INHALATION OF BLOOD, SALIVA, AND ALCOHOL : CONSEQUENCES, MECHANISM, AND TREATMENT

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The inhalation of body fluids as a main or contributory cause of morbidity and death has been recognized in only a few conditions.

The aspiration of saliva and gastric content was found to be the cause of death in 92 out of 11,000 patients submitted to general anaesthesia (Edwards, Morton, Pask, and Wylie, 1956). Delayed gastric emptying during parturition was suggested to account for the relative frequency with which aspiration of vomitus contributes to maternal death (Mendelson, 1946 ; Parker, 1954). Half the mortality rate in severe head injuries is said to be due to inhalation of saliva, vomitus, blood, and cerebrospinal fluid (Maciver, Frew, and Matheson, 1958 ; Zündel, 1961). The respiratory distress syndrome of the newborn (at present the main cause of perinatal mortality) is regarded by some (Barnett, 1959) as a consequence of amniotic fluid inhalation. Severe haemoptysis may occasionally result in respiratory failure (Brown, Nour-Eldin, and Wilkinson, 1960). A lack of response to 100% oxygen breathing is a common and ill-understood feature in these severely cyanotic patients.

There is some indication that the real frequency of body fluid inhalation may be much higher than is generally recognized. In the absence of specific clinical signs suggestive of fluid inhalation the diagnosis is based on post-mortem findings. However, unless the fluid inhaled was excessive in volume, irritative to the tissues, or a carrier of particulate (or coagulable) material it is rapidly absorbed, leaving no structural changes behind. Pathologists therefore find it difficult to substantiate the clinical claim and feel justified in arguing that the inhaled fluid, provided that there was such, had been disposed of before death and could hardly have made a major contribution to the ultimate outcome.

Inhaled water is absorbed within minutes across the huge alveolo-capillary surface (Courtice and Phipps, 1946 ; Halmagyi, 1961), but the physiological alterations, which have been found to be independent of the amount inhaled, remain unchanged for some time (Halmagyi and Colebatch, 1961 ; Colebatch and Halmagyi, 1961a). The finding that the pulmonary response to inhaled water is predominantly reflex in nature (Colebatch and Halmagyi, 1961b) has resolved these apparent contradictions.

The absorption from the lung of isotonic solutions or of fluids containing protein is slower than that of water (Courtice and Phipps, 1946 ; Courtice and Simmonds, 1949 ; Halmagyi, 1961). The aspiration of alcohol is reported to have produced microscopical damage in the lungs (Moran and Hellstrom, 1957), but inhaled water did not. It seemed therefore of interest to determine if inhaled fluids other than water would have similar effects and if the implications for treatment arising out of the studies on water inhalation have a similar application.

EXPERIMENTAL DESIGN

Cardiac output, systemic and pulmonary arterial pressure and resistance, venous admixture, ventilation, lung compliance, mean frictional resistance, and elastic work of breathing were measured in lightly anaesthetized sheep before and five minutes after the intratracheal administration of 1 ml./kg. blood, saliva, physiological saline, and dilute alcohol. Subsequently the lungs were inflated and lung compliance was repeatedly measured. The effect of the administration of atropine and of isoproterenol was also studied in some animals.

METHODS

Sixteen sheep weighing 31 to 44 kg. were used in these experiments. The supine animals were anaesthetized with thiopentone, heparinized, and

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intubated. A cardiac catheter was passed via the femoral vein into the pulmonary artery, a cannula was introduced into the femoral artery, and intrapleural pressure was taken via a needle introduced into the third or fourth interspace.

Pressures were measured with Sanborn transducers and recorded on a Sanborn multi-channel direct-writing oscillograph. Intravascular pressures were expressed in mm. Hg and intrapleural pressure in cm. H₂O relative to atmosphere.

