Air Ions and Physiological Function

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ABSTRACT Although gaseous ions possess no obvious physical properties which would predict a capability to influence living cells or tissues they can be shown to produce functional changes. The physiological effects so far demonstrated are limited in extent. In the mammalian trachea air ion action appears to depend upon the release of bound 5-hydroxytryptamine by CO_2^+ and upon O^--induced acceleration of its metabolic destruction.

INTRODUCTION

Early in the course of studying the world around him, man noted and was deeply impressed by the ability of living organisms to survive and flourish in vastly diverse environments. The broad evolutionary adaptations to specialized conditions and the facile individual adjustments required with variations in temperature, pressure, humidity, light, etc., are matters of obvious biological importance. As these studies progressed, a good deal was learned about the extent to which ordinary environmental changes affect man himself and currently, in preparing for extended exploration by submersible and space capsule, information is accumulating very rapidly about what novel and greater than ordinary changes do to him.

In addition to the severe and drastic environmental fluxes that may result in disability or even death, there are others so tenuous that they are not readily detected. This is the case with air ionization, a subtle factor whose role in the maintenance of health and comfort is as yet imperfectly defined.

The notion that atmospheric electricity may exert an influence on the human economy is not new; in 1780 Abbé Bertholon (1) published a book presenting his observations on the response of normal individuals and of patients suffering from various diseases to changes in the electrical state of the ambient air. Subsequently a great deal of speculating was done on this intriguing subject but little of a definitive character was accomplished until 1899 when Elster and Geitel (2) laid the foundations for scientific inquiry by proving the existence of electrically charged atmospheric constituents—the classical air ions. It then became possible to explore the effects of atmospheric electricity

in terms of naturally occurring ions and to develop the equipment required for their measurement and artificial production.

The technical advances of the early part of this century paved the way for an enormous amount of research directed largely toward evaluating the therapeutic potentialities of air ions and to a lesser extent toward determining the more fundamental physiological responses of cells and tissues. Despite the fact that many of these studies were poorly controlled and often neglected the interference of gaseous pollutants produced by electrical discharges employed to generate ions, the investigators displayed surprising unanimity in attributing to excessive concentrations of positive ions generally harmful effects and to negative ions stimulating or beneficial effects.

The physical facts about air ions taken by themselves would furnish no basis for predicting any sort of influence on cell function or structure. An air ion is simply a group of 4 to 12 gaseous molecules randomly clustered around an electrically charged atom or molecule of gas. It moves slowly and, even in an artificially ionized atmosphere, exists in such strikingly sparse numbers that the ratio of ions to non-ionized molecules rarely exceeds $1:1 \times 10^{12}$. There is therefore no reason to anticipate either damage to cells on impact or stimulation of cellular activity. Nevertheless, experimentation has demonstrated that gaseous ions can induce definite and quantitatively reproducible physiological changes although it appears evident that these changes are of a low order of magnitude.

Generation and Measurement of Gaseous Ions

In nature, radiation and ionization are intimately related environmental factors and at the surface of the earth the radioactivity of the soil is the principal source of gaseous ions. Cosmic rays, another source of gaseous ions, become more important as altitude increases.

For laboratory experimentation air ions may be generated by a variety of means including high voltage electrical fields, incandescent materials, ultraviolet light, x-ray, and α- or β-radiation from radioisotopes. Electrostatic, ultraviolet, and thermionic generators are capable of producing high densities of gaseous ions initially but they tend to undergo a rapid deterioration of output. Furthermore, ozone, a very undesirable pollutant, is almost always a by-product of high voltage and ultraviolet generators.

When precise ion control is required with a uniform output of one or both polarities of ions adjusted to meet specific conditions, radioisotopic generators are to be preferred (3). We use 50 millicuries of tritium gas sealed in zirconium and deposited on a stainless steel foil. It is a low energy source of β-radiation (0.0185 Mev: half-life 13 years) which ionizes air through a range of slightly more than 1 cm.

An electrical potential difference varying from 300 to 2000 volts DC is used to separate ions of opposite charge before they are lost through recombination in the dense ion plasma surrounding the foil. Ions of the desired charge can then be disseminated through migration in the same electrical field or through transport in an air current directed over the ion source. This type of generator will produce not less than 1×10^9 ions per second and is particularly desirable for scientific work, since it creates no ozone or oxides of nitrogen and does not fluctuate in ion output.

