AN ANALYTICAL MODEL DESCRIBING THE EXCHANGE PROCESSES
OF ALCOHOL IN THE RESPIRATORY SYSTEM

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Summary

The diffusion processes of ethanol in the respiratory system are analyzed and simulated in a model consisting of 3 compartments with lumped parameters. The areas of exchange are differentiated into the alveolar space, the upper respiratory tract and the mouth-throat cavity. The underlying processes such as diffusion through membranes, air mixing and convection of ethanol gas are approximated by numerical equations processed through a digital computer using the ventilation as loop controlling variable. The parameters of the model were optimized by direct comparison of its behaviour with measured time courses of expired breath alcohol concentration obtained in drinking experiments. From their data "standard parameters" were derived and used for studying the influence of ventilation on the breath alcohol concentration. In this way it can be shown that the mucous layer on the respiratory duct is heavily involved in ethanol exchange during respiration.
Introduction

Quantitative, evidence-quality breath alcohol analysis has become of increasing interest during the last few years. This interest seems to parallel motor vehicle density. It is very easy for non-physicians to obtain breath samples and the results of the analyses are immediately available.

Some instruments possess sufficient accuracy and precision for in vitro measurements to justify their consideration for quantitative forensic purposes. However, the transition to in vivo determinations is accompanied by a reduction of correlation between concentration of alcohol which is in the breath and blood. This is caused partially by physiological variations of the blood/breath alcohol partition ratio and by variations of the subject's ventilation pattern when providing a breath sample. This reduced correlation has been the subject of debate in medical-legal circles for years. The study described is an effort to explain some of the reasons for discrepancies.

The Effect of Ventilation

The influence of ventilation before and during the delivery of a breath sample on the expired breath alcohol concentration (BRAC) is demonstrated qualitatively in Figure 1. Normal breathing conditions lead to a BRAC time course corresponding to curve a). Within short time a concentration is reached which is related to the alveolar equilibrium concentration. In the case of breath-holding for several seconds before the test, a higher slope at the beginning of the expiration can be observed (b) favouring a faster approach to equilibrium conditions. Reverse effects are found for forced ventilation before the test. A premature termination of expiration (e.g. after 4 seconds) would lead to a substantially lower answer.
Figure 1: Effects of different breathing patterns on the expired breath alcohol concentration.

The purpose of this paper is to try to explain the quantitative relations between inspired/expired volume and exhaled BRAC by using a computer-simulated model of the respiratory system.

Ethanol Transfer in the Lung

Membrane diffusion, evaporation, air mixing, and convection are involved with the transfer of alcohol molecules through the blood-air barrier into the vapour head space. The efficiency of diffusion depends on the surface/thickness ratio according to FICK's laws. In the alveolar re-
gion with an effective membrane thickness of about 0.6 \( \mu \) and a surface area of 80 \( m^2 \) /1/ the diffusional flow is so high that even under hyperventilation conditions no significant reductions of alveolar alcohol concentration will occur. Different situations are found in the various conducting airways. In the upper respiratory tract, for example, which shows a membrane thickness of 40 \( \mu \) combined with a surface of 0.6 \( m^2 \), the diffusional flow is 10\(^4\) times less than in the alveoli. The whole surface of the respiratory system is covered by a thin mucous layer /2/. Its volume has been estimated at 7 ml in the alveolar space and at 3 ml in the upper respiratory tract /3/. From there the alcohol molecules evaporate into the head space within about 10\(^{-5}\) seconds, where an equilibration between the gaseous and liquid phases takes place with a breath/blood partition ratio of about 1:2300 /4/. This means that under equilibrium conditions the concentration not only in the mucous layer but also in the membrane tissue and blood is by far higher than in breath so that these substances possess an enormous storage capacity for alcohol.

JONES et al. have mentioned the special role of these liquid surface layers for the exchange of alcohol /5/. During inspiration they will lose some alcohol to the air passing. This evoked concentration deficiency in the conducting airways can be fully compensated for only from alcohol-saturated alveolar air during expiration. Increasing ventilation leads to a stronger reduction of the surface concentration so that more alcohol molecules will be withdrawn from the expired breath. This effect might explain the mentioned dependence of BRAC time courses from ventilation.

In addition to JONES's statement, it is necessary to say that not only the mucous layers are involved in this exchange process, but also all proximal zones of the membrane tissue. This has to be considered for the model formation of the blood-air barrier.
Formation of the Lung Model

Taking into account the functional and morphometric properties of the different sections of the respiratory system a multi-compartment structure was chosen for the model (Figure 2). The areas of exchange are divided into three compartments with lumped parameters: the alveolar space, the upper respiratory tract, and the mouth-throat cavity. Between these compartments, time lag systems (TL1-3) are situated representing the respective anatomical dead spaces. The upper time lag system simulates the dynamic properties of the breath alcohol testing device. The blood alcohol concentration (BAC) serves as a common input variable, breath alcohol concentrations within each compartment are expressed by BRAC1-3. Mass transfer between the compartments is provided by the time course of ventilation V and its direction IN/EX.

