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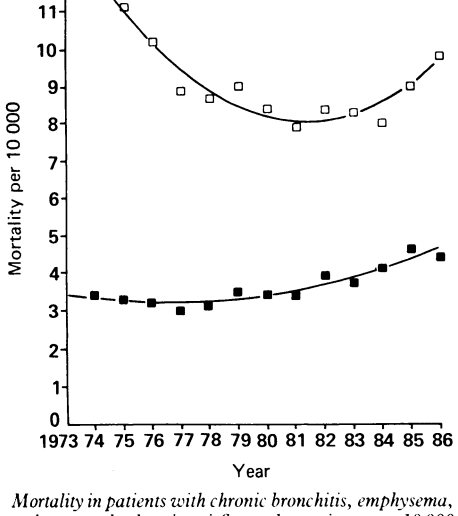
Prevalence and diagnosis of chronic respiratory symptoms

SIR,—Dr Peter Littlejohns and colleagues have reported a reduced prevalence of disability associated with chronic respiratory symptoms among patients in south west London compared with that in 1961.[1] The extent to which prevalence was reduced was, however, fairly small and in women was probably not significant (2·5% compared with 3% in 1961). The analysis did not take into account non-pulmonary causes of disabling breathlessness, including excess weight and "silent" ischaemic heart disease, so that the true prevalence of respiratory disability cannot be deduced from these findings. In conjunction with the national mortality and morbidity statistics Dr Littlejohns and colleagues interpreted the position as improving, but this may be wishful thinking.



Mortality in patients with chronic bronchitis, emphysema, asthma, and chronic airflow obstruction per 10 000 population aged 55-64, 1973-86

Among women aged 55-64 mortality in diseases associated with airflow limitation has increased over the past few years, and there seems to be an upward trend among men (figure). The position has deteriorated since 1981, when a report of the Royal College of Physicians made recommendations for management of what is mainly a preventable condition.[1] Unfortunately, a high proportion of the patients in greatest need do not receive specialist advice, and their treatment commonly leaves much to be desired.[4] In addition, Dr Littlejohn and colleagues' study showed a high proportion of undiagnosed cases.

As a profession we are having only limited success in treating this type of patient; we need to do more to bring such patients to treatment and to curb smoking, which remains the principal cause of their disability.

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Non-ionic versus ionic contrast media

SIR,—Minerva,[1] relying on the work of Eyes and Goldman,[2] asks why any patient undergoing urography should be exposed to the risks of the old method of urography using ionic contrast media.

Eyes and Goldman argue that by using a half dose of non-ionic contrast medium the cost is reduced by a half and the urogram is subjectively acceptable, but their work[4] has been criticised[4] and other authors studying longer series have found no reason to prefer non-ionic media[5]; sodium salts gave a slightly better urogram than non-ionic media.[6] Non-ionic low osmolar media are supposed to be safer than ionic media but this has yet to be established by clinical trial. Indeed one trial has shown a greater number of delayed reactions to iopamidol than to iothalamate (Conray 320).[7]

Low osmolar media are so expensive (even in half doses) that they have been termed "liquid gold"[8] and the cost of saving a life given reasonable assumptions is estimated at £500 000 to £1m,[9] about 10 times the amount the NHS can afford for proved treatments with known effects.[10] The concept of risk factors for predicting reactions to contrast media is seriously flawed as the incidence of important reactions, even in patients with so called risk factors, is extremely low[7] and the relevance of most of them has not been tested in controlled trials. Nevertheless, up to one half of patients have such risk factors.[10]

The answer to Minerva's question is that low osmolar media are very expensive; though they are more comfortable for the patient, it has not been satisfactorily shown that they are safer in clinical use, and a technically better urogram results from using sodium salts of ionic media.

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Guidelines on HIV infection

SIR,—Last year two publications arrived on my doorstep on the same day. The first was a copy of the *BMA Guidelines for Doctors on HIV Infection.* The second was a copy of *New Scientist*, which carried the first report that a gene multiplication technique had identified the HIV genome in the blood of a person who was at risk for the disease 36 months before subsequent seroconversion. The guidelines for doctors were based on the stated assumption that the absence of HIV antibodies three months after an accident to a health worker was a reliable indication that infection had not occurred.

It is particularly unfortunate that Dr Jonathan A Shapiro's article, which aims at encouraging a positive attitude towards AIDS in health workers, should reach me alongside another copy of *New Scientist*, which reports a paper in the *New England Journal of Medicine* confirming that silent infection may persist for an uncertain number of years, certainly for more than four.[2]

The BMA booklet is now clearly misleading and should be withdrawn immediately. It seems probable that HIV infection with a small number of virions in an otherwise healthy person usually leads to silent infection. The results of gene multiplication studies in a representative group of health workers are urgently needed.