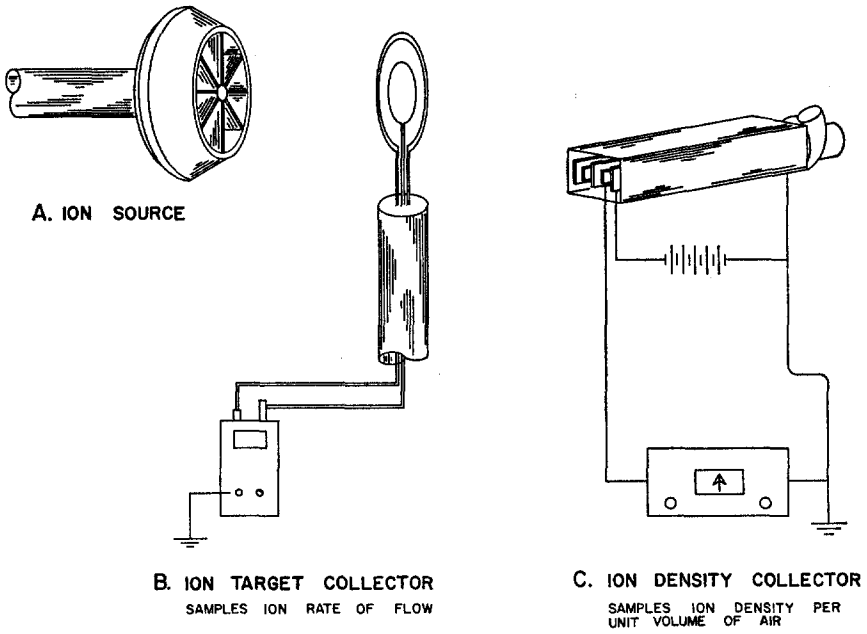

FIGURE 1. Methods of quantitation for gaseous ions. Ions generated by *A* are collected on surface of target probe *B* providing a measure of numbers of ions/cm²/sec. or are measured as numbers of ions/cc of ambient atmosphere by ion collector *C*.

The improved ion collectors now in general use provide a small ion mobility spectrum accurate to within approximately 15 per cent under varying conditions of atmospheric pressure, temperature, and humidity. These devices draw air through an electrostatic field between parallel plates or concentric cylinders; the ions are collected on the plates, the resulting ion current is measured with the aid of a micromicroammeter, and is converted into the number of ions/cm³ (Fig. 1).

In experiments requiring measurement of the numbers of ions impinging on a tissue per unit of time, an electrostatically shielded metal disc is connected to an electrometer (Fig. 1). By substituting the probe for the tissue one can meas-

ure accurately the rate of ion flow in an electrical field from ion source to tissue.

Some Observations on the Biological Effects of Gaseous Ions

Some 6 years ago we began a series of experiments designed to detect air ion effects on single celled organisms (bacteria) and on tissues. It soon became evident that the experimental design would have to include instrumentation for monitoring ion densities to which the cells or tissues were exposed and some procedure for providing air free from pollutants.

Ion densities may vary widely without warning, due to such simple factors as the condensation of water vapor on the tritium foil; the variations are apt to go undetected unless monitoring is included as a routine measure. A suitable ion collector and micromicroammeter connected to a recorder permit continuous monitoring of the numbers of ions of either polarity and various sizes per milliliter of air.

Air pollutants are capable of depleting small ion density by combining with newly formed air ions and converting them into undesired charged complexes. Removal of air pollutants is a formidable problem but the installation shown in Fig. 2 maintains the laboratory atmosphere within satisfactory limits.

In our earlier experiments on bacteria we found that air ion effects were detectable only when cells suspended in small volumes of water were stirred so that contact with ions at the air-water interface was facilitated (4). Even then the only clear-cut action attributable to air ions was an increase in the rate of death. Although this lethal action of ions of either charge has been found to occur in other forms such as *Neurospora* (5) and *Penicillium* (6) and *E. coli* (7) the order of magnitude is small and the underlying mechanism is as yet undetermined.

