01$).

In a paper examining smoking and chronic respiratory symptoms in 11 to 15-year-old children, Benatar[45] examined 605 children. Of these 290 were coloured, predominantly social classes 3 and 4 and 315 were white, predominantly social classes 1 and 2. It was found that 76% of the white children and 59,6% of the coloured children were non-smokers and had no past or present symptoms of chronic lung disease. Of the white children, 2,5% were smokers, as compared to 15,2% of the coloured children. Of the 52 children who smoked 12 had chronic respiratory symptoms: 1 had asthma, 9 had chronic cough and sputum and 2 had shortness of breath on exertion. Among the non-smoking group, 13,6% of the white children and 7,9% of the coloured children gave a history of past or present asthma or wheezy chest. In his discussion the author indicates that the prevalence of smoking history in the white cohort was probably an underestimate since many white children refused to participate for fear of being reprimanded for smoking. The author points out that there was no difference in the prevalence of chronic respiratory symptoms in smoking and non-smoking children and also no difference in the simple measures of ventilatory function. "This is not surprising in view of the fact that the majority of the children who smoked had done so for less than one year."

An important study was conducted by Vermeulen[46] to explore the factors responsible for the significant difference in prevalence rates of airway hyper-responsiveness found among urban and rural communities. A previous study by van Niekerk[47] had showed that an urban group of Xhosa children (aged 6 to 9 years) had a prevalence rate for asthma of 3,17% as compared to 0,14% in their rural counterparts. Van Niekerk used an exercise challenge test to identify his asthmatic cases.

Vermeulen set out to repeat this work by using a histamine challenge bronchial provocation test on 1 014 children in rural Transkei. One hundred and forty five cases were identified as having bronchial hyper-responsiveness, yielding a prevalence rate of 14,2%. The importance of this study, although it did not investigate smoking history, is that it showed a higher prevalence of bronchial hyper-responsiveness in a rural African population than previously suspected. A study by Luyt, *et al.* investigated the profile of asthmatic children attending Baragwanath Hospital.[48] No mention is made of smoking history; the commonest precipitants were exercise, cold weather and upper respiratory tract infections.

Deaths from asthma in Cape Town were investigated by Benatar and Ainslie.[49] During this 3-year period, 351 patients were certified as having died from asthma in the Cape Town City Council area. Of the 231 patients certified as having died from asthma only, 179 (77,5%) were over the age of 40. The investigators examined the circumstances surrounding death in 28 of the remaining 52 patients under the age of 40 years. It was found that the incidence of death from asthma in Cape Town is three times greater than in the UK. Of the aforementioned 28 patients, 3 were or had been smokers. Sixteen patients (57%) had been admitted to hospital previously for acute asthma, 8 of these within one month of death.

Current Concepts

The authors of *Crofton and Douglas' Respiratory Diseases*[50] provide a global perspective on the prevalence and causation of asthma. Studies are quoted indicating that "general surveys of random samples of adult populations in Britain, the US and other westernised countries indicated that current prevalence of diagnosed asthma may be around 2 - 6% and cumulative prevalence (current and/or a history of asthma) around 3 - 9%." The same authors regard the following factors as being responsible for inducing or aggravating asthma: food, drink and drugs (see Food Additives and Chronic Asthma below), infection, air pollution (see Environmental Air Pollution and Chronic Lung Disease below), tobacco smoking, psychological factors, gastro-oesophageal reflux, exercise (may aggravate asthma in pre-existing asthmatics) and occupational factors. On smoking, the following comment: "smokers appear to be at greater risk of developing asthma and have a higher prevalence of hyperreactivity" of the airways.

DAGGA (CANNABIS) SMOKING AND CHRONIC LUNG DISEASES

Studies performed in South Africa would suggest that dagga smoking is prevalent throughout South Africa and may thus constitute a significant health problem. Authors indicate that the prohibition of dagga smoking has tended to complicate studies in this area.

Simon[51] conducted 17 informal interviews and analysed 1 597 questionnaire responses among South African university students. He noted a significant discrepancy between the interview-related data and the data derived from the questionnaires. It was found that of those who completed the questionnaire, 25,1% indicated that they had smoked dagga and 7,2% that they had taken dagga in other forms. An earlier study by Hare and Morley[52] among 788 white South African undergraduates indicated that 23,9% had tried illicit drugs on at least one occasion and of these 92,1% had tried dagga. Unfortunately the publication does not describe the sampling frame procedures. A study by Levin, *et al.*[53,54] examined 1 020 undergraduate medical students at the University of Witwatersrand and elicited an 85,1% return of questionnaires. It was found that 32,4% had tried dagga in the past and 16,4% were currently using the drug. Of the students who were still smoking dagga, 10% were light smokers (twice or less in the past 6 months) and 48% were heavy smokers (more than 10 times in the past 6 months) - the others were in the intermediate category.

Studies among South African adolescents have indicated disturbing trends. A study by Disler, *et al.*[55] investigated the prevalence of use of habit-forming drugs in a large co-educational Cape Town high school. It was found that a total of 26,6% of pupils of all ages admitted that they had used

cannabis and 13,2% were using it at the time of the survey on a regular basis; 2,6% were using cannabis more than once per month. The prevalence rose significantly with age. It was found that 24,6% of girls had used cannabis as compared to 20,3% of the boys. Unfortunately this study does not make any comment on socio-economic status and other influences that may be relevant in the prevalence of drug use.

