Alcohol Concentrations in Blood, Breath and Urine
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A comprehensive study of the uptake, distribution and elimination of volatile agents in the animal body is in progress. As part of this study, the distribution of alcohol in blood, breath and urine in relation to time after administration is being investigated in animals and man. For the determination of alcohol levels in urine and blood the macro-method of Nickolls (1960) is widely used by forensic laboratories but this method requires an excessive volume of blood. We now use the micro-method of Conway (1950) having verified that good agreement can be obtained between the two methods. The time variation of the alcohol concentration has been followed in mixed venous, arterial, and peripheral venous blood. The mixed venous levels were the highest during the initial period of active absorption of alcohol. Peripheral venous levels were substantially lower than either mixed venous or arterial levels during this period.

In the United Kingdom the courts accept a ratio of 4:3 for urine to blood levels; in Holland this ratio is taken as 3:2. Such ratios have been obtained from a statistical analysis of several thousand cases. Whilst these ratios represent the mean figures, a wide distribution occurs on either side of the mean. Sampling directly from the ureters of dogs, we have shown that the urine/blood ratio is not a constant but varies with the time following the administration of alcohol.

In the breath a blood level of alcohol of 100 mg/100 ml is equivalent to 243 parts per million by volume at 34°C assuming a blood/breath ratio of 2,000:1. For such breath measurements we have used a sensitive infra-red gas analyzer with a full scale sensitivity of 400 p.p.m. v/v alcohol. An automatic syringe method has been developed to allow accurate calibration of the analyzer to be made. The analyzer requires a sample volume of 110 ml, and this has been found satisfactory for end-tidal samples. Simultaneously, mouth temperature is recorded with a thermocouple and the expiratory carbon dioxide plateau monitored with a rapid-response carbon dioxide analyzer in order to ensure that a true end-tidal sample is reaching the alcohol analyzer. Preliminary experiments have brought out clearly the effect of fatty stomach contents in reducing breath levels, and also the fact that the alcohol excretion pattern can vary markedly from subject to subject. This confirms the suggestion that breath sampling should not be undertaken until the elapse of 1 hour from drinking.

Current work is directed towards the use of a helium-neon gas laser for the determination of alcohol vapour. The discrete wavelength generated by the laser removes interference from carbon dioxide and water vapour in the breath and will allow the use of a sample cell volume of some 1.5 ml.

REFERENCES

A Comparative Evaluation of Corticoids in the Treatment of Acute Adrenal Insufficiency
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Cortisol which has a mixed glucocorticoid and mineralocorticoid action is of proven value in the

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therapy of acute adrenal insufficiency. Recently, synthetic steroids have become available with a pure glucocorticoid action (table I), which are claimed not to cause complications resulting from water and electrolyte imbalance. However, it is uncertain whether these steroids are as effective as cortisol in episodes of acute adrenal failure.

In order to throw some light on this problem, an investigation was carried out on adrenalectomized rats, subjected to a standardized formalin trauma. The protection afforded by the two pure glucocorticoids (dexamethasone and betamethasone) was compared with that obtained following the mixed corticosteroids (cortisol and cortisone). The efficacy of aldosterone was also investigated.

**Technique.**

Bilateral adrenalectomy was performed 7 days prior to the standardized trauma; postoperatively these animals received normal food and were offered physiological saline to drink (tap water was given in one series for the final 3 days). Steroids were administered intramuscularly 2 hours, 24 hours, and in one series 48 hours, prior to trauma. In some rats the adrenals were inspected at operation but the glands were not removed: these animals became one of the control groups (mock adrenalectomy).

**Results.**

Following the standardized trauma, "mock adrenalectomized" animals showed a mortality of 5–10 per cent, while adrenalectomized animals without steroid therapy showed a mortality of 95–100 per cent.

Two series of adrenalectomized steroid-treated animals were studied. The first were treated with slowly acting water-insoluble steroid. Among these, cortisol reduced the mortality to 20 per cent and the pure glucocorticoids reduced it to 2.5 per cent (40 animals tested with each drug). Aldosterone only reduced the mortality to 65 per cent. The mortality in this series was not influenced by whether the animals received water or saline during the final 3 days.

The second series were pre-treated with rapid-acting water-soluble steroids, and a more severe trauma was inflicted. The mortality following cortisol (2.5 mg X 2) was reduced to 60 per cent while with the glucocorticoid (dexamethasone, 0.08 mg X 2) it was reduced to 32 per cent (25 animals tested with each drug).

**Conclusion.**

In adrenalectomized rats, subjected to the type of trauma employed in this investigation, the pure glucocorticoids were at least as effective as the mixed corticosteroids in reducing mortality. Provided adequate glucocorticoid steroid is already present in the body, the mineralocorticoid fraction of the adrenal steroids does not appear to play a significant role in stress states.