Since the completion of our experiments on bacteria we have undertaken a study of the effects of gaseous ions on the mammalian trachea. The trachea was selected because it is a primary zone of contact with inhaled air ions and it is conveniently accessible for observation. The tracheal mucosa is representative of that which covers the major channels of the respiratory tree and consists of a unique combination of cells with cilia on a free border and cells able to form mucus; this anatomical structure is responsible for the surface-clearing function of the respiratory tract. Inhaled particulate matter is trapped in the mucus film coating the epithelium and is carried out of the body through the wave-like action of the cilia, beating at rates approximating 900/min.

Observations on excised tracheal strips and on exposed tracheas of anesthetized rabbits, mice, rats, guinea pigs, and monkeys have indicated that positive ions produce: (*a*) decreased ciliary activity, (*b*) contracture of the posterior tracheal wall, (*c*) exaggerated vulnerability to trauma (EVT), (*d*) vasocon-

striction, and (*e*) increased rate of respiration. All five effects are seen in the anesthetized tracheotomized animal and the first three are seen in the isolated strip. Negative air ions reverse these effects (8–10).

In these experiments all the gaseous components of the atmosphere were subjected to ionization and it was impossible to infer which particular gaseous

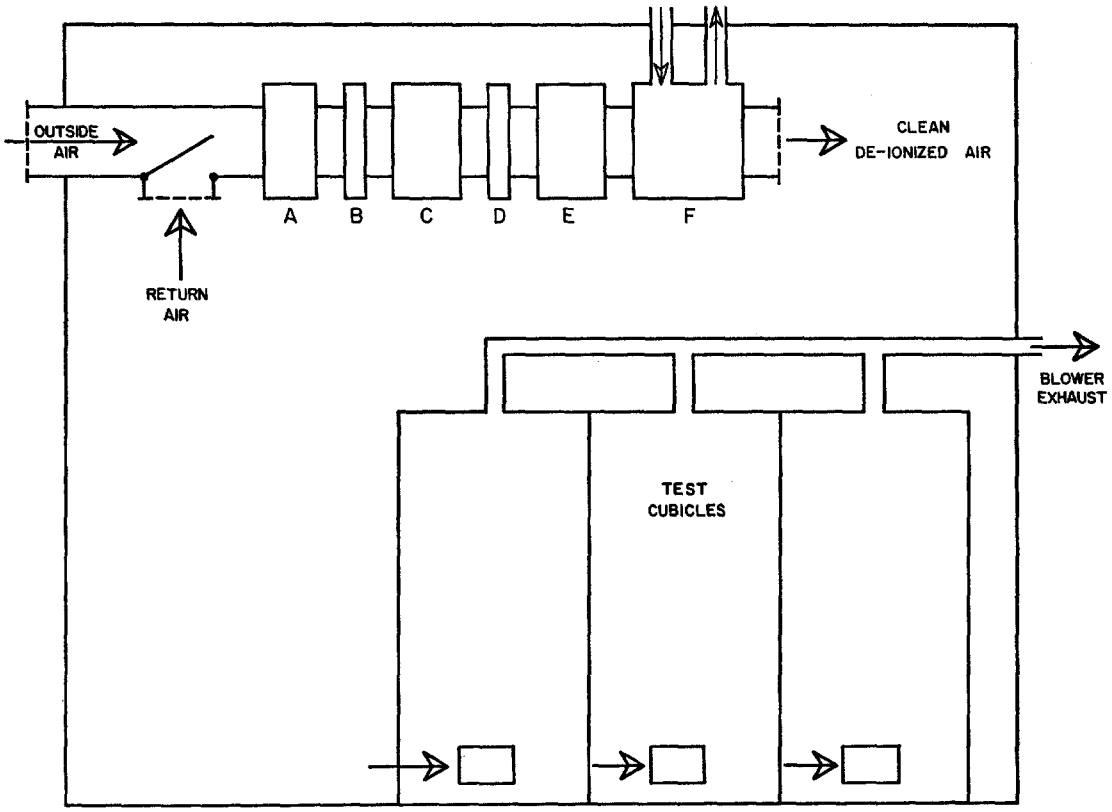

FIGURE 2. Diagram of air purification unit designed to provide clean air for gaseous ion investigations. *A*, electric duct heater. *B*, prefilter for *C*. *C*, electrostatic precipitator. *D*, negative ion source to neutralize excess positive ions generated in *C*. *E*, activated carbon filter. *F*, air conditioner.