Oxygen saturation and haemoglobin content of the arterial and mixed venous blood were measured spectrophotometrically. Oxygen uptake and ventilation were measured with a twin spirometer ("Pulmotest," Godart) while the animal was breathing air. Air flow rate and tidal volume for the lung mechanics measurements were obtained with a Godart pneumotachometer and integrator.

Blood flows, ventilated volumes, and resistances were expressed on the basis of 1 m.² body surface area (B.S.A.). Lung compliance was expressed in ml./cm. H₂O/kg., elastic work of breathing in kg.-m./min./10⁻², and mean frictional resistance in cm. H₂O/l./sec.

Details of our techniques are described elsewhere (Halmagyi and Colebatch, 1961; Colebatch and Halmagyi, 1961a).

Statistical methods were used as recommended by Snedecor (1956).

PROCEDURE.—After a control period a thin polyethylene catheter attached to a syringe was passed just beyond the distal end of the endotracheal tube.

The following fluids, 1 ml./kg., were injected intratracheally at a rapid rate: own heparinized blood (five sheep); own saliva (five sheep); a mixture consisting of three parts of saliva and one part of absolute alcohol (three sheep); and isotonic saline (three sheep).

Pressures were recorded continuously; measurements were repeated five minutes after the fluid aspiration. All animals were then subjected to lung inflation with a pressure of 30 mm. Hg followed by repeated determinations of lung compliance.

Different types of treatment were then given in 10 out of 16 sheep (three blood, five saliva, and two alcohol). The animals were first given 0.2 to 0.3 mg./kg. atropine sulphate intravenously and the measurements were repeated after lung inflation. In five of these animals this régime was followed by the administration of isoproterenol hydrochloride. In two sheep this substance (Isuprel, Winthrop) was injected as a continuous intravenous infusion (0.33 µg./kg./min.), the lungs were inflated, and measurements repeated while the infusion was in progress. The infusion was then discontinued and the measurements were repeated 10 minutes later. Three animals were subjected to a five-minute period of 1% Neopline (Burroughs Wellcome) inhalation. The aerosol was administered with a Mark 8 Bird respirator using an inflating pressure of 20 cm. H₂O

and four to six inspirations at a pressure of 40 cm. H₂O. After this period the measurements were repeated.

In one animal fluid inhalation was followed by a constant intravenous infusion of 0.4 µg./kg./min. adrenaline; in one other the injection of atropine preceded the inhalation of alcohol; in a further animal the inhalation of alcohol was followed by the continuous breathing of 100% oxygen. Blood samples were taken after 12 minutes.

RESULTS

The results are summarized in Table I.

TABLE I
CARDIORESPIRATORY EFFECTS OF THE INHALATION OF BODY FLUIDS IN SHEEP

Fluid inhaled		Blood	Saliva	Alcohol
No. of animals		5	5	2
Cardiac output	B*	3.29	2.56	4.41
(l./min./m. ² B.S.A.)	A	3.52	4.06†‡	5.76
Femoral artery mean pressure	B	119	109	102
(mm. Hg)	A	121	116	110
Systemic arterial resistance	B	3.005	3.694	1.860
(dynes-sec.-cm. ⁻⁵ /m. ² B.S.A.)	A	2.924	2.722	1.526
Pulmonary artery mean pressure	B	16	13	14
(mm. Hg)	A	17‡	18	19
Pulmonary artery resistance	B	394	441	256
(dynes-sec.-cm. ⁻⁵ /m. ² B.S.A.)	A	413‡	411‡	270
Arterial oxygen saturation (%)	B	80.6	92.8	88.4
	A	62.1†	69.7†	53.9
Venous admixture (% of cardiac output)	B	35	7	20
	A	54†	42†	64
Ventilation	B	10.2	9.7	8.5
(l./min./m. ² B.S.A.)	A	13.9	15.9†	10.8
Tidal volume	B	254	235	265
(ml./m. ² B.S.A.)	A	275	316†	224
Rate of breathing (min.)	B	41	36	32
	A	49	45	71
Mean frictional resistance (cm. H ₂ O/l./sec.)	B	1.74	2.24	2.00
	A	4.40†	5.72	8.60
Lung compliance	B	2.89	3.20	2.02
(ml./cm. H ₂ O/kg.)	A	1.26†	0.95	0.65
Elastic work of breathing (kg.-m./min./10 ⁻²)	I	2.00	1.15	0.97
	B	12	10	15
	A	42	79†	77