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**The secretary writes: "Detection of HIV genetic material by DNA amplification (polymerase chain reaction) was first reported at the Stockholm conference in 1988 after the BMA guidelines had been published. The article in the *New England Journal of Medicine* contains several caveats, though, reporting positive results with the polymerase chain reaction in three men at up to 35 months before seroconversion and isolation of HIV in 27 in whom seroconversion was not observed at 28-36 months of follow up. The subjects were at high risk of sexual exposure to HIV, in contrast to direct inoculation of HIV, which seems to be more likely to lead to defined seroconversion events. Whether isolation of HIV or positive results by the polymerase chain reaction in the absence of seroconversion implies infection with an HIV strain capable of in vivo replication and pathogenesis has yet to be proved. The results cannot provide an estimate of the proportion of HIV infections that do not stimulate measurable antibody.

"Absolute certainty is rarely possible in medicine, and there is no unequivocal test for absence of HIV infection. We do not judge it necessary to modify our guidance at present. Health workers are not a high risk group for AIDS, and in the rare cases when accidental inoculation leads to HIV infection

this will generally be detectable within a few months afterwards by conventional testing for antibody."—ED, *BMJ*.

Sudden infant death syndrome in Hong Kong

SIR,—Dr Millard Bass, commenting on our paper on sudden infant death syndrome in Hong Kong,[1] wrongly asserted that the controls we used were unsuitable.[2]

According to basic epidemiological principles, controls should not have the disease or condition under investigation but should be similar to cases in regard to past potential for exposure. We used one community control and one hospital control for each dead child, and we consider that neither group was subject to selection bias. The controls suggested by Dr Bass included babies dying suddenly of various conditions. Some of these babies may be diagnosed as dying of the sudden infant death syndrome, depending on the diagnostic fashion. Hence one would create the undesirable condition of misclassification—that is, comparing cases with cases. Moreover, the background of such dead babies is likely to be similar to that of babies with the sudden infant death syndrome—that is, overmatching of controls to cases. For example, Dr Bass suggested that poor judgment by the carer was a likely cause of the sudden infant death syndrome. It is quite obvious that hyperthermia or smothering may result from poor judgment by the carer too, and if such controls were used the relation of the risk factor with sudden infant death syndrome would not be discerned.

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Lake Nyos disaster

SIR,—Dr Peter J Baxter and colleagues suggested that carbon dioxide was responsible for most deaths in the Lake Nyos disaster.[1] Though I accept that a large scale release of carbon dioxide occurred, the "killer gas" may have been carbon monoxide.

As long ago as 1895 Haldane showed that considerably less than 1% carbon monoxide in inspired air was sufficient to kill mice.[2] Furthermore, when the oxygen concentration was reduced a carbon monoxide concentration of as little as 0·25% was sufficient to cause coma. Studies of patients rescued from fires or exposed to car exhaust fumes have clearly shown that carbon monoxide can cause coma, convulsions, and death; early skin necrosis over pressure points may be a useful indicator of such exposure.[3] In lower concentrations carbon monoxide can produce symptoms of fatigue, headache, confusion, dizziness, chest pain, nausea, vomiting, abdominal pain, and diarrhoea.[3] These symptoms and signs have many similarities with those reported in the survivors of the Lake Nyos disaster.[1]

Carbon monoxide has an affinity for haemoglobin 300 times that of oxygen.[4] As little as 0·1% in inspired air can produce a carboxyhaemoglobin concentration of 50% in humans—that is, it halves the oxygen carrying capacity of haemoglobin. In addition, carbon monoxide shifts the oxyhaemoglobin dissociation curve to the left, causing any remaining oxygen to be more tightly bound to haemoglobin and so reducing still further the availability of oxygen to the tissues.[4] Percentage carboxyhaemoglobin is determined by (*a*) the fractions of inspired air that are carbon monoxide and oxygen (a high oxygen fraction reduces percentage carboxyhaemoglobin); (*b*) the duration of exposure to carbon monoxide; (*c*) minute ventilation; and (*d*) cardiac output.[6] At the tissues carbon monoxide binds to myoglobin and poisons many of the enzymes responsible for cellular respiration, including cytochrome *c* oxidase.[6] Removal of carbon monoxide from haemoglobin is slow—the time taken to halve the arterial concentration of carboxyhaemoglobin is about five hours; concentrations in the tissue are likely to fall much more slowly.[7] Given these facts, it is easy to see how a small amount of carbon monoxide may produce profound cellular hypoxia and even death.