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**ASSESSMENT OF CAPILLARY pH ELECTRODE AND MICRO-TONOMETER SYSTEM**

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The assessment of a patient's acid-base state is commonly made using a capillary glass pH electrode in conjunction with a micro-tonometer unit (Siggaard-Andersen et al., 1960). The Radiometer equipment is widely used for this purpose, but there is, to our knowledge, no published account of its accuracy.

It was found that the glass electrode consistently read low with a single blood sample of usual size (40 μl). This error was partly, but not
completely, prevented by flushing between readings with isotonic saline instead of with the recommended distilled water. Constant readings were then obtained with subsequent aliquots of 40 μl, the replicability having a standard deviation of 0.0044 pH unit for blood, and 0.0018 pH unit for buffer. We have not found it possible to obtain consistent readings when sampling from a single limb of the micro-tonometer since this only contains about 60 μl. It is, therefore, our practice to sample from both limbs before reading the pH and to pause 10 seconds between the two samples (no intermediate flushing).

The most important factor affecting the performance of the micro-tonometer was the amplitude of vibration. Optimum amplitude was 1.4 mm which gave equilibration within 2 minutes. Neither flow rate of equilibrating gas (25–250 ml/min) nor volume of sample (30–70 μl) was critical provided that amplitude was optimum. During equilibration the approach of Pco₂ values (derived from pH) to the final value was approximately exponential. Final values showed random scatter for equilibrations on aliquots of the same blood sample (standard deviations 0.004–0.008 unit).

pH/log Pco₂ plots were confirmed as linear within the range Pco₂ 20–150 mm Hg, and the slope accorded with the haemoglobin concentration, although it lacked sufficient precision to offer a practicable method of measuring the haemoglobin concentrations to the customary degree of accuracy. The mean intercept of the buffer lines of 24 hospital outpatients was pH 7.373 at 40 mm Hg Pco₂. This corresponds to a calculated standard bicarbonate of 22.5 m.equiv/l.

Studies of blood equilibrated in a Torres type tonometer (Torres, 1963) showed no significant systematic error between Pco₂ of tonometer gas measured with a CO₂-sensitive electrode and Pco₂ of blood calculated by interpolation of pH on the buffer line. The random error had a standard deviation of 1.74 mm compared with 1.16 mm Hg for simultaneous observations of blood Pco₂ made with a CO₂-sensitive electrode.

REFERENCES


HYPERVENTILATION AND ACID-BASE BALANCE
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The changes in acid-base balance occurring during hyperventilation were studied in dogs anaesthetized with pentobarbitone. In arterial blood samples the pH, Pco₂ and Po₂ were determined using the appropriate electrode systems; the concentration of carbon dioxide and oxygen, using techniques developed employing the Pco₂ and Po₂ electrodes (Linden, Ledsome and Norman, 1965), and the haematocrit were measured.

Five dogs were ventilated using a Starling pump and during the first 2 hours the ventilation was adjusted to aim at a Pco₂ of 40 mm Hg. At the end of this period the pH (mean, ± SD) was 7.38 (±0.03), Pco₂ 43.7 mm Hg (±5.4), plasma HCO₃⁻ 22.8 mM/l. (±1.5) and pK 6.139 (±0.012). The animals were then hyperventilated by increasing the rate and stroke of the pump. After 40 minutes the pH was 7.66 (±0.06), Pco₂ 22.9 mm Hg (±4.4), plasma HCO₃⁻ 19.2 mM/l. (±2.4) and pK 6.209 (±0.023). After 4 hours hyperventilation the pH was 7.69 (±0.05), Pco₂ 18.9 mm Hg (±2.6), plasma HCO₃⁻ 17.4 mM/l. (±2.0) and pK 6.211 (±0.023). The ventilation was then reset to the initial value. After 40 minutes the pH was 7.42 (±0.06), Pco₂ 36.4 mm Hg (±4.3), plasma HCO₃⁻ 20.9 mM/l. (±1.7) and the pK 6.132 (±0.028). After 2 hours of normal ventilation the pH was 7.385 (±0.05), Pco₂ 39.2 mm Hg (±5.1), plasma HCO₃⁻ 21 mM/l. (±2.0) and pK 6.131 (±0.039).

Thus, hyperventilation induced a respiratory alkalosis. There was no sign of any non-respiratory acidosis during the 4 hours of hyperventilation. Return to the initial ventilation led to a return to the same pH, and the slight decrease in plasma HCO₃⁻ was similar to that seen in a control group of 5 dogs anaesthetized and breathing spontaneously for 8 hours.
During hyperventilation the pK of the blood samples increased significantly \((P<0.01)\) and in an opposite direction to that of blood equilibrated with various \(PcO_2\) levels in vitro (Severinghaus, Stupfel and Bradley, 1956).