Flischer, *et al.*[56] performed a study in collaboration with the MRC to determine the prevalence of "risk-taking behaviour of Cape Peninsula high-school students". A cluster-sampling technique was used to yield a sample of 7 340 students from 16 schools in the three major education departments. A self-administered questionnaire was completed by each student under conditions approximating those of examinations. Means were weighted to account for the fact that different proportions of students were selected from each education department. Of the total sample, 7,5% reported that they had ever smoked cannabis, while 2,4% reported using cannabis at least once in the past 7 days. A relatively large proportion of Xhosa-speaking males reported smoking cannabis on 4 or more occasions during the previous 7 days: 5,9% of this group reported having done so, compared with less than 1,8% of every other standard/gender and language/gender group. The proportion of Xhosa-speaking females who had used cannabis was particularly small. The authors conclude that "of all subgroups it emerges that Xhosa-speaking males are possibly most at risk for continued drug use and its negative consequences. Their behaviour goes further than experimentation." The authors conclude that this study is consistent with the findings of five earlier studies that the extent of drug use among South African adolescents was considerably lower than suggested by media sentiment. Furthermore, for all drugs the extent of use among Cape Peninsula adolescents is markedly less than observed in Australia and the USA. A study from the USA is quoted where 59% of students had previously used cannabis and 6,3% were using it on a daily basis.

The studies quoted above all refer to the prevalence of dagga usage among young South Africans. By inference (see Current Concepts below) certain respiratory health effects are likely to arise from excessive dagga smoking.

Mechanisms

No South African publications have appeared in which the mechanisms by which dagga may cause or aggravate COPD or chronic asthma have been published.

Social Impact

No South African study has been published in which the impact of dagga on respiratory disability is examined.

Current Concepts

Two studies published in the prestigious journal, *American Review of Respiratory Disease*,[57,58] have shown that dagga smoke is significantly more toxic to the lungs than cigarette smoke. Tashkin, *et al.*[57] showed that smoking 3 or 4 dagga cigarettes a day was associated with the same frequency of symptoms of acute and chronic bronchitis as smokers of 20 tobacco cigarettes a day would experience. Gong, *et al.*[58] made similar observations regarding the type and extent of epithelial damage of the large airways of the lung. A study by Wu, *et al.*[59] showed that the pulmonary toxicity of dagga appears to be unrelated to tetrahydrocannabinol content; it would appear that there is a substantially greater respiratory burden of carbon monoxide and tar in dagga smoke as compared to a similar quantity of tobacco smoke.

FOOD ADDITIVES AND CHRONIC ASTHMA

A feature of a modern, westernised lifestyle is a diet consisting largely of processed foods, preserved and enhanced in taste and appearance by food additives. It is generally recognised that

a number of food additives may induce the asthmatic state in individuals that have a genetic predisposition to such induction or may aggravate the severity and frequency of attacks in patients with asthma.

A number of ingested agents which are capable of precipitating asthma attacks have been identified. Broadly these fall into two classes, namely natural food substances inducing allergy and food additives which may induce or aggravate allergic conditions, including asthma. Because of the overlap of these classes of ingested agents and the complexity of Western diets, the need for placebo-controlled double-blind food challenge has become imperative in describing the prevalence of adverse reactions to food additives. Commonly recognised food additives that may induce or aggravate asthma are depicted in Table II.

Table II. Food additives that may provoke allergic reactions

Sulphur dioxide
Sodium and potassium bisulphite
Sodium and potassium meta-bisulphite
Other sulphites
Sodium benzoate
Sodium or potassium nitrite or nitrate
Tartrazine
Colourants (dyes)

In the USA legislation has been in place since 1990 enforcing labelling on all foodstuffs including nutrients and their quantities. However, in the United Kingdom and Europe technical matters regarding free trade in the EEC have acted as a barrier to the introduction of mandatory labelling.[60] The Allergy Society of South African has been active in lobbying for appropriate legislation through a number of working documents, a "food allergy tolerance workshop" held in Durban in July 1993,[61] a number of press releases and direct discussions with the Food Legislative Advisory Group (FLAG). As a result of lobbying by ALSSA the Foodstuffs, Cosmetics and Disinfectants Act of 1972 (Act 54 of 1972) has been modified to make provision for fairly extensive food labelling as published in the Government Gazette of 29 October 1993.

Mechanisms

A study by Borock, *et al.*[50] suggested that the likelihood of exercise-induced asthma was reduced if dietary factors and inhaled allergens were reduced in 6 asthmatics. Unfortunately the abstract does not report which foods were eliminated and whether food additives were implicated.

Social Impact

A survey by Steinman and Weinberg[63] indicated that 27% of a cohort of children with asthma gave a history of being sensitive to sulphites in soft drinks.

A study by Steinman, *et al.*[64] showed that 16 of 37 asthmatic children (43,2%) challenged with apple juice containing the preservative sodium metabisulphite had a significant fall in their forced expiratory volume in one second (FEV_1). None of 22 control asthmatic children who were

challenged with pure apple juice had a significant fall in FEV_1. Reactions occurred in spite of maintenance medications; one child became severely distressed and two had prolonged attacks, requiring nebulised bronchodilator treatment. The authors draw attention to the fact that reported prevalence of sulphite-sensitive asthmatics range between 3,9 and 10% in adult asthmatics and 35,3 and 65,5% of children with chronic asthma.[65-68] The authors draw attention to the fact that hidden, unlabelled sources of sulphur dioxide, sodium and potassium bisulphite and sodium sulphite in foodstuffs remain a problem in South Africa.

ENVIRONMENTAL AIR POLLUTION AND CHRONIC LUNG DISEASE

It is generally believed that environmental air pollution is a source of chronic lung disease.[69] While it is recognised that acute, heavy exposure to certain pollutants will cause illness, the data regarding the health effects of chronic, lower dose exposure is less persuasive.

Mechanisms

No South African studies have been done in this field.