The disaster examined by Dr Baxter and colleagues could be accounted for by the release of fairly small concentrations of carbon monoxide (<1%) with carbon dioxide; the carbon dioxide would greatly increase the rate of uptake of carbon monoxide into the body by increasing minute ventilation and cardiac output. Carbon dioxide would also reduce the available oxygen concentration by an amount equal to its own concentration. In addition, carbon dioxide would increase oxygen demand by increasing oxygen consumption—all at a time when oxygen delivery to the tissues was reduced by carboxyhaemoglobin. Furthermore, if the inhabitants were also anaemic oxygen delivery would be even further compromised. Severe cellular hypoxia and even death seem probable with this lethal mixture of carbon monoxide and carbon dioxide.

If carbon dioxide were the only killer gas concentrations in excess of 30% would probably have had to have been present, as Dr Baxter and colleagues stated, but this seems unlikely in terms of the scale of carbon dioxide emissions required to account for the disaster. If the increase in carbon dioxide concentration in the local atmosphere is assumed to have been gradual rather than instantaneous circumstantial evidence of extreme agitation before convulsions, coma, and death should have been found as the ventilatory response to carbon dioxide varies with age and not all subjects would have been struck down instantaneously. By contrast, carbon monoxide in combination with small concentrations of carbon dioxide could easily have caused minimal apparent upset to individual subjects or families. As indicated above carbon dioxide would not need to have been a "substantial component" of the gas to have been lethally effective with carbon dioxide.

The forensic studies that were performed several days after the disaster confirmed the release of carbon dioxide in large quantities; they cannot, however, determine the percentage carbon dioxide in the local atmosphere at the time of the disaster or reliably exclude the emission of carbon monoxide in fairly small but clinically important amounts. Carboxyhaemoglobin concentrations were not assayed in survivors: had high concentrations been found, this might have supported the hypothesis of carbon monoxide poisoning with inhalation of carbon dioxide. Unfortunately, if carbon monoxide poisoning did occur neuropsychiatric sequelae may occur in up to 40% of survivors.[8]

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AUTHORS' REPLY,—As we explained in our paper there are two competing theories to account for the Lake Nyos disaster. According to the limnological theory, large amounts of gas stored under pressure in the lower layers of the lake were suddenly released by an overturning of the water or by some other mechanism. Alternatively, the gas cloud was emitted from a volcanic eruption beneath the lake.

The limnological explanation is the one favoured by most experts, but in this there is seemingly no role for carbon monoxide, which was not detectable in samples of lake water. Thus if this theory turns out to be correct the medical findings will probably have to be explained by the presence of carbon dioxide alone. However, if the cloud of carbon dioxide had been erupted then we agree with Dr Lanigan that carbon monoxide could also have been present but other gases such as hydrogen sulphide, which is also lethal in low concentrations, are likely to have been components as well.

Carboxyhaemoglobin levels were measured in necropsy material from two victims who had died two days after admission to hospital and six days after the gas release and in one exhumed victim, but these were not raised.[1] Dr Lanigan has already referred to the short half life of carboxyhaemoglobin, and we do not consider that these sparse negative findings rule out carbon monoxide. We are, however, reluctant to speculate further on the role of carbon monoxide in the absence of evidence for its presence.

An important lesson was relearnt at Lake Nyos—namely, that urgent investigations by medical scientists are an indispensable part of the emergency response to any major toxic incident, including volcanic eruptions. If performed in time, detailed necropsy and toxicological studies could have been crucial in showing which of the competing theories was correct or at least have shed more light on volcanic processes. The issue is of more than academic importance as the limnological theory offers the prospect of monitoring suspect lakes for the build up of carbon dioxide whereas eruptions are inherently unpredictable; the future safety of populations by other lakes in Cameroon, as well as settlers in the Lake Nyos area, might therefore depend on its resolution.

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1 Kling GW, Clark MA, Compton HR, *et al*. The 1986 Lake Nyos gas disaster in Cameroon, West Africa. *Science* 1987;**236**: 169-75.

Monitoring resuscitation

SIR,—I would like to reinforce the comments made by Mr David Skinner in his excellent editorial.[1] We have recently studied the relation between blood pressure as measured by an occlusive cuff over a limb and by an indwelling arterial catheter in patients immediately after cardiac arrest.[2] There is very little correlation between cuff blood pressure and true mean arterial pressure at this time. Five out of 15 patients had an "unrecordable" blood pressure yet the mean arterial pressure ranged from 58 to 89 mm Hg (mean 72 mm Hg).

It is known that a rise in peripheral vascular resistance in the presence of a low cardiac output will make Korotkoff sounds inaudible even when