AVIATION MEDICINE - SELECTED REVIEWS

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Edited by
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CONTENTS

INTRODUCTION
AND
PAPER SUMMARIES

CLAYTON S. WHITE

INTRODUCTION

IN the course of assessing recent advances in instrumentation and related methodology which might be of value to those interested in Aviation Medicine, twelve senior scientists were stimulated to prepare papers reviewing selected topics relevant to some of the biomedical aspects of flight. The authors working in technical areas in which each was experienced, perused a considerable number of publications, over seven hundred of which were cited as references to valuable scientific material. The aim was to document condensed sources of information summarizing specialized portions of the aeromedical and related sciences.

A total of twelve manuscripts were prepared and all are reproduced in this volume, not only for the convenience of physicians who are aeromedically oriented but for a wide variety of other scientists who need and desire a condensed guide to specialized sources of data. Too, many busy and curious people who wish to stay generally well informed will find the several papers of aid in staying abreast of advancements in instrumentation, methodology and analytical techniques.

As an aid in becoming oriented to the several papers which follow, a brief summary of each review has been prepared to familiarize the reader more fully with the contents of each author's contribution.

PAPER SUMMARIES

(a) *Spirometric methods by* Dr. ULRICH C. LUFT.—Spirometric methods as used by investigators concerned with respiratory physiology and metabolism were reviewed, beginning with the initial employment of the spirometer for vital capacity measurements by HUTCHINSON in 1846. Subsequent modification of the early methods and extension of the techniques were discussed under two headings; namely, (1) *Direct spirometry and spirography*, and (2) *Indirect spirometry*. With regard to the former, the use of open and closed spirometric circuits during rest and exercise for determining and (or) recording tidal volume, vital capacity, inspiratory capacity, inspiratory and expiratory reserve volumes, oxygen consumption, carbon dioxide output and the respiratory quotient, whether pressure breathing or not, were described. Also, bronchospirometry—the measurement of ventilation and gas exchange in each lung separately—was mentioned.

The author discussed a variety of approaches to indirect spirometry and the techniques which have been developed and employed primarily to determine the functional residual volume and hence the total lung volume, assessment of which cannot be made directly. Dilution methods using indicator gases and clearance methods were both described and the major sources of difficulty encountered with each technique applied to normal and pathological subjects were critically discussed.

(b) *High-speed motion picture photography as an aid in bio-medical investigation by* MERRILL A. PALMER.—The author discussed the uses of high-speed photography in a variety of biological problems and emphasized the potential value of photography by noting in some detail the characteristics of intermittent and continuous film cameras. As examples, attention was directed to the performance capabilities and limitations of Kodak and Fastax series high-speed cameras, and the importance of adequate operating techniques was pointed out. Problems surrounding choice of field, illumination, film, exposure, speed and analysis as they influence obtaining desired data were all mentioned. A few specific instances of the employment of rapid cinematography to document function and response of biologic media were cited.

(c) *The measurement of atmospheric ozone by* I. GERALD BOWEN.—Ozone was considered a possible, though unproven, toxicological threat to aviation personnel. Concentrations of ozone present at various altitudes was set forth, along with the more useful methods of measuring it. The expression of ozone concentration as the volume ratio to air used by upper atmospheric physicists was transformed and plotted using more common physiologic terminology; e.g. partial pressure as a function of altitude. Employing the above data, the partial pressure of ozone which might occur in the lung was computed on the " wet " basis as a function of cabin pressure and altitude. These data, combined with those setting forth the limits for ozone concentration allowable in industry, indicated a potentially dangerous situation. However, the rather wide discrepancies in the medical literature relevant to toxic concentrations of ozone, along with the instability of the gas, particularly at high temperatures, did not allow the statement of a firm opinion regarding the existence of a hazard. The author suggested actual determination of ozone concentrations in the cabins of pressurized and non-pressurized high-flying aircraft as an initial step in proving or disproving the existence of a toxicologic problem attributable to ozone.