Social Impact

An important study was performed by Zwi, *et al.*[70] among white schoolchildren in 11 schools in a high pollution environment (Eastern Transvaal Highveld) and 11 schools in non-polluted Transvaal towns. The study involved approximately 1 000 subjects in each limb. A questionnaire was completed by each child's mother and spirometry was recorded. Cough, wheeze, asthma and chest illness were more frequently reported from polluted areas compared with non-polluted areas, after allowance had been made for parental smoking and home cooking fuel. After correcting for age, children in the polluted area were 0,83 cm shorter, $P<0,035$. However, there were no significant differences in forced vital capacity and forced expiratory volume in one second in children from the two groups. The authors draw attention to the fact that levels of air pollution by smoke and SO_2 are not high by international standards in the Eastern Transvaal Highveld. They refer to a study done in the European community on 22 000 children aged 6 - 11 years, which showed no consistent relationship between air pollution levels and respiratory health.[71]

A study by Terblanche, *et al.*[72] had the aim of monitoring air pollution as well as a programme to assess health effects in the Vaal Triangle. Air pollution was determined by monitoring outdoor air pollution levels, indoor air pollution monitoring as well as personal monitoring. The pollutants that were monitored included SO_2, NO_x, particulate matter (PM), O_2, NH_3, H_2S and CO. A health questionnaire was distributed to 11 000 white and 1 500 black children and medical examination of the upper respiratory tract and lung function tests as well as immunological tests on sputum and blood in selected volunteers were done. Urine cotinine tests were also performed. Initial results of the cross-sectional phase of the study revealed that among 10 187 children, 24,1% of children considered by their parents to have been exposed to an environment with heavy air pollution had had lower respiratory tract illnesses (bronchitis, chronic cough and chronic illnesses) as compared to 16,3% of children not so exposed. It is noteworthy that a statistically significant higher prevalence of lower respiratory tract illnesses was reported in children exposed to parental smoking (25,7%) as compared to households where parents did not smoke (20,8%).[73]

The importance of indoor air pollution has attracted comment from several South African investigators. Truter, *et al.*[74] draws attention to the fact that children spend the majority of their time indoors and that major sources of indoor pollution in South Africa include tobacco smoke, coal stoves, wood smoke, paraffin and gas stoves (sources of respiratible particles, NO_x, CO, CO_2), plywood, glues, carpets and furniture (formaldehyde, radon, volatile organic compounds, asbestos, sulphur dioxide). The reference quoted[74] describes the protocol for a study; the final results have not yet been published. Von Schirnding[75] describes a study in which the type of fuel used in the home was found to be a risk factor for certain respiratory symptoms in urban coloured children.

Von Schirnding and Aucamp[76] drew attention to the observation that "there is a dirth of information on prevailing pollution levels and respiratory illness rates in the black urban townships." There is an urgent need to investigate the levels of pollution in these environments, particularly since the indoor air pollution level might be extremely high and may contribute to chronic lung disease. Coetzee, *et al.*[77] performed a study in the Sasolburg area showing that there was a significant difference in the FEV_1 of primary school boys in a polluted area and a relatively unpolluted rural area. A study by Klopper, *et al.*[78] showed evidence that there was no gross short-term public health hazard associated with air pollution in areas of heavy pollution.

Truluck[79] studied the hospital admission patterns of children with respiratory illnesses in Cape Town and investigated air pollution and meteorological factors associated with these admissions over 3 years. More than 15 000 admissions to the Red Cross War Memorial Children's Hospital and Tygerberg Hospital were due to respiratory illnesses, comprising 47,3% of the total number of admissions. Acute respiratory infections accounted for 63,6% and asthma accounted for 37,4% of these respiratory admissions. Air pollution data were obtained from the Cape Town City Council monitoring programme; during the study period monitors were located in Bellville South (a large coloured residential area) and another in the Cape Town central business district. None of the monitors were appropriately sited to monitor air pollution experienced on the Cape Flats. The data showed significant associations between acute respiratory infections and environmental prevalence of oxides of nitrogen, pollution index and temperature; acute asthma attacks were associated with a high level of NO_x; total admissions were associated with pollution index, average temperature and minimum temperature (negative). The author concluded that "despite generally low levels of air pollution in Cape Town, childhood respiratory admissions (to the two hospitals) were statistically significantly associated with some ambient air pollution as well as temperature."

In addition to the publications quoted above, a list of references of other reports (not available in the general literature) is provided as references 80 to 99.

Current Concepts

Recent work has strongly suggested that a greater level of discrimination with regard to the pollutant substance in the environmental air might show associations with respiratory disease to greater effect. Thus, a Swiss study[100] on preschool children in two cities in Switzerland showed that the total suspended particulates were more significantly predictive of the duration of any respiratory symptom than NO_2. This applied to coughing episodes and, to a marginal extent, as a predictor of upper respiratory episodes. Their study, however, did not provide any longitudinal data and refers to acute episodes only.

A study from Boston[101] investigated the indoor and outdoor particulate level on respiratory health in 1 576 never-smokers aged 40 to 69 years in industrial, residential and suburban areas. Households with coal stoves were found to have substantially higher indoor particulate levels than those with gas stoves. Persons who lived in houses where coal stoves were used for cooking and heating had significantly higher odds ratios for chronic phlegm, bouts of coughing and phlegm, wheeze and wheeze with shortness of breath than those who were not so exposed. The odds ratios for chronic cough and shortness of breath were similarly higher in the former category although these results were not significant. It was found that the particulate level was the highest in the industrial area and lowest in the suburban area. There was an excess risk of all respiratory symptoms among subjects who lived in industrial and residential areas as opposed to suburban areas with an increase in symptom prevalence commensurate with outdoor particulate levels. This study would suggest that in South Africa, where coal and wood are common sources of domestic fuel, generating high levels of particulates, we are likely to find an increased disease burden due to this exposure.