* B = before, A = 5 min. after fluid inhalation; I = after inflation of lung; † difference from control value (B) statistically significant (P < 0.05); ‡ difference from corresponding change after fresh water inhalation statistically significant (P < 0.05).

CIRCULATORY RESPONSE

Fresh Water.—The immediate circulatory response to the inhalation of 1 ml./kg. fresh water is shown in Fig. 1.

Blood.—The inhalation of blood had no immediate (Fig. 2) or delayed (Table I) effect on the pulmonary circulation.

Saliva.—There was no abrupt change (Fig. 3), only a small gradual rise (Table I) in pulmonary arterial pressure after the inhalation of saliva. Pulmonary arterial resistance was unchanged after five minutes. This was significantly different from the corresponding changes obtained after fresh water inhalation (Halmagyi and Colebatch, 1961).

The inhalation of saliva resulted in a marked increase in cardiac output from 2.56 to 4.06

FIG. 1.—Effect of the inhalation of 1 ml./kg. fresh water. “Asystolic” periods represent electrical mean pressures. PL=intraleural pressure.

FIG. 2.—Effect of the inhalation of 1 ml./kg. heparinized blood. Black box at the bottom shows time of blood inhalation. PL=intraleural pressure. Paper speed as in Fig. 1.

FIG. 3.—Effect of the inhalation of 1 ml./kg. saliva. PL=intrapleural pressure.

l./min./m.² B.S.A.; this was significantly different from the corresponding change after water inhalation. Because of the slight increase in the mean average pulmonary arterial pressure from 13 to 18 mm. Hg and the gross rise in cardiac output, right ventricular activity was significantly increased.

Saliva and Alcohol.—The changes were virtually identical with those caused by saliva alone.

Physiological Saline.—The intratracheal administration of physiological saline was followed by a pulmonary hypertensive response (Fig. 4) similar to that caused by the inhalation of water.

CHANGES IN BLOOD OXYGEN AND VENOUS ADMIXTURE.—The increase in venous admixture and the fall in arterial oxygen saturation were essentially similar in all four types of fluid inhalation. There was a gross arterial hypoxaemia, and venous admixture in several animals exceeded 50% of the cardiac output.

In the one animal which had been given 100% oxygen breathing after alcohol inhalation arterial oxygen saturation increased from 64.5% to only 75.6%.

VENTILATORY RESPONSE.—In about half of the animals the inhalation of blood or saliva caused transient apnoea. The inhalation of alcohol resulted in a transient apnoea in two out of two untreated animals. Breathing always returned spontaneously.

An increased rate and depth of breathing resulted in a varying degree of hyperventilation after the inhalation of all four types of fluid. A significant rise in ventilation and tidal volume occurred only after the inhalation of saliva.

CHANGES IN THE MECHANICS OF BREATHING.—A rise in the intrapleural pressure swing was obtained in all cases. This occurred rapidly when preceded by apnoea and more progressively in other animals. The mean average intrapleural pressure swing five minutes after saliva inhalation was 17 cm. H₂O, and five minutes after blood inhalation it was 12 cm. H₂O.

FIG. 4.—Effect of the inhalation of 1 ml./kg. 0.85% physiological saline. Black box at the bottom shows time of administration of saline.

FIG. 5.—The effect of inflation of the lung (infl.) and the injection of atropine (atrop.) and isoproterenol (isupr.) after the inhalation of saliva. Mean values obtained in three experiments. "Elasticity of breathing" means the elastic work of breathing.