(d) *Methods and apparatus for the study of stress reactions and metabolic changes by* Dr. BERNARD B. LONGWELL.—By way of introduction, the environmental variations associated with flying, by producing deviations in homeostasis in the several systems of the body, was considered to be a potentially " stressful " situation. Thus, the general concept of evaluation of " stress ", not only through studies of various organs but also by the integration of these studies to the end that the response of one system requires evaluation of its effect on all others, was established. Since such a broad concept included the regulatory effect of both the nervous and endocrine systems upon metabolic processes of almost, if not all tissues of the body, the author was forced to limit his dissertation primarily to methods and apparatus which had been or could be applied to the study of " stress " on the endocrine system and certain closely related metabolic processes.

Specifically, the endocrine glands and electrolyte and water balance studies were chosen as subjects for discussion. With regard to the former, recent and current methods applicable to the pituitary and endocrine system were covered; e.g. the thyroid by assay of serum protein-bound iodine and radioactive iodine uptake; the pituitary by assay of thyrotropic hormones; the adrenal cortex by chemical and bio-assay determinations of the corticosteroids in human urine and blood; and the adrenal medulla through determination of the plasma and urinary contents of epinephrine and norepinephrine. Recent methods and techniques suitable for determining variations in water and electrolyte balances produced by short periods of acute stress were reviewed. Particularly, electrolyte variations in plasma and urine, blood volume changes, alterations in total extracellular fluid, water balance and the relation of these to hormonal control by aldosterone were covered.

Lastly, as an aid to the reader, highly selected and useful references were cited.

(e) *Dosimetry of ionizing radiations* by JOHN L. HOWARTH.—The general significance in science and medicine of the expanding activities in the field of nuclear energy was mentioned initially, as was the importance of detecting and measuring the several varieties of radiations in aviation medicine, specifically. Hazards from the use of nuclear weapons, cosmic rays, nuclear power plants for manned aircraft and the wide employment of radioisotopes were cited as particularly pertinent to aviation biologists. As background to discussions of dosimetry, an informative summary of the interaction processes between ionizing radiations and matter was presented, following which the fundamental principles of dosimetry, including definition of physical and biological units, were discussed in some detail. Lastly, the general principles of ionization instruments were covered, along with references to the literature adequate for orienting the reader to all but highly specialized detection and measuring techniques.

(f) *Some technical developments applicable to problems in pathology* by Dr. THOMAS L. CHIFFELLE.—The author prepared a rather broad survey and in some respects a fairly detailed summary of recent developments and techniques which have been and will be of considerable use to the experimental pathologist and anatomist. Corrosion cast and injection procedures and their application in examining gross specimens were described in general. Tissue disintegrators were mentioned briefly and the problems surrounding the proper choice of the multitude of available tissue fixatives were covered in considerable detail. The relatively recent use of rapid freezing with vacuum dehydration of tissues was mentioned as often the only means of processing material for certain special studies. Histochemistry and cytochemistry, including dye metachromasia, detection of lipoids and neutral fats, autofluorescent techniques, the use of polarized light and the detection of ethylenic linkages, steroids, and phospholipines were given considerable attention. Further, the special approaches offered by electron microscopy, radioautography, microradiography and X-ray microscopy as they might interest the experimental and clinical pathologist were mentioned. A fairly lengthy reference list was also included.

(g) *Temperature measuring techniques for aviation physiological research by* Dr. F. G. Hirsch.—Remarks relevant to the relationship between man and his temperature environment were presented as background information illustrating the utilization which has been made of temperature measuring techniques in aviation biology; i.e. monitoring the environmental temperature exchange as a function of time, the accompanying biological heat storage and loss as a function of time, the design of personal equipment and clothing to protect men against high and low temperatures and the importance of understanding the general principles utilized in thermal sensing instruments. Thermocouples, resistance thermometers, including the relatively new thermistors, calorimetry, telemetering and miscellaneous techniques (temperature tapes and temperature sensitive paints), were briefly discussed.

(h) *The analysis of respiratory gases by* Dr. Clayton S. White.—By way of introduction the author pointed to the limitations of non-continuous and manual methods of respiratory gas analysis, mentioned the development of continuous and automatic techniques of value in physiology, and emphasized the need for a simultaneous, continuous and rapid analytical method capable of processing each individual respiratory gas at the same speed. Several of the more useful automatic methods currently employed were reviewed and discussed in detail; e.g. (1) those based on thermal conductivity principles, (2) paramagnetic properties of gases, (3) combinations of (1) and (2) above, (4) refractive index analyzers utilizing interferometric and refractometric methods, (5) acoustic analyzers, (6) critical flow methods, and (7) spectrometric techniques including absorption and emission methods and the principle of the mass spectrograph. The spectrographic approach was dealt with in considerable detail, particularly the use of absorption in the infrared for carbon dioxide analysis and the use of emission phenomena produced inside a variety of small volume discharge tubes energized with d.c. and r.f. for analysis of nitrogen and carbon dioxide and possibly oxygen and water-vapor. Illustrative material was prominently employed and the bibliographic documentation of each section of the report was highly selective, but adequate.

