A STUDY OF THE ARTERIAL CLEARANCE OF XENON 133 IN MAN

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SUMMARY

Arterial xenon 133 concentrations have been measured after inhalation of the isotope in anaesthetized and conscious human patients. The anaesthetized patients were ventilated by either a mechanical or a manual method. The arterial concentration of xenon 133 was compared with the pulmonary radioactivity measured by external scintillation counting during clearance of the gas. The rates of arterial clearance of xenon 133 were expressed as the length of time taken to fall to 10 per cent of the original level of radioactivity. In the control group this value was 3.5 minutes. Pulmonary external scintillation counting did not reflect the concentration of arterial xenon 133 accurately. The significance of these findings was discussed with particular reference to the determination of cerebral blood flow.

Radioactive isotopes of the inert gases krypton and xenon are being increasingly used to measure regional blood flow in man. So far, however, few basic observations on the distribution and elimination of these gases have been made following their administration to human subjects.

In the present study the gamma-emitting isotope of xenon (xenon 133 half-life=5.2 days) is used to elucidate the pattern of behaviour of the arterial concentrations of this gas after its inhalation.

METHODS

The majority of the observations were made on anaesthetized patients during abdominal operations. More recently the work was extended to include conscious patients awaiting operation.

In the anaesthetized patient 1 mc of xenon 133 was introduced into a closed anaesthetic circuit of 1.5 l. cubic capacity. The patient breathed a mixture of anaesthetic (halothane in oxygen) and xenon 133 for 6 minutes, after which time the circuit was opened and the patient cleared the xenon 133.

In the conscious patients a similar type of circuit was used; a xenon 133-air mixture was substituted, but in all other respects the technique remained the same.

During the last 2 minutes of the uptake phase and the first 6 minutes of the clearance phase, measurements of the arterial concentration of xenon 133 were made. Arterial samples were withdrawn from the brachial artery at half-minute intervals into heparinized syringes. These were sealed immediately. Each sample was transferred to a constant-volume cuvette by a closed technique and counted in a well-type scintillation counter (Ekco N664A). This was connected to an automatic scaling unit (Ekco N530F). Under these conditions the background count rates were of the order of 5 c.p.s. and the count rates from the samples collected at the beginning of clearance were of the order of 500 c.p.s.

The arterial concentrations of xenon 133 were expressed as percentages of the activity reached at the end of the uptake phase.

In five of the patients in the anaesthetized group, concurrent with arterial sampling, the rate of fall of pulmonary radioactivity was measured by a directional scintillation counter (Labgear Type D 4133) positioned anteriorly over the right upper lobe. Count rates of the order of 1000 c.p.s. were recorded over the lung at the beginning of clearance.

In two conscious patients the experiment was repeated to assess the effect of breathing a 5 per cent carbon dioxide mixture on the arterial clearance of xenon 133. This mixture was breathed for the last 2 minutes of the uptake phase and the first 4 minutes of the clearance phase, and the arterial samples were collected as previously described.

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Finally, three conscious patients were given a rapid intravenous injection of 1 mc of xenon 133 dissolved in 20 ml of normal saline. Count rates were recorded over the parietal region of the skull by a directional scintillation counter (Labgear Type D 4133). These were of the order of 80 c.p.s.

The integrated body dosage of radioactivity during these procedures was calculated to be less than 0.32 millirads (Gilbert, personal communication, 1963).

**RESULTS**

Twenty anaesthetized subjects were investigated but, owing to technical difficulties in collection of the blood samples, the results were discarded in three of these. The results from the seventeen subjects in whom satisfactory samples were obtained were divided into three groups.

In one group of six patients the lungs were manually ventilated by the anaesthetist, and in the second group of six patients the lungs were mechanically ventilated by a Blease Pulmoflator. The results of these two groups are shown in figures 1 and 2 respectively. It is seen that in both of these groups the rate of arterial clearance of xenon 133 is relatively slow; in the manually ventilated group there is a larger standard deviation and a slower rate of arterial clearance of xenon 133 than in the mechanically ventilated group. In the latter group the concentration of xenon 133 takes 3.5 minutes to fall to 10 per cent of its original value (90 per cent clearance) whilst in the former group this level is not reached within 5 minutes.

The third group of five patients were those in whom arterial sampling and external pulmonary counting were undertaken simultaneously, and these subjects were manually respired. The results are shown in figure 3 and it is apparent that although neither curve reaches 90 per cent clearance in under 5 minutes the initial fall in pulmonary radioactivity is greater than the initial fall in arterial radioactivity due to xenon 133 and after 2 minutes clearance the curves appear to become parallel.

In three conscious patients with normal respiratory function the pattern of arterial clearance of xenon 133 is very similar to that found in the anaesthetized and mechanically ventilated group (fig. 4). The effect of 5 per cent carbon dioxide in these patients is to increase the rate of fall of the arterial concentration of xenon 133 so
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The mean rate of fall of arterial and pulmonary radioactivity at minute intervals from the onset of clearance in five manually ventilated anaesthetized patients. The standard deviations of each mean are represented by the vertical lines.

FIG. 3

The mean rates of arterial clearance in conscious and anaesthetized patients at minute intervals from the onset of clearance.

1 = Chronic bronchitic
2 = Manually ventilated
3 = Normal
4 = Mechanically ventilated
5 = General anaesthesia

FIG. 5

A ratemeter tracing from a cerebral external scintillation counter following intravenous injection of xenon 133. Trace reads from right to left and arrow indicates time of injection. Horizontal scale: Time in minutes. Vertical scale: c.p.s.

that 90 per cent clearance is reached in 2 minutes compared with the control determination of 3.5 minutes.