A gross fall in lung compliance resulted from the inhalation of all types of fluid. After the inhalation of blood this fall appeared to be somewhat less marked and inflation of the lung seemed to restore compliance more readily than in the other groups; the difference was, however, not statistically significant. The correlation between compliance fall and increase in venous admixture was identical with that already described for water inhalation (Colebatch and Halmagyi, 1961a).

The rise in mean frictional resistance appeared to be more marked after the inhalation of blood than after that of water, and more marked after the inhalation of saliva than after that of blood. The difference between the rise in mean frictional resistance after water and after saliva inhalation was statistically significant. The gross rise in the average value of mean frictional resistance after

the inhalation of alcohol was due to an excessive increase in one animal and a small rise in the other.

Elastic work of breathing increased significantly in all groups. The smallest rise occurred after the inhalation of blood; the difference was, however, not statistically significant.

EFFECT OF THERAPEUTIC PROCEDURES.—The effect of the administration of atropine and isoproterenol is illustrated in Fig. 5. The diagram represents mean values obtained in three experiments. The injection of atropine was followed in this case by a marked rise in ventilation, lung compliance, and arterial oxygen saturation. These changes were further augmented by the infusion of isoproterenol which also caused a marked increase in cardiac output. When the infusion of isoproterenol was discontinued cardiac output

returned to normal, ventilation decreased, and there was a slight diminution of lung compliance. Elastic work of breathing decreased gradually throughout the entire procedure.

In one sheep, in which the inhalation of alcohol was preceded by the administration of atropine, lung compliance decreased from 1.59 ml./cm. H_2O /kg. to only 1.33 ml./cm. H_2O /kg.

DISCUSSION

These studies re-emphasize the severity of the arterial hypoxaemia that invariably follows the inhalation of even small amounts of fluids. Its onset and extent seem to be largely independent of the chemical composition or origin of the fluid inhaled.

Pulmonary hypertension, a characteristic response to the inhalation of water, was completely absent after the inhalation of blood. Iso-osmoticity could hardly account for the absence of this reaction, as the inhalation of physiological saline had effects similar to those of water. The increase in pulmonary arterial pressure after the inhalation of saliva was accompanied by a rise in cardiac output. As a result, pulmonary arterial resistance remained unchanged. In normal circumstances a similar increase in flow is unlikely to affect pulmonary arterial pressure. We suggest therefore that an increase in pulmonary arterial tone has occurred. We cannot at this stage offer any explanation for these remarkable differences in the pulmonary vascular reaction.

Alveolar oxygen tension was invariably normal after the inhalation of 1 ml./kg. water (Halmagyi and Colebatch, 1961) and there was a marked drop in the saturation of the arterial and mixed venous blood. It has been suggested, as summarized by Fishman (1961), that pulmonary precapillary resistance increases not only during alveolar hypoxia but also after a marked drop of the saturation of arterial or mixed venous blood. Our experiments failed to confirm this hypothesis. The oxygen saturation decreased significantly after the inhalation of blood, yet pulmonary hypertension was absent. This is consistent with our previous conclusion that pulmonary hypertension caused by the inhalation of water is unrelated to hypoxaemia.

No explanation is offered for the marked rise in cardiac output after the inhalation of saliva. In these animals the extent of arterial hypoxaemia, a possible stimulus for increased blood flow, was comparable to that of other groups.

A gross fall in lung compliance was the most important physiological consequence of the

inhalation of these small amounts of fluid. The changes in lung mechanics were essentially similar to those described after fresh water aspiration (Colebatch and Halmagyi, 1961a) and seem to account for the severe respiratory embarrassment and cyanosis encountered in clinical fluid inhalation (Gardner, 1958).

Because the anaesthetized animal tends to breathe at a fixed tidal volume, i.e., a constant transpulmonary pressure swing, compliance is likely to remain reduced until a large inflation is performed. The apparent duration of the stimulus responsible for the fall in compliance, or, alternatively, the effect of any therapeutic procedure, can only be assessed by the effect of inflation on the restoration of compliance.