(i) "*Aerosols: physical properties, instrumentation and techniques*" by Dr. Arnold E. Reif.—The paper on aerosols proved to be a very scholarly, complete and excellent review of fifteen of the most important and useful physical properties of aerosols, along with applicable theory, related instrumentation and techniques used in quantitative measurement of the liquid or solid components of an aerosol. No attempt was made to cover the chemical and physiological properties of aerosols. Neither were the methods of aerosol production nor the biological effects, beneficial or pathological covered in the discussion.

The properties of aerosols which were dealt with in detail incorporated the following: (1) assessment of the *representative diameter* and physical and statistical methods of its determination for solid and liquid, including volatile, aerosols. (2) *Density*, its determination and corrections to unit density for comparative purposes. (3) *Terminal settling velocity*, its direct and indirect measurement employing elutriation along with the use of the property in separating aerosols of different sizes and densities. (4) *Stirred settling.* (5) *Brownian motion* for smaller particles and the influence of this on rate of flocculation and respiratory retention of an aerosol. (6) *Diffusion* and the related development of the " diffusion battery " of use in determining particle size and mass. (7) *Centrifugal motion*, the related uses and application of the conifuge for sizing techniques and the industrial use of "cyclone" separation to remove aerosol material from polluted industrial gases. (8) *Impingement* and the use made of impingers, konimeters and cascade impactors in aerosol methodology. (9) The complex process of aerosol *filtration*, the important related physical properties, and the widespread industrial applications of filters and filration. (10) *Thermal precipitation*, including the use of thermal precipitators in laboratory research. (11) *Electrostatic precipitation* incorporating methods of charging particles (d.c. or a.c. precipitators) and a brief discussion of the widespread industrial applications. (12) *Sonic coagulation* and the contributions made by covibration, hydrodynamic forces, radiation pressure and vortex motion, along with laboratory and industrial applications, including fog dispersal. (13) *Droplet growth and evaporation* as related to vapor pressure, curvature, evaporation rates, along with the production of uniformly sized and stable liquid aerosols, as influenced by electrostatic charge, dissolved substances, variation in surface tension with curvature and critical nucleation diameter. Further, the associated problems of stability of fogs and " smogs " and the control of droplet growth were also mentioned. (14) *Coagulation* (coalescence and cohesion) as it influences the size or state of aggregation of aerosol particulates. (15) Lastly, the *optical properties* were dealt with in considerable analytical detail.

With regard to optical properties of aerosols, a number of interesting phenomena were discussed, such as higher order Tyndall spectra, along with the " Owl ", an instrument of use in accurate determination of homogeneous aerosols of appropriate size. Further, the polarization of light by homogeneous aerosols was noted as was the utility of this fact in checking uniformity in droplet size. Coronae—the rings of colored light surrounding a point of light located in a fog (or a beam of light shining through the fog)—and their application to particle size determination in fogs was also explained. Likewise, light transmission and total and relative light scattering, the basis for development of Tyndallometers and " Slope-o-meters " for determining mass concentration of liquid aerosols, proved particularly fascinating. Also of considerable interest were the relation of day and sunset sky color to " aerosology ", the association between visibility and particle size, the use of visibility meters automatically and continuously to monitor urban atmospheres, the adaptation and employment of optical methods automatically to size and count aerosol particulates by cleverly arranging to scan slides by " spot " and " slit " light beams, sometimes employing " guard " spots, " arrested-scan " techniques and " memory " methods. The last two practical, optically oriented methods mentioned for aerosol studies, consisted of direct aerosol photography and electron microscopy.

The aerosol review was thorough and elegantly done. The paper consisted of 124 typewritten pages, 30 illustrations and 164 separate references.