ions produced the positive and negative effects. Consequently the experiments were repeated, replacing the air in the exposure chamber successively with N_2, O_2, CO_2, and the rare gases. Under conditions permitting positive ion formation, typical results were obtained only with carbon dioxide and negative ion effects were observed only when oxygen was present. It was concluded therefore that negatively charged oxygen (O^-) and positively charged carbon dioxide (CO_2^+) are the mediators of physiological effects occurring in the trachea as a result of atmospheric ionization (11, 12).

We subsequently observed that all the tracheal effects attributed to CO_2^+ can be duplicated by the intravenous injection of 5-hydroxytryptamine (5-HT) (13). Like positive ion effects, the 5-HT effects can be reversed by treatment with O^-. On the basis of these facts it was postulated that CO_2^+ ions are serotonin releasers and that a local accumulation of 5-HT in the trachea is the immediate cause of functional changes produced by positive ions. It was further postulated that O^- reverses positive ion effects by speeding up the rate at which free 5-HT is oxidized (Fig. 3). The enzyme involved, monamine oxidase, is thought to consist of a dehydrogenase linked to a re-

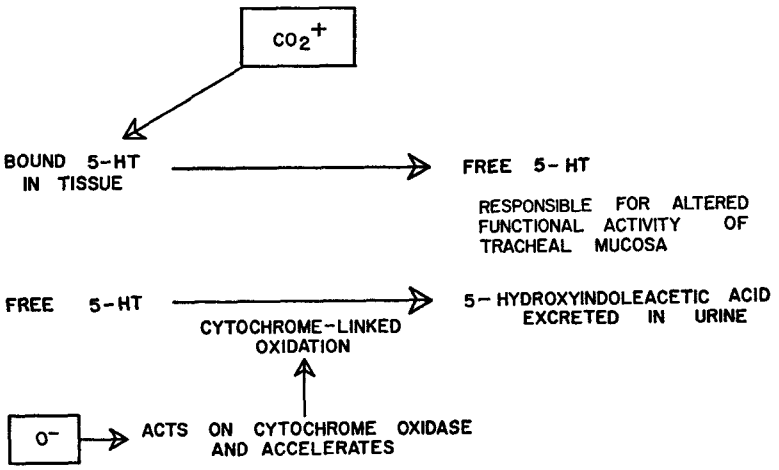

FIGURE 3. Diagram of gaseous ion action on tracheal mucosa. CO_2^+ converts bound 5-hydroxytryptamine to free 5-HT which alters functional activity of mucosa. O^- accelerates normal metabolic conversion of 5-HT to 5-hydroxyindoleacetic acid through action on cytochrome oxidase.

spiratory chain which may include cytochromes or flavins. In studies of gaseous ion effects on the catalytic activity of a modified Keilin-Hartree pig heart homogenate (14), we found that O^- ions have a direct effect on cytochrome oxidase and accelerate the cytochrome-linked conversion of succinate to fumarate. This would suggest that the same action may produce a cytochrome-linked oxidation of 5-HT.

Indirect confirmation of this hypothesis is provided by experiments with reserpine and iproniazid. Reserpine is believed to cause 5-HT to be momentarily released and then rapidly destroyed by monamine oxidase so that the tissues quickly become depleted of 5-HT. According to our hypothesis, reserpine would produce a condition in the trachea resembling that induced by O^-. Moreover, one would expect CO_2^+ ions to be unable to produce their characteristic effects on reserpine-treated animals, since the 5-HT necessary

for positive ion action is lacking. Both these expectations have been realized experimentally.

Iproniazid has shown to block monamine oxidase, preventing the metabolic removal of 5-HT and thus causing its accumulation in the tissue. One would expect an iproniazid-treated animal to display tracheal effects resembling those produced by CO_2^+ ions and to resist the action of O^- ions in reversing these effects. Again, both these expectations have been experimentally confirmed.