Inflation of the lung was hardly effective after the inhalation of saliva or alcohol and restored compliance only partially after the inhalation of blood. The amount of fluid administered was only 5% of the resting lung volume of the sheep and could hardly account for the sustained depression of lung compliance amounting to 30 to 70%.

Inflation after the administration of atropine, isoproterenol, or both resulted in a significant increase in lung compliance. This effect is similar to that seen after water inhalation (Colebatch and Halmagyi, 1961b). We suggest therefore that the inhalation of these fluids caused an intrinsic reaction in the lung similar to that caused by water, consisting of a reflex constriction of the musculature in the terminal (unsupported) airways. The airway closure reduced the amount of lung, i.e., the number of distensible units participating in expansion, and was measured as a fall in lung compliance. The continued perfusion of non-ventilated areas produced a shunt of venous blood to the systemic circulation which was responsible for hypoxaemia and could be represented as venous admixture.

Breathing of 100% oxygen after alcohol inhalation failed to restore arterial oxygen saturation. This is consistent with the effect of self-breathing of oxygen after water inhalation (Colebatch and Halmagyi, 1961a) and indicates that a diffusion defect or uneven ventilation could hardly account for the severe hypoxaemia.

In the majority of experiments the injection of atropine resulted in a satisfactory improvement in arterial oxygen saturation and elastic work of breathing. In some cases, however, the response was unsatisfactory and isoproterenol was more effective. The reason for this occasional unresponsiveness to atropine has to be further investigated.

Assuming that fluid aspiration in humans has effects similar to those we have described in lightly anaesthetized sheep, then the implications of our findings for clinical management can be briefly outlined. The essential measurement for assessment and as a guide to the efficiency of treatment is arterial oxygen saturation.

It follows from the mechanism of hypoxaemia that the collapsed areas of the lung must be re-inflated, otherwise the persistence of a high venous admixture will prevent satisfactory levels of arterial oxygen saturation being attained. The maximum safe inflating pressure should be available for artificial respiration or assisted breathing; 30 mm. Hg is a reasonable upper limit. Large inflations should be given at a relatively slow (8 to 12 per minute) rate. In these circumstances the expiratory phase may be four to six times as long as inspiration. This ensures a low mean airway pressure, and so avoids any significant depression of cardiac output. For restoration of normal oxygen saturation in the arterial blood a combination of 100% oxygen with intermittent positive pressure breathing is essential (Colebatch and Halmagyi, 1961a). The additional 2 volumes % of physically dissolved oxygen in the arterial blood is only one factor of the effect of oxygen; it also relieves pulmonary vasoconstriction and facilitates airway opening.

The dose of atropine that was effective in restoring lung compliance in these experiments was many times more than that used in clinical medicine. Smaller amounts, even when given as a constant intravenous infusion, as suggested by Ursillo (1961), were considerably less effective. However, the effect of a smaller relative dose should be assessed in man.

The amount of isoproterenol found to be effective in these experiments was well within the human therapeutic range. A particularly favourable feature of its effect was full efficiency in aerosol form. This, when combined with intermittent positive pressure breathing using 100% oxygen, would appear to represent the most efficient method in the management of patients who have inhaled any type of fluid.

SUMMARY

The cardiorespiratory effects of the inhalation of 1 ml./kg. blood, saliva, and alcohol were studied in sheep. The effect of different types of treatment was also assessed.

The inhalation of blood failed to affect the pulmonary circulation; a minor rise in pulmonary arterial pressure was observed after the inhalation of saliva. This contrasted with the marked pulmonary hypertension following water inhalation.

The intratracheal administration of these small quantities of all three types of fluid caused a marked fall in lung compliance resulting in severe arterial hypoxaemia. The injection of atropine and the injection or inhalation of isoproterenol greatly reduced these changes.

The implications of these findings in the management of patients who have inhaled fluid are discussed.

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