(j) *Transducers.*—A short paper was written by JAMES CLARK under the title *Transducers: pressure-transformer type.* The author pointed out the need for pressure transducers of high output and sensitivity and proceeded to describe the general design and characteristics of three units which he had developed and used, employing the electromagnetic characteristics of transformers. One unit utilized two transformers placed symmetrically on each side of a circular, pressure-sensitive diaphragm and was recommended for use as a differential pressure-sensing instrument. The other two instruments employed a single transformer and both were flush diaphragm units. One was of conventional size, but the other was a subminiature unit, 0.100 in. in diameter and 0.250 in. long. The latter was suitable for bonding to a No. 8 catheter and thus was appropriate for use inside the bodies of even small animals.

Recommended electrical components of the equipment required to use the transducers were described and examples of employment in biological work were given.

(k) *Spectrometric methods.*—A technical paper was prepared by Drs. CLAYTON S. WHITE and W. RANDOLPH LOVELACE II under the title *Spectrometric methods—gas analysis by quantitative emission spectroscopy.* This paper reviewed the history of the use of emission spectrographic methods to analyze nitrogen starting with the original work of Lilly and Anderson. Modifications of the method were described and the complex spectral problem was reviewed. Recent satisfactory calibration procedures were noted and the necessary techniques and precautions to obtain quantitative data with existing equipment adequate for respiratory experiments were emphasized. The paper covered experience with d.c. activated discharge tubes operated under carefully controlled conditions when light or spectral isolation was accomplished by broad-band pass filters with cut-off below and above 3000 and 4000 Å, respectively.

(1) *Gas sampling methods.*—Dr. NILS P. V. LUNDGREN prepared a brief, but excellent paper entitled *Comparision of the Rahn–Otis technique with other methods of intermittent and continuous sampling of expired air.* The author described an arrangement for sampling end-expiratory air from the upper respiratory tract which allowed the use of automatic gas analyzers, along with Haldane analysis. Use with a closed- or open-circuit experiment was possible, though employment in the latter was more satisfactory. It was established directly that samples taken from the mouth in open-circuit experiments contained gases having concentrations very close to those obtained with the Rahn–Otis end-expiratory technique. Following a sharp change in the content of inhaled gases, accomplished by shifting from air to oxygen breathing, a mixing delay in the latter sampling method was documented primarily using rapid nitrogen analysis, but the delay proved significant only during the first 3 min following a change in the content of inspired gas.

SPIROMETRIC METHODS

ULRICH C. LUFT

INTRODUCTION

Measurements of the gas content of the respiratory tract and the range of its excursions (*Fig. 1*) are frequently required for diagnostic purposes in clinical medicine as well as in medical research. Since HUTCHINSON[1]

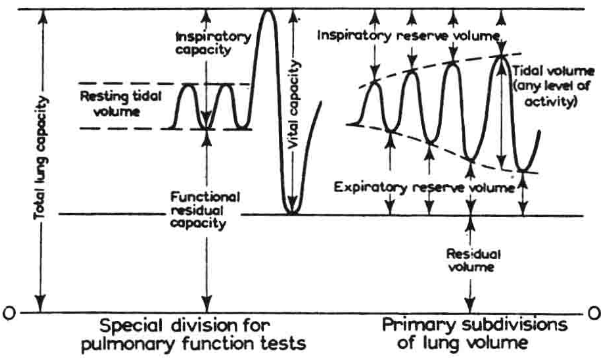

Fig. 1. Subdivisions of lung volume with the terms proposed by J. R. PAPPENHEIMER *et al. (Fed. Proc. Vol. 9, pp. 602–605, 1950).*

first introduced the spirometer to measure the vital capacity in 1846, this device has undergone innumerable modifications adapting its use beyond the direct reading of vital capacity and its subdivisions (*direct spirometry*) to the determination of the residual volume and functional residual capacity (*indirect spirometry*) and the continuous recording of tidal volume to obtain the total ventilation per unit time (*spirography*) frequently combined with the measurement of oxygen consumption.