Further support for the hypothesis has been provided by recent experiments in which O^- ions were found to decrease 5-HT concentrations in excised strips of rabbit trachea and in the respiratory tracts of living mice (15). Guinea pigs exposed to O^- ions displayed a transient rise in urinary 5-hydroxyindoleacetic acid excretion; this compound is the specific metabolite of 5-HT.

The 5-HT mechanism of air ion action outlined above may not be limited to the trachea but conceivably could apply to other areas; *e.g.*, burned tissues. It has been reported that exposure of burned patients to negatively ionized air results in prompt relief of pain (16). 5-HT is known to be released in zones of inflammation and it causes pain in dilutions as high as 1×10^{-8} gm/ml (17). If 5-HT is a major pain-producing agent in burned tissues the relief of pain could be attributed to O^--induced acceleration of 5-HT destruction by monamine oxidase.

It is appropriate also to point out that the 5-HT mechanism represents only one of many possible channels through which air ions may influence physiological functions. For example, Frey (18) has proceeded on the hypothesis that negative ions stimulate the secretion of the adrenal gluco-corticoids while positive ions either stimulate the secretion of the mineralo-corticoids or inhibit gluco-corticoid secretion. He has called attention to the similarities between corticoid and ion effects in a variety of conditions such as the allergies.

Some of the leading Russian investigators consider the respiratory tract to be the primary trigger area for air ion action. Vasil'yev (19) has presented evidence that air ions act on the endings of pulmonary afferent neve fibers, altering the functional state of the central nervous system and through it the peripheral organs. He also attaches importance to the effect of air ions on the surface charge of erythrocytes and on the serum proteins. According to his observations an increase in the negative charge of blood colloids and cellular elements favorably influences the functional activity of the central nervous system and the body's tissues in general. Positive air ions exert an opposite action.

C. W. Hansell (20) has emphasized the need for a unifying concept of air ion action and has suggested a model consisting primarily of an automatic negative feedback control system for regulating bodily processes. The system operates to compensate for or to oppose environmental changes and exhibits

two major types of response: fast (minutes) and slow (weeks). Air ions absorbed during respiration produce effects enormously greater than the energies involved in direct chemical reactions of their own, because they influence the course of reactions of much greater magnitude and energy exchange. Hansell feels that alternate exposure to (+) and (−) ions may strengthen the fast acting feedback control system and adjust the slow acting mechanism toward a more normal range.

It is tempting to make some comments on general and specific areas of research devoted to detecting the biological effects of air ions. Based on the experience of the past 6 years in non-clinical aspects of the problem certain points seem noteworthy:

1. Pioneers in this field were handicapped by deficiencies of instrumentation and in consequence the literature, while voluminous, is frustratingly inconclusive. Nevertheless, the early workers successfully demonstrated that air ions are biologically active, and correctly concluded that positive and negative ions often elicit opposing reactions.

2. It is only comparatively recently that strictly controlled work in this area has become possible through the development of adequate ion generators and suitable instruments for the quantitative determination of air ions. Modern generators produce relatively large numbers of air ions free from gaseous by-products (ozone and the oxides of nitrogen) and enable the investigator to maintain constant ion densities in the ambient atmosphere. Advances in electronics have brought about the design and production of excellent ion collectors, ion probes, micromicroammeters, and recorders which combine to permit great accuracy in the quantitation and monitoring of atmospheric ion concentrations as well as in the measurement of the numbers of ions impinging on an exposed surface per unit of time.

3. The biological (non-clinical) effects produced by atmospheric ions are not dramatic; on the contrary they tend to be limited in degree. Nevertheless, there exists convincing evidence that gaseous ions produce functional changes in individual cells and in cells organized into tissues.

4. The mechanisms underlying air ion effects are slowly becoming apparent. In our own work on the mammalian trachea the evidence suggests that gaseous ions probably react with water (cell fluids) to form active radicals which then elicit various cellular responses. CO_2^+ seems to be the essential positive air ion and its important primary action is the release of 5-HT. This powerful neurohormone is the proximal cause of all the alterations in tracheal function which follow exposure to positive air ions. The opposing action of negative air ions depends upon the ability of O^- (through a derivative radical formed in water) to react with cytochrome oxidase, thereby accelerating the metabolic destruction of 5-HT.

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