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Metabolic and environmental origins of volatile organic compounds in breath

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Abstract

Although more than 200 volatile organic compounds (VOCs) have been identified in human alveolar breath, their origins are still mostly unknown. An attempt was made to determine whether the major VOCs in breath were derived from inside or outside the body—that is, were they products of metabolism or contaminants from the environment? The concentrations were measured of the 24 most abundant VOCs in the alveolar breath of 12 normal volunteers and also in the air they inspired. The polarity of the mean alveolar gradient (concentration in breath minus concentration in inspired air) was positive in 15 VOCs and negative in nine. The mean alveolar gradient varied from strongly positive (for example, 2,3,3-trimethylpentane), consistent with a metabolite manufactured in the body, to strongly negative (for example, isoprene), consistent with ingestion of an air pollutant which was then catabolised in vivo or excreted via an extra-pulmonary pathway.

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More than 200 volatile organic compounds (VOCs) have been identified in normal human breath,[1–3] but their origins and importance are still largely unknown. Breath VOCs might originate from either inside or outside the body, as endogenous products of metabolism or from exogenous sources such as air, food, and water. Previous studies of the VOCs in alveolar breath have generally not addressed the question of their primary source. The distinction between the endogenous and exogenous origin of a VOC has assumed greater importance in recent years with the recognition that the composition of breath VOCs may be substantially altered in conditions such as lung cancer,[4 5] liver failure,[6] acute myocardial infarction,[7] and schizophrenia.[8]

We have already reported a method for the collection and analysis of VOCs in alveolar breath and inhaled air,[9] and have shown that carbon disulphide has a negative alveolar gradient in most normal subjects, consistent with an exogenous origin from polluted air.[10] We undertook this study to determine whether the most abundant breath VOCs were of endogenous or exogenous origin.

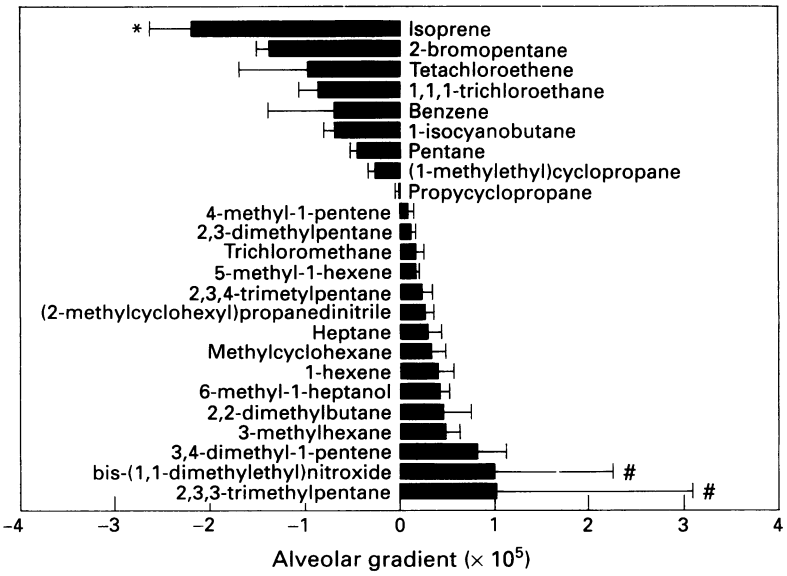

*Figure 1 Alveolar gradients of the most abundant VOCs in breath: solid bars indicate the mean alveolar gradient of a VOC in the breath of normal subjects; error bars indicate standard error of the mean (# = reduced X 0·1, * = reduced X 0·5). Units are AUC of the chromatographic peaks. Positive polarity indicates probable manufacture in the body; negative polarity indicates a probable environmental origin.*

Methods

Twelve normal volunteers with no known medical problems were studied. All breath samples were donated between 0700 hours and 1100 hours, after written informed consent to participate in this study had been obtained. The study was approved by the Institutional Review Board of St. Vincent's Medical Center of Richmond.