DIRECT SPIROMETRY AND SPIROGRAPHY

In the simplest form of spirometry the exhaled gas is collected in a small HUTCHINSON[1] spirometer (6–9 l.) for a single vital capacity measurement or for continuous breathing through a one-way valve system in a large TISSOT[2] spirometer of 100–600 l. capacity (*Fig. 2*). The expired air may also be conveniently collected in one or more portable bags (DOUGLAS[3]) and subsequently emptied through the spirometer. The open systems are not suitable for close observation of the respiratory pattern nor can they be used to follow changes in the respiratory level and for indirect spirometry.

Closed spirometer circuits which include a medium for the absorption of carbon dioxide such as the KROGH[4] (*Fig. 3*), the BENEDICT-ROTH[5] and the KNIPPING[6] apparatus are much more versatile and are widely used in respiratory laboratories for testing ventilation and metabolism. The smaller capacity of the spirometers (6–9 l.) employed in the closed circuit technique permits greater accuracy of measurement.

In those apparatus in which the circulation of gas is maintained solely by the respiratory efforts of the subject, it is essential to reduce the flow

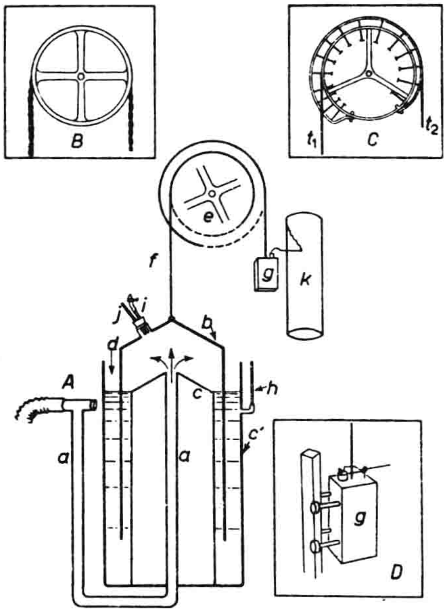

Fig. 2. Tissot spirometer. A, a–inlet airway with 38 mm inside diameter; b–floating bell; c–inner shell; d–water seal; e–pulley; f–chain; g–counterbalance; k–pen and recording drum; B–concentric pulley with chain counterbalance; C–eccentric pulley with varying lever arm; D–recording pen on guided counterbalance. (Methods in Medical Research Vol. 2, p. 96, 1950).

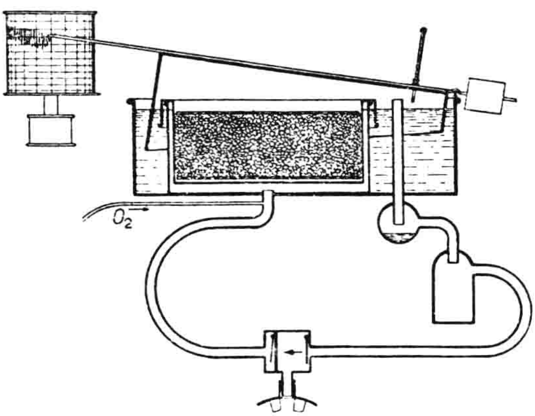

Fig. 3. Krogh spirometer[4] with closed circuit for breathing oxygen to measure respiratory volume and oxygen consumption.

resistance offered by the valves, tubing and carbon dioxide absorbent to a minimum. It is recommended that the inner diameter of all tubing and connections should be at least 25 mm in studies at rest and 38 mm for use during physical activity or hyperventilation[7]. The spirometer bell and recording attachments should be perfectly counterbalanced and of light material to reduce inertia in rapid movements. Precautions must also be taken to minimize the dead space at the mouthpiece to avoid rebreathing.

Many investigators prefer to include a pump in the spirometer circuit which maintains a rate of flow at least equal to the peak flow rate of breathing to eliminate the resistance and insure rapid mixing of gas (KNIPPING[6]). Other advantages of such an arrangement are the complete absence of valves, the use of more efficient carbon dioxide absorbers without adding to the resistance for breathing and the optional use of either a mouthpiece or breathing mask, sometimes preferable in clinical work. The usefulness of the closed system for experiments with strenuous exercise is limited by the high flow rates required of the circulating pump to avoid resistance and rebreathing. The pump would have to match peak respiratory flow velocities of approximately 500 l./min attained under these circumstances and the absorption of carbon dioxide would become inadequate. FLEISCH[8] has solved this problem by introducing a " double-coupled spirometer ". The spirometer bell (*Fig. 4*) is divided into two equal chambers by a partition. One chamber is connected to the expiratory tube, the other to the inspiratory side. With this modification the circulation rate in the system can be reduced to one-half of the peak flow velocity of breathing. Assuming the subject inhales 8 l./sec and the pump ventilation supplies only 4 l./sec, the remaining 4 l./sec are gained from chamber (I) of the spirometer which simultaneously releases 4 l./sec from the other chamber (*E*) downstream to the pump. There is no flow in the expiratory tube, *Te*, at this time and consequently no rebreathing.