In an authoritative review of subjects in medical clinics of North America[102] it is noted that "some environmental exposures are known to be clinically relevant." These include ambient air pollution

which "remains a concern as a source of morbidity, particularly for susceptible populations such as persons with asthma, chronic obstructive pulmonary disease or cardiac disease and the elderly." It is noted that several components of indoor air pollution have been shown to have adverse effects on health; these include environmental tobacco smoke, fungi (thermophilic actinomycetes) that may contaminate ventilation systems and in the home fungus spores that may aggravate asthma. The author holds the view that evidence is less compelling for a link between other exposures and disorders of the respiratory tract.

A retrospective survey of deaths during the period 1973 to 1980 in Philadelphia suggested a significant positive association between total mortality (mean of 48 deaths per day) and total suspended particulates and SO_2. Of these, the particulate pollution was the more significant and had a greater effect on subjects older than 65 years of age. The authors point out that "there is an accumulating body of evidence showing that particulate pollution is associated with increased daily mortality at current levels in the United States."[103] Reviewing 32 publications, Austro[104] noted that the association between air pollution (measured as particulate matter) and mortality has been reported from several locations, over a wide range of climates and different populations. He noted that the more powerful investigations were the time-series studies which examined the joint occurrence of daily fluctuations in air pollution and mortality - these provided the strongest evidence of a true association. The author is cautious about the extrapolation of these results to infer causality, averring that consistency of the results needs to be explored; when the studies were converted into a common metric, a "striking consistency in the results was observed." The fulfilment of other criteria for causality, including specificity, presence of dose-response relationship and coherence of results was felt to lend strong support to the existence of an actual association between particulate matter and mortality. It would appear that the last criterion of causality, namely the biological mechanism, is not yet well understood.

In a prospective cohort study of 811 adults in six USA cities, the 14 to 16 mortality rates were investigated in relation to smoking history and environmental pollution exposure.[105] It was found that mortality rates were most strongly associated with cigarette smoking. After adjusting for smoking, it was found that the mortality-rate ratio for the most polluted cities was significantly higher than the least polluted cities. Air pollution was positively associated with death from lung cancer, cardiac pulmonary disease but not with death from other causes. Mortality was most strongly associated with air pollution with fine particulates, including sulphates.

CONCLUSIONS AND RECOMMENDATIONS

The percentage of total deaths attributable to chronic lung disease in South Africa is steadily increasing, with a figure of 4% of all deaths in 1990. The racial distribution (with a higher incidence among the white and coloured population groups) would suggest that chronic lung diseases occur to a greater extent among more affluent population groups. This is almost certainly a feature of the higher smoking habit currently found among more affluent South Africans but there is disconcerting evidence that smoking trends are increasing in both male and female blacks. Respiratory disease was the fourth most common cause of death among the black elderly population and the third most common among the elderly white, coloured and Asian population groups in a recent survey. The impact of deaths due to chronic lung disease among the economically active age group (15 to 64 years) in white South Africans is substantial; this disease group accounts for 3,5% of total deaths in this age group.

South African studies in the field of the mechanism of *tobacco smoke* and lung disease have tended to focus on the way in which oxygen radicals released by inflammatory cells behave when antioxidants such as various vitamins and drugs are administered in humans and rats. Studies of the social impact of tobacco smoking on chronic lung disease have been done among schoolchildren, suggesting a positive association between smoking, chronic cough and a history of dyspnoea on exertion. Studies in South Africa among adults (graduates from medical schools) and a community-based study in Bellville, a study among industrial workers and miners showed loose

associations between cigarette smoking and respiratory symptoms. A disconcerting projection by two workers from the MRC suggested that tobacco consumption among the black population may increase by 140 to 1226% over the 1984 rate by the year 2000. Despite the failure of South African studies to show a convincing relationship between smoking and chronic lung disease, a number of European and North American studies have shown a very convincing association between tobacco smoking and mortality from chronic bronchitis. It is recommended that the MRC should preferentially fund studies that will monitor tobacco consumption, particularly among the black population, and studies that will investigate the most effective means of curtailing tobacco consumption among all population groups in the country. It seems unlikely (and pointless) that we will be able to duplicate the massive studies that have been done in the Northern hemisphere to prove that tobacco smoking causes excess mortality due to chronic lung disease. Studies on the mechanisms of tobacco smoke-induced injury on the lung and ways to counteract these appear to be pure folly in the face of so obvious a need in the field of preventative epidemiology.

The mechanisms by which *tobacco smoke* may induce or aggravate *asthma* have not been investigated by South African workers. However, there is sufficient evidence in the world literature to link childhood asthma to tobacco smoke in the domestic environment, i.e. particularly related to parental smoking. Regarding the social impact of tobacco smoking on asthma, a hospital-based study suggested that smoking was a contributory factor in 56 to 86% of patients attending an allergy clinic. A study of smoking habits among 605 schoolchildren found that 25% of children who smoked had chronic respiratory symptoms (although not specifically asthma). An investigation of asthma deaths in Cape Town did not have sufficient power to examine the impact of smoking. However, it is generally accepted by experts in Europe and North America that smoking plays a significant contributory role in developing and aggravating asthma. It is recommended that the problem of smoking in asthmatics be dealt with by mass education of all asthmatics regarding the deleterious effects of smoking on asthma and that existing channels such as the South African Pulmonology Society and the primary health care network be used to convey this message through pamphlets in all languages.