Each compartment contains the formal description of the blood-air barrier structure including the mucous layer and the vapour head space. The mathematical solution of FICK's diffusion laws is based on numerical approximation methods which require the quantisation of time and space /6/. From the resulting equations an equivalent electrical network is derived consisting of a chain of resistors (R) and capacitors (C). The potentials along this RC-chain correspond to the local concentration distribution within the membrane structure. As source acts the BAC, as drain the capacity of the mucous layer together with the vapour head space (C_M).

The behaviour of the entire model is determined by the lumped parameters R, C and C_M of each compartment. The model answer was adapted to empirically determined BRAC time courses by computer-aided parameter optimisation methods, the ventilation V serving as loop controlling variable. Figure 3 shows the experimental arrangement for the registration of BRAC and ventilation data. For these purposes a new Infra-Red spectrometer developed by ADRIAN and
input signals

V(t)
IN/EX

output signals

environment

inspir.

expir.

BAC: blood alcohol concentration

V: ventilation

BRAC: breath alcohol concentration

TL: time lag system

COMP: compartment

Figure 2: Schematic structure of the lung model.
BORKENSTEIN was used [7]. At the inlet of its sample chamber a specially developed thermistor anemometer measuring the ventilation is installed. Output signals of both instruments are registered and stored in the transient recorder and at the end of each test fed to the tape punch for later computer data treatment.

Figure 3: Experimental arrangement for the registration of BRAC and ventilation data.

Drinking experiments were carried out with two male and two female subjects of varying vital capacities (VC). During the test they showed BRACs between 0.95 and 1.54 °/oo. For the evaluation of model behaviour under variable ventilation conditions they were to exercise the following two breathing patterns:

- Hypoventilation: a deep inspiration followed by breath holding for about fifteen (15) seconds and finally full expiration. The intention is to reach complete equilibration in all sections of the conducting airways.
- Hyperventilation: three cycles of inspiration
Figure 4: Comparison between model behaviour and empirical concentration time courses under hypoventilation condition.
and expiration within a short time lead to a strong vitiation of alcohol exchange.

Results

The following diagrams (Figure 4 and 5) which were selected from all twenty-two (22) tests allow direct comparisons between model behaviour (dotted lines) and measured BRAC time courses (continuous line). A square symbol denotes the model output concentration based on individually optimized parameters. Since statistical methods applied on these "optimal parameters" of all tests did not show significant differences, "standard parameters" of general validity could be derived from them. They were used for the second simulated expiration curve (triangle symbol). All concentrations are referred to \(1\%\) BRAC.

Figure 4 gives a typical example for hypoventilation. The simulation on the basis of optimal parameters is in good accordance with the actually expired BRAC. This is expressed by a mean error (ME1) of 1.8% which is slightly increased by using the standard parameters (ME2). A similar good agreement between recorded concentration data and model simulation is found in the case of hyperventilation (Figure 5). Since BRAC was registered only during the third expiration phase, no comparisons with the preceding expirations are made possible.

Overall, this hyperventilation condition shows that this model closely resembles the dynamic exchange processes of alcohol in the respiratory system. Therefore, several typical breathing patterns were programmed leading to quantitative relations between ventilation and expired breath concentration.

An example for this kind of simulation is presented in Figure 6. The subject is instructed to inspire during four seconds then hold his breath for about two seconds. Inspiration volumes between 20 and 100% of the vital capacity evoke varying reductions of the concentration at the mouth.
Figure 5: Comparison between model behaviour and empirical concentration time courses under hyperventilation condition.
Figure 6: Simulated concentration at the mouth.
(left part of the diagramm) which can not be fully reequilibrated within the breath-holding phase (middle). Thus the BRAC during a full expiration within ten seconds is lowered with increasing inspiration volume. However, the asymptotic rise is still significant because after discarding 40% of the vital capacity (i.e. after four seconds) in all cases 75% of the end-expiratory BRAC is reached. This is an important statement for judging incomplete breath samples occurring rather often under practical test conditions.

From this diagram it is now possible to give quantitative predictions on the time course of exhaled BRAC under defined ventilation conditions. The example shown assumes a vital capacity of 5 litres, but further simulations with 2.5 and 7.5 litres show very similar results.

It can be concluded from the behaviour of the single compartments that the exchange processes on the surface of the conducting airways strongly influence the expired breath alcohol concentration. These results were achieved by the use of advanced electronics combined with a digital computer. They demonstrate the advantages of mathematical-technical methods for answering physiological questions.

References


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