If plotted on an Astrup nomogram the results show an apparent non-respiratory alkalosis. If these results are taken in conjunction with those of Robinson (1960) (from hyperventilated human subjects) and those following the inhalation of high carbon dioxide mixtures (Cohen, Brackett and Schwartz, 1964) it would appear that the response of the whole body to changes in alveolar \(PcO_2\) is more like that of plasma equilibrated with carbon dioxide in vitro than that of whole blood. In conditions in which the alveolar \(PcO_2\) changes, values such as buffer base or standard bicarbonate derived from whole blood equilibration curves may be misleading.

REFERENCES

Effects of Anaesthetics on Postganglionic Sympathetic Discharge

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An increase in the impulse discharge rate of preganglionic sympathetic nerves was shown previously during administration of constant inspired concentrations of cyclopropane, halothane, and diethyl ether (Millar and Biscoe, 1964). The experimental technique has been described briefly (Biscoe and Millar, 1964). However, these anaesthetics also cause depression of the postganglionic response to a synchronous preganglionic volley, interpretable as partial ganglion block (Biscoe and Millar, to be published). The effects of the three inhalation agents have therefore been studied on (postganglionic) cardiac, carotid, and hypogastric nerves, in rabbits lightly anaesthetized with pentobarbitone and given gallamine triethiodide. The nerves were dissected with the aid of an operating microscope in order to obtain multifibre strands, the activity of which was recorded with the aid of a pulse height selector and integrating ratemeter.

In association with a maximum rise in arterial pressure occurring after 4–10 minutes, 50 per cent cyclopropane greatly increased the impulse discharge rate in postganglionic nerves. Arterial pressure was reduced subsequently when high concentrations were continued, but sympathetic activity remained above the control level.

Changes in postganglionic discharge during anaesthesia with 3 per cent halothane were assessed arbitrarily at levels of arterial pressure 30 and 60 per cent below control; cardiac nervous activity was then significantly increased, by 65 and 84 per cent above the pre-anaesthetic level. Less pronounced excitation occurred in the hypogastric nerve. In five of six rabbits, postganglionic carotid sympathetic discharge was increased significantly, but in one animal there were reductions in activity in a multifibre nerve strand which had shown an increased discharge with cyclopropane.

The activity in these postganglionic nerves was increased by ether (7–14 per cent), in association with generally small changes in arterial pressure.

During administration of these high anaesthetic concentrations of cyclopropane, halothane, or ether over periods up to 30 minutes, no evidence was obtained of central vasomotor depression; the relevance of sympathetic ganglionic blockade to the circulatory actions of the anaesthetics requires further examination.

REFERENCES
Method of Recording the Minute Volume of Respiration

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If one wishes to record the average value of the inspiratory flow rate, one will wish to suppress variations due to the individual respirations. But the frequency spectrum of a regular respiratory flow pattern contains no component below the fundamental frequency of respiration; if variations at that frequency and above can be suppressed, while passing slower variations and the steady component (i.e. if a sharp cut-off, low pass filter can be constructed) a rapid instrument response to changes in the minute volume rate can be preserved. Although such a record describes only a single parameter of respiration, and there are obvious disadvantages in this simplification, there are also advantages in being able to compress the time scale and obtain an overall picture of respiratory changes occurring over a period.

An instrument has been constructed to perform this function; it has been made very compact by using a rotating vane flow sensing head similar to that used in the respirometer described by Wright (1955) in which, instead of activating a gear train through a mercury seal, the shaft moves freely on pivots. As the vane rotates it passes close to, but does not touch, two metal plates, and in doing so varies the coupling between a high frequency generator and an amplifier.

The rate of rotation is measured electronically; the apparatus required for this, with its associated battery, has been made compact, so that using a small battery-operated chart recorder, recordings can continue while the patient is in transit on his trolley. The filter circuit used is a specially devised one which uses a transistor, so connected that it passes the steady component and slow variations, but opposes the transmission of variations of greater frequency than 10 cycles per minute. The instrument response (15 sec for 90 per cent response after the sudden start of respiration) is much faster than with a simple CR circuit and better than the compound CR circuits which were also tried.

The calibration curve is substantially linear but errors of the type described by Nunn and Ezi-Ashi (1962) occur at low flow rates.

REFERENCES


ASSOCIATION OF ANAESTHETISTS OF GREAT BRITAIN AND IRELAND

The next Annual Meeting of the Association of Anaesthetists of Great Britain and Ireland will be held at the Assembly Rooms in Edinburgh, on October 13, 14 and 15, 1965.

Those wishing to read papers or display scientific exhibits should submit their applications to the Hon. Secretary, Association of Anaesthetists, Royal College of Surgeons, Lincoln’s Inn Fields, London, W.C.2, not later than May 6, for consideration by the programme committee.

Papers should be in the form of a 200–500 word summary and details of the scientific exhibits should include an estimate of the space required.