The impact of *dagga* (cannabis) on chronic lung disease is surprisingly poorly documented in South Africa. Although a number of studies have investigated the prevalence of dagga smoking among schoolchildren and university students, no published South African study could be found which investigated the respiratory effects of dagga smoking. Studies which have been performed in North America have showed that the pulmonary toxicity of dagga cigarettes appears to be significantly greater than tobacco cigarettes (a ratio of 5:1). It is recommended that a concerted effort be made to investigate the impact of dagga smoking on health in South Africa. Little scientifically based information appears in the lay press regarding the potential health effects of dagga and the level of knowledge of the toxic effects of dagga among health care workers is very low. Clearly the use of dagga is hardly curtailed by the present legislation and it does not appear sufficient to leave this matter in the hands of the law enforcement authorities - there is enough evidence to bring this harmful habit/addiction into the ambit of health care.

The fact that many *food additives* aggravate chronic asthma is well recognised in the medical literature. In South Africa relatively few studies have been done; the most important additive is the preservative sulphur dioxide which is commonly used in fruit drinks and a wide variety of other preserved foods and drinks. The general impact of food preservatives on the health of South Africans has not been studied. However, it has been shown that 43% of asthmatic children had significant episodes of bronchospasm in response to drinking apple juice containing sodium metabisulphite. Considering that approximately 5% of the general population have asthma, the impact of sulphites on the nation as a whole could be substantial. An active lobby (the Allergy Society of South Africa) has succeeded in having legislation gazetted to the effect that food labelling should commence. It is recommended that research into specific questions around food labelling should be supported in order to enhance the effectiveness and appropriateness of food labelling.

The impact of environmental *air pollution* on aggravating or causing chronic lung disease has

undergone a surge of active investigation (both South African and abroad) in the past 5 years. The impact of outdoor air pollution on health (particularly schoolchildren) as shown by the South African studies has been relatively slight. The more important question of indoor air pollution in South Africa is currently being studied. Preliminary results would suggest that the type of fuel used in South African homes could be a risk factor for certain respiratory symptoms in urban coloured children. However, there is still a dearth of information regarding prevailing pollution levels and respiratory illness rates in the black urban townships. A number of recent papers from the USA have strongly pointed to the importance of respirable particulates from indoor fuel sources in causing or aggravating chronic respiratory diseases and, more importantly, resulting in a significantly higher incidence of death, particularly among the elderly. It is recommended that investigations on the impact of indoor fuel source on respiratory disease and death in South Africa be urgently investigated. This is a health priority which relates closely to socio-economic factors, particularly as manifested by primary fuel source. Such investigations would equip health policy-makers and health economists to make informed strategic decisions in terms of preventing illness.

ACKNOWLEDGEMENTS

The author is indebted to the Deans of all Medical Faculties and the Heads of Department for providing lists of publications; similarly the CSIR, HSRC, the South African Pulmonology Society and the Allergy Society of South Africa who were very helpful. Ms Cornelia Stander gave valuable assistance in the literature search, obtaining documents, theses and other publications from institutions throughout South Africa; I am grateful to Ms Sue Botha who tirelessly typed the manuscript.

REFERENCES

1. Seaton A, Seaton D, Leitch AG. *Chronic bronchitis and emphysema.* Chapter 19. In: Crofton and Douglas's Respiratory Diseases. Oxford: Blackwell Scientific Publications, 1989.
2. Snider GL, Kleinerman J, Thurbeck WM, Bengalie ZH. The Definition of Asthma. Report of a National Heart, Lung and Blood Institute, Division of Lung Diseases Workshop. *Am Rev Respir Dis* 1986;**132**:182.
3. Department of National Health and Population Development. *Health Trends in South Africa.* Pretoria: Government Printer, 1992:56-58.
4. Steyn K, Fourie J, Bradshaw D. The impact of chronic diseases of lifestyle and their major risk factors on mortality in South Africa. *SAMJ* 1992;**82**:227-231.
5. Bradshaw D, Dorrington RE, Sitas F. The level of mortality in South African in 1985 - what does it tell us about health? *SAMJ* 1992;**82**:237-240.
6. Wyndham CH. The loss from premature deaths of economically active manpower in the various populations of the RSA. Part I. Leading causes of death: health strategies for reducing mortality. *SAMJ* 1981;**60**:411-419.
7. Wyndham CH. Deaths from destructive lifestyles (largely preventable) among economically active Whites in South Africa, 1968 - 1977. *SAMJ* 1982;**62**:1017-1026.
8. Wyndham CH. Deaths from and mortality rates for largely preventable causes of death in whites in the RSA. Comparison of the situations in 1970 and 1980. *SAMJ* 1985;**67**:975-976.
9. Epstein L, Sayed AR, Bourne DE, Benatar SR. Variations in mortality of the coloured, white and Asian population groups in the RSA, 1978 - 1982. Part IV. Respiratory diseases. *SAMJ* 1987;**72**:559-563.
10. Wyndham CH, Irwig LM. A comparison of the mortality rates of various population groups in the Republic of South Africa. *SAMJ* 1979;**55**:796-802.
11. Van der Burgh C. Smoking behaviour of White, Black, Coloured and Indian South Africans. Some statistical data on a major public health hazard. *SAMJ* 1979;**55**:975-978.
12. Steyn K, Jooste PL, Langenhoven ML, *et al.* Smoking patterns in the coloured population of the Cape Peninsula (CRISIC study). *SAMJ* 1987;**71**:145-148.
13. Coetzee AM. Rook en gesondheid - feite en statistiek (Letter). *SAMJ* 1978;**54**:425-426.
14. McIntyre DE, Taylor SP. Economic aspects of smoking in South Africa. *SAMJ* 1989;**75**:432-435.
15. Mayet FGH. Lifestyle and disease. Disease patterns in Indian South Africans. *SAMJ* 1982;**61**:968-972.
16. Benatar SR, Saven A. Morbidity trends in the medical wards at Groote Schuur Hospital - 1971 and 1982. *SAMJ* 1985;**67**:968-974.
17. Reeve PA, Falkner MJ. Disease patterns in a rural black population. *SAMJ* 1986;**69**:551-552.
18. Bloom B, Bourne D, Sayed AR, Klopper JML. Morbidity patterns from general practice in Cape Town. A pilot study. *SAMJ* 1988;**73**:166-168.