An arterial clearance curve for xenon 133 obtained from a conscious patient with severe bronchopulmonary disease (VC=0.7 l.; FEV₁ = 0.35 l.) is shown to approximate closely to that obtained in the manually ventilated group under general anaesthesia (fig. 4). Ninety per cent arterial clearance is reached in 5 minutes, and breathing a 5 per cent carbon dioxide mixture does not alter this rate.

The cerebral count rates of those patients who were given an intravenous injection of 1 mc of xenon 133 rise to from forty to sixty times the background activity. This level is reached rapidly and takes more than 8 minutes to return to background levels (fig. 5).

DISCUSSION

It has been stated previously that "xenon is almost completely cleared from the bloodstream in a single passage through the pulmonary circu-
lation so that during the clearance phase it is possible to neglect the arterial concentration" (Veall and Vetter, 1958). This statement was based on work in dogs in which the arterial concentrations of xenon 133 were estimated after inhalation of the gas (Pittinger et al., 1956). These authors stated that "something of the order of 95 per cent of the xenon . . . present in the pulmonary capillary blood was excreted in one passage" through the lungs. They also demonstrated that when a xenon 133-oxygen mixture was breathed for several minutes there was a high arterial concentration of xenon 133 during the early part of the clearance phase and this concentration took at least 2 minutes to fall to 10 per cent of its original value.

In the present investigation a similar pattern of clearance was demonstrated in man although the rate of arterial clearance was slightly slower. It is suggested that the explanation of these apparently conflicting observations is that after xenon 133 has been administered by inhalation over several minutes, the tissues of the body act as a reservoir for the xenon 133 and thus, even with a high pulmonary efficiency for a single "bolus" of xenon 133, significant arterial levels will remain for some time after clearance has commenced.

Pulmonary clearance of xenon 133 has not been measured directly in the present study, but the high count rates recorded over the head after intravenous injection of the isotope suggests that pulmonary efficiency for this gas may not be as high as the 95 per cent reported in dogs. Tobias and colleagues (1949) investigated the rate of xenon 133 exchange in the human hand and found that it was slower than the rate predicted from solubility considerations alone. It is possible that the size of the xenon molecule itself may be responsible for both of these findings since according to Graham's law the rate of diffusion of a noble gas varies inversely with the square root of its molecular weight.

The difference between the arterial clearance rates in the manually and mechanically respired groups of patients and the similarity between the rates of clearance in this latter group and the conscious patients suggested that manual artificial ventilation was a poor substitute for normal spontaneous respiration.

Carbon dioxide was found to increase the rate of clearance of arterial xenon 133 in normal conscious patients; however, this effect was not demonstrated in the patient with severe bronchopulmonary disease, in whom gaseous exchange was already proceeding at its maximum rate.

Xenon 133 was first used in the measurement of cerebral blood flow by Conn (1955). He stated that the rate of loss of such a gas from the brain was dependent upon blood flow when arterial influx of the gas was negligible. No blood sampling was necessary since the passage of inert gas through the tissue could be followed by external (gamma) counting. In evaluating a method of this nature the history of the arterial concentration of the tracer must be examined (Sokoloff, 1961).

The present study measured arterial concentrations of xenon 133 after the gas had been administered in the manner described previously for the determination of cerebral blood flow in man (Schofield, Isbister and Torrance, 1963; Mallet and Veall, 1963) and throws considerable doubt upon the assumption that there is an insignificant amount of xenon 133 present in arterial blood during cerebral clearance.

If the extracranially recorded xenon 133 clearance curve of brain is analyzed by the method of resolving it into two components (Mallet and Veall, 1963), the high initial arterial concentration of xenon 133 must contribute to the fast component and thus invalidate any absolute value obtained for cerebral blood flow, unless some correction can be made.

It has been suggested that external pulmonary counting may be of use to monitor the arterial concentration of xenon 133 (Veall, personal communication, 1962), but our experimental findings do not substantiate this. Theoretically, it is impossible for an externally recorded "pulmonary" clearance curve to represent the rate of arterial clearance. The "pulmonary" radioactivity measured under these conditions represents the sum of the concentrations of xenon 133 in the chest wall, the alveolar gas, the pulmonary vascular bed and the bronchial tree, and since these systems do not clear at the same rates a composite clearance curve must be produced.

Although it may be possible to apply a correction for the arterial recirculation of xenon 133 dur-
ing the measurement of organ blood flow it is difficult to conceive of any method short of direct arterial sampling that would be satisfactory. If, however, the rate of pulmonary ventilation and therefore pulmonary efficiency for xenon 133 clearance remains unaltered during a series of observations on the same patient, it may be justifiable to ignore arterial recirculation in the analysis of externally recorded xenon 133 clearance curves for qualitative and comparative estimates of organ blood flow.

CONCLUSION
Arterial clearance of xenon 133 is slow and incomplete after a single pulmonary circulation. Arterial recirculation of the gas is, therefore, significant and unless a correction is made for this the xenon 133 clearance technique cannot be used in a quantitative study of organ blood flow.

ACKNOWLEDGMENT
We would like to express our gratitude to the Geigy Pharmaceutical Company who provided a research scholarship for one of us (W.H.I.), and to the Board of Governors of the United Manchester Hospitals for a research grant for another of us (P.F.S.).

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