Samples (10·0 litres) of alveolar breath and unfiltered room air were collected sequentially using a transportable apparatus which captured the VOCs on an adsorptive trap containing activated carbon and molecular sieve. The method has been described before.[9]

The VOCs were subsequently desorbed from the adsorptive trap in a microprocessor controlled thermal desorber and concentrated by two-stage cryofocusing in sequential cold traps at −150°C. The concentrated sample was then separated by gas chromatography and analysed by mass spectroscopy with an ion-trap detector.

Results

The mass spectra of the VOCs in the samples were tentatively identified from a computer based library, and their concentrations were determined from the area under curve (AUC) of the chromatographic peaks. AUC values were determined for the 24 major VOCs detected in the samples of room air and alveolar breath, and the mean alveolar gradient was determined for each compound (AUC in alveolar breath minus AUC in room air) (fig 1).

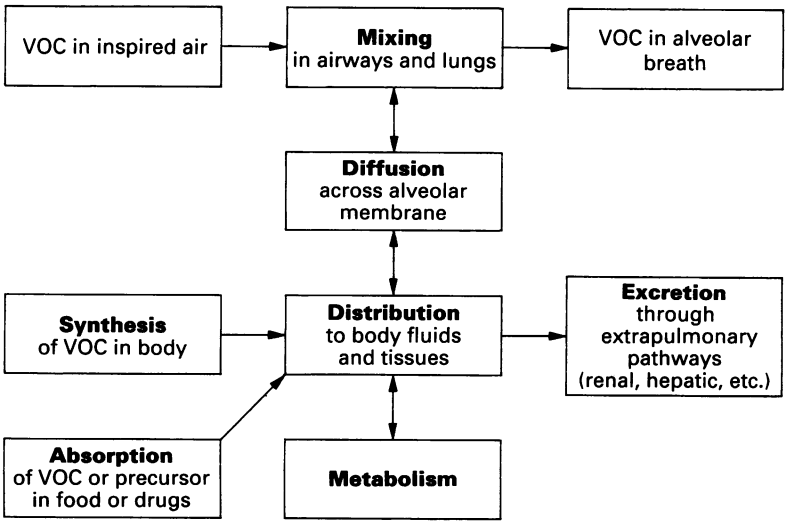

Figure 2 Sources of VOCs in the alveolar breath: this figure shows that VOCs in the breath may be derived from sources either inside the body (as products of metabolism) or outside the body (VOCs in the inspired air, food, and drugs).

The mean alveolar gradient of all VOCs exhibited either positive or negative polarity, ranging from the most positive (2,3,3-trimethylpentane) to the most negative (isoprene).

Discussion

Based on what is known of the physiology of pulmonary gas exchange, the polarity of the alveolar gradient appears to depend mainly on whether a VOC originates from inside or outside the body. Like water flowing down a hill, a VOC diffuses across the pulmonary alveolar membrane from the compartment with the higher vapour pressure to the lower, from the air into the blood, or vice versa. The equilibration between VOCs in the blood and in the alveolar air is rapid and probably near complete. The pathways of potential sources of breath VOCs are shown in fig 2. A positive alveolar gradient (concentration higher in breath than in air) indicates that more of the VOC was excreted than ingested through the lungs; therefore, these VOCs were either synthesised in the body, or absorbed from another site, possibly as a drug or in the food. The dietary intake of the volunteers was not controlled, so it is possible that some of the VOCs with a positive alveolar gradient may have originated in food or water. Conversely, a negative alveolar gradient indicates that a VOC originated outside the body and was then either catabolised or excreted via an extrapulmonary pathway (such as the kidneys or the liver). The situation is less clearcut with respect to those VOCs with alveolar gradients close to zero. These compounds may have been room air pollutants which were not significantly catabolised or excreted, so that their concentrations in blood and air were about equal.

These findings show, for the first time, that the alveolar gradients of the most abundant VOCs in breath may exhibit either positive or negative polarity, consistent with an endogenous or an exogenous origin. Further studies are now needed to clarify the synthetic pathways responsible for endogenous manufacture of VOCs, as well as the catabolic pathways responsible for the degradation of VOCs ingested as environmental pollutants.

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