19. Reilly WK. Special Report. Respiratory health effects of passive smoking: lung cancer and other disorders. *Tobacco Control* 1993;2:71-79.
20. Van Antwerpen L, Theron AJ, Myer MS, *et al.* Cigarette smoke-mediated oxidant stress, phagocytes, vitamin C, vitamin E, and tissue injury. *Ann NY Acad Sci* 1993;**686**:53-65.
21. Richards GA, Theron AJ, van Rensburg CEJ, *et al.* Investigation of the effects of oral administration of vitamin E and beta-carotene on the chemiluminescence responses and the frequency of sister chromatid exchanges in circulating leukocytes from cigarette smokers. *Am Rev Respir Dis* 1990;**142**:648-654.
22. Van Antwerpen L, Theron AJ, Myer MS, *et al.* Cigarette-smoke mediated oxidant stress, phagocytes, vitamin C, vitamin E and tissue injury. South African Pulmonary Society Congress. Oral Abstract No 24, 1993:15.
23. Theron AJ, Richards GA, van Rensburg AJ, van der Merwe CA, Anderson R. Investigations of the role of phagocytes and anti-oxidant nutrients in oxidant stress mediated by cigarette smoke. *Internat J Vit Nutr Res* 1990;**60**:261-266.
24. Anderson R, Theron AJ, Richards GA, Myer MS, van Rensburg AJ. Passive smoking by humans sensitizes circulating neutrophils. *Am Rev Respir Dis* 1991;**144**:570-574.
25. Richards GA, Theron AJ, van der Merwe CA, Anderson R. Spirometric abnormalities in young smokers correlate with increased chemiluminescence responses of activated blood phagocytes. *Am Rev Respir Dis* 1989;**139**:181-187.
26. Anderson R, Theron AJ, Ras GJ. Regulation by the antioxidants ascorbate, cysteine, and dapsone of the increased extracellular and intracellular generation of reactive oxidants by activated phagocytes from cigarette smokers. *Am Rev Respir Dis* 1987;**135**:1027-1032.
27. Anderson R, Theron AJ, Ras GJ. Ascorbic acid neutralizes reactive oxidants released by hyperactive phagocytes from cigarette smokers. *Lung* 1988;**166**:149-159.
28. Anderson A. Assessment of the roles of vitamin C, vitamin E, and ß-carotene in the modulation of oxidant stress mediated by cigarette smoke-activated phagocytes1-3. *Am J Clin Nutr* 1991;**53**:358S-61S.
29. Anderson R. The role of phagocytes in oxidant stress mediated by tobacco smoke. *BJCP* 1990;**44 (2)**:45-47.
30. Maritz GS. Maternal nicotine exposure and carbohydrate metabolism of fetal and neonatal lung tissue: response to nicotine withdrawal. *Respiration* 1987;**51**:232-240.
31. Maritz GS, Woolward KM, Du Toit G. Maternal nicotine exposure during pregnancy and development of emphysema-like damage in the offspring. *SAMJ* 1993;**83**:195-199.
32. Maritz GS, Burger B. The influence of maternal nicotine exposure on neonatal lung carbohydrate metabolism. *Cell Biology International Reports* 1992;**16 (12)**:1229-1236.
33. Maritz GS. Effect of maternal nicotine exposure on growth in vivo of lung tissue of neonatal rats. *Biol Neonate* 1988;**53**:163-170.
34. Maritz GS, Woolward K. The effect of maternal nicotine exposure on neonatal lung development: a morphological study. *S Afr J Sci* 1990;**86**:537.
35. Maritz GS, Woolward K. Effect of maternal nicotine exposure on neonatal lung elastic tissue and possible consequences. *SAMJ* 1992;**81**:517-519.
36. Prout S, Benatar SR. Smoking in White high-school children in Cape Town. *SAMJ* 1983;**63**:483-486.
37. Coetzee AM. Die rookgewoonte by en gesondheid van dokters wat aan die Universiteit van Pretoria gegradueer het. 'n Voorlopige verslag. *SAMJ* 1981;**60**:31-34.
38. Wicht CL, Kotze TJvW. Die invloed van die rookgewoonte op die simptome van die diffuse obstruktiewe pulmonale sindroom. *SAMJ* 1981;**60**:26-30.
39. Wicht CL, de Kock MA, Kotze TJvW, *et al.* An epidemiological study of the diffuse obstructive pulmonary syndrome. *SAMJ* 1977;**Suppl 24 December**:1-15.
40. Sluis-Cremer GK, Harrison WO, Pearson RCT. Respiratory symptoms and lung function in black and white mining and non-mining industrial workers in South Africa. *SAMJ* 1981;**59**:672-675.
41. Yach D, Joubert G. Deaths related to smoking in South Africa in 1984 and projected deaths among coloureds and blacks in the year 2000. *SAMJ* 1988;**73**:400-402.
42. Fletcher C, Peto R. The natural history of chronic airflow obstruction. *BMJ* 1977;**1**:1645.
43. Ehrlich RI. Parental smoking and childhood asthma. Editorial. *SAMJ* 1992;**81**:443-444.
44. Joubert JR, Brink S, Hentzen GM. Allergic asthma in different population groups in the western Cape. Causative and complicating factors. *SAMJ* 1988;**73**:150-154.
45. Benatar SR. Smoking and chronic respiratory symptoms in 11 - 15 year old children. *SAMJ* 1979;**56**:301-304.
46. Vermeulen J. Airway hyperresponsiveness. *Respiratory Focus* 1990;**2**:6-8.
47. Van Niekerk CH, Weinberg EG, Shore SC, *et al.* Prevalence of asthma: a comparative study of urban and rural Xhosa children. *Clinical Allergy* 1979;**9**:319-324.
48. Luyt DK, Davis G, Wilson WE. Baragwanath Hospital Childrens' Asthma Clinic: a synopsis. Poster Abstract No 37.
49. Benatar SR, Ainslie GM. Deaths from asthma in Cape Town, 1980 - 1982. *SAMJ* 1986;**69**:669-671.
50. Seaton A, Seaton D, Leitch AG. *Asthma.* Chapter 26. In: Crofton and Douglas's Respiratory Diseases. Fourth Edition. London: Blackwell Scientific Publications, 1984.
51. Simon AM. A study of drug abuse in a group of South African university students. *SAMJ* 1982;**61**:666-668.
52. Herr P, Morley JE. Drug use patterns among South African undergraduates. *SAMJ* 1972;**46**:1404-1406.
53. Levin SM, Berman C, Cobb H, McIlraith J. Dagga (cannabis) usage among medical students in Johannesburg. *SAMJ* 1983;**63**:607-609.
54. Levin SM. Dagga use amongst University of the Witwatersrand medical students - the first longitudinal study. In: Proceedings South African Conference on Dagga. Durban: University of Natal, Sept 1983:27-30.
55. Disler SA, Epstein LM, Disler PB, Rip MR, Klopper JM, Kibel MA. Lifestyles of adolescents. A study in a Cape Town High School. II. Use of alcohol and habit-forming drugs. *Community Health in South Africa* 1989;**4**:8-12.
56. Flisher AJ, Ziervogel CF, Chalton DO, Leger PH, Robertson BA. Risk-taking behaviour of Cape Peninsula high-school students. Part V. Drug use. *SAMJ* 1993;**83**:483-485.
57. Tashkin DP, Coulson AH, Clark VA, *et al.* Respiratory symptoms and lung function in habitual heavy smokers of marijuana alone, smokers of marijuana and tobacco, smokers of tobacco alone, and nonsmokers. *Am Rev Respir Dis* 1987;**135**:209-216.
58. Gong H, Fligiel S, Tashkin DP, Barbers RG. Tracheobronchial changes in habitual, heavy smokers of marijuana with and without tobacco. *Am Rev Respir Dis* 1987;**136**:142-149.
59. Wu T-C, Tashkin DP, Djahed B, Rose JE. Pulmonary hazards of smoking marijuana as compared with tobacco. *N Engl J Med* 1988;**318**:347-351.
60. Steinman H. Now is the time for mandatory food labelling. *Current Allergy* 1992;**5**:11-12.
61. Hromic AA. ALLSA food allergy and intolerance workshop. Report. *Current Allergy* 1993;**6**:14-23.
62. Borok G, Loots JM, Daehne HO, Schultz CM. Exercise induced asthma: without food and inhalants exercise may not induce asthma. Abstract. South African Pulmonology Society, 1990.
63. Steinman HA, Weinberg EG. The effects of soft-drink preservatives on asthmatic children. *SAMJ* 1986;**70**:404-406.

64. Steinman HA, Le Roux M, Potter PC. Sulphur dioxide sensitivity in South African asthmatic children. *SAMJ* 1993;**83**:387-390.
65. Taylor SL, Bush RK, Selner JC, *et al*. Sensitivity to sulfite and foods among sulphite-sensitive subjects with asthma. *J Allergy Clin Immunol* 1988;**81**:1159-1167.
66. Bush RK, Taylor SL, Busse W. A critical evaluation of clinical trials in reaction to sulfites. *J Allergy Clin Immunol* 1986;**78**:191-202.
67. Stevenson DD, Simon RA. Sensitivity to ingested metabisulfites in asthma subjects. *J Allergy Clin Immunol* 1981;**68**:26-32.
68. Friedman ME, Easton JG. Prevalence of positive metabisulfite challenges in children with asthma. *Pediatr Asthma Allergy Immunol* 1987;1:53.
69. Speizer FE. *Environmental lung disease.* In: Petersdorf RG, Adams RD, Braunwald E, Esselbacher KJ, Martin JB, Wilson JD, eds. Harrison's Principles of Internal Medicine. 10th ed. New York: McGraw-Hill 1983, 1521-1532.
70. Zwi S, Davies JCA, Becklake MR, Goldman HI, Reinach SG, Kallenbach JM. Respiratory health status of children in the eastern Transvaal highveld. *SAMJ* 1990;**78**:647-653.
71. Florey CdV, Swan HV, Van der Lende R, *et al*, eds. Report on the EC Epidemiological Survey on the relationship between air pollution and health in primary school children. Brussels: European Community, 1983.
72. Terblanche AP, Opperman L, Nel CME. Vaal Triangle air pollution health study: design and preliminary results. In: Proc of Symposium on Air Pollution and the Environment, Vol 2. Durban: November 1991.
74. Truter R, Terblanche APS, Ijsselmuiden CB, Kocks DJ. Monitoring indoor air pollution in homes: a protocol for the Vaal Triangle air pollution health study. In: Proc of Symposium on Air Pollution and the Environment, Vol 1. Durban: November 1991.
75. Von Schirnding YER. Environmental determinants of acute respiratory symptoms and diarrhoea in coloured children living in urban and peri-urban areas in South Africa. *SAMJ* 1991;**79**:457-461.
76. Von Schirnding YER, Aucamp PJ. Urbanisation and environmental health. Editorial. *SAMJ* 1991;**79**:414-415.
77. Coetzee AM, Smith FCA, van der Merwe CA, Dreyer RJ. Die invloed van lugbesoedeling op gesondheid in the Sasolburg-gebied. *SAMJ* 1986;**70**:339-343.
78. Klopper J, Bourne D, Harrison JA, Rip MR. A study of possible health effects associated with air pollution in the greater Cape Town area. *Community Health in South Africa* 1988;**3(4)**:2-4.
79. Truluck TF. Hospital admission patterns of childhood respiratory illness in Cape Town and their association with air pollution and meteorological factors. MA Thesis, Department of Environmental and Geographical Science, UCT, April 1993.
80. Terblanche APS, Murray PWLeR, Fourie PB. Evaluation of the potential for Epidemiological study of Radon Exposure in South Africa. (Report to the Foundation for Research Development, CSIR). May 1989.
81. Terblanche APS. Potential health effects of air pollution in Witbank. Report to the Environmental Impact Assessment Unit at UCT, July 1990.
82. Terblanche APS. Health effects of motor vehicle emissions. Report to the Residents of Knysna, December 1990.
83. Terblanche APS. Report on the 1st International Meeting on Total Exposure Assessment Methodology: A New Horizon, Las Vegas, Nevada. Submitted to the MRC, January 1990.
84. Terblanche APS, Mouton BJ. Gesondheidsgevare van koolstofmonoksied blootstelling. Report to Sperotek, February 1990.
85. Terblanche APS, Nel CME, Opperman C. Health and safety aspects of domestic fuels. Report to the National Energy Council, March 1992.
86. Terblanche APS. National perspective on air pollution: Special reference to the Vaal Triangle, the Cape Peninsula, Edenvale, Secunda and Sharpeville. CSIR Report EMAP-C 92038, 1992.
87. Burger LW, Gertenbach JP, Terblanche P. An assessment of the environmental health and social impact of Sanachem. Phase II: Atmospheric dispersion modelling and air quality monitoring network design. CSIR Report EMAP-C 92032. Report to Sanachem, 1992.
89. Terblanche APS, Ellerbeck R. Evaluation of particulate concentrations and potential health hazards in Sasol's polypropylene plant. CSIR Report EMAP-C 92057, 1992.
90. Danford IR, Terblanche APS, Baunok I, Roos C, Elphinstone C. Comparative evaluation of human exposures to air pollution from low-smoke and conventional household coal usage. CSIR Report EMAP-C 92055, 1992.
91. Terblanche APS, O'Beirne S, Oosthuizen R, Brassel K. Air quality assessment and community respiratory disease survey. Airkem Final Report. CSIR Report EMAP-C 93018, 1993.
92. Terblanche APS. Health impact of three electrification scenarios for urban areas in South Africa. Report to Eskom, TRI, 1993.
93. Terblanche APS, Nel R, Danford I. Health and safety aspects of household fuels Phase II. CSIR report EMAP-C 93017. Report to the Department of Mineral and Energy Affairs, 1993.
94. Terblanche APS, Opperman L, Nel, CME, Reinach SG, Tosen G, Cadman A. Preliminary results of exposure measurements and health effects of the Vaal Triangle Air Pollution Health Study. *SAMJ* 1992;**81**:550-556.
95. Terblanche APS, Uys L, Smit HE. The Vaal Triangle Air Pollution Health Study: Study Design. *S Afr J Epidemiol Infect* 1991;**6(2)**:23-25.
96. National Association for Clean Air, Western Cape. Photochemical smog/brown haze in Cape Town. One Day Seminar: Oude Libertas, Stellenbosch, 12 August 1992.
97. National Association for Clear Air, Western Cape. Air Pollution Update. One Day Seminar: University of Stellenbosch Seminar Centre, Annendale Road, Lynedoch, 25 August 1993.
98. Murray BWLeR, Terblanche APS. Aldehydes in the atmosphere: A review of its adverse effects. (Report to the Department of National Health and Population Development). October 1988.
99. Terblanche APS, Murray PWLeR. Health aspects of diesel emissions. (Reports to the Department of National Health and Population Development). February 1989.
100. Braun-Fahrlander C, Ackerman-Leibrich U, Schwartz J, *et al*. Air pollution and respiratory symptoms in preschool children. *Am Rev Respir Dis* 1992;**145**:42-47.
101. Xu X, Wang L. Association of indoor and outdoor particulate level with chronic respiratory illness. *Am Rev Respir Dis* 1993;**148**:1516-1522.
102. Utell MJ, Samet JM. Environmentally mediated disorders of the respiratory tract. (Review). *Med Clin North Amer* 1990;**74**:291-306.
103. Schwartz J, Dockery DW. Increased mortality in Philadelphia associated with daily air pollution concentrations. *Am Rev Respir Dis* 1992;**145**:600-604.
104. Ostro B. The association of air pollution and mortality; examining the case for inference. (Review). *Arch Environ Hlth* 1993;**48**:336-342.
105. Dockery DW, Pope AC, Xu X, *et al*. An association between air pollution and mortality in six U.S. cities. *New Engl J Med* 1993;**329**:1753-1759. [Comment in: *N Engl J Med* 1994;**330**:1237-1238.]