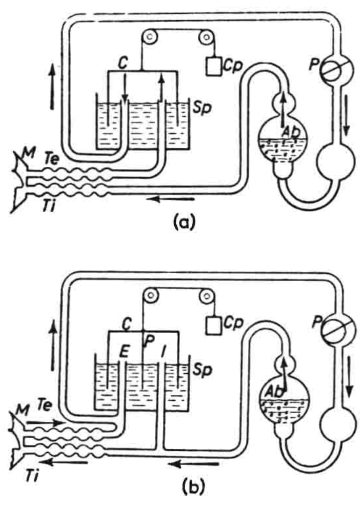

Fig. 4. (*a*) *Standard spirometer circuit with pump* (*P*) *and carbon dioxide absorber* (*Ab*). (*b*) *double-coupled spirometer. M = mask; Te = expiratory tube; Ti = inspiratory tube; C. = bell; Cp = counterbalance; E = expiratory chamber; I = inspiratory chamber.* (FLEISCH[8]).

In the original type of closed circuit spirograph it is necessary to fill the spirometer system with high concentrations of oxygen, as otherwise the oxygen removed by the subject from a relatively small volume would lead to hypoxia in a short time, particularly in studies involving physical activity. A normal inspiratory oxygen tension is desirable in most clinical function tests and precise control of oxygen tension is a necessity in respiratory research. The closed circuit technique has, therefore, been modified in various ways to meet these requirements. One method[9,10] is to add oxygen from a second spirometer into the circuit initially filled with air in such a manner that the end-expiratory level on the spirogram tracing remains constant. This arrangement can also be used to produce either hypoxia or hyperoxia in the subject by the proper control of oxygen added to the system. Disturbance of the spirograph record by the intermittent addition of oxygen can be avoided by a simple gear mechanism suggested by v. TAVEL[11] whereby the differential movements of both spirometers are recorded. Fully automatic oxygen stabilizers with electrical controls have been designed by WIESINGER *et al.*[12], ROSSIER and WIESINGER[13], FLEISCH[8] and VAN VEEN *et al.*[26]. Another technique introduced by DONALD and CHRISTIE[14] lends itself well to studies breathing air or gas mixtures of any desired composition (*Fig. 5*). It furnishes a record of tidal and cumulative

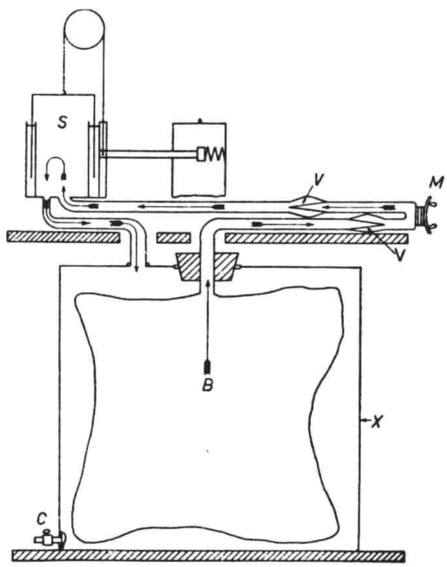

Fig. 5. Spirometer circuit of DONALD *and* CHRISTIE[14]. *S = recording spirometer; M = mouthpiece; V = valves; B = light rubber or plastic bag of 80 l. capacity in metal drum or box of 100 l. capacity; C = stopcock. Direction of airflow indicated by arrows.*

ventilation and either oxygen consumption or the expiratory exchange ratio of CO_2 and O_2. The operating principle is similar to that of DUSSER DE BARENNE and BURGER[15] in that inhaled and exhaled gas are kept separate in a common closed pneumatic system. This is accomplished by conducting the expired gas from the spirometer into a rigid tank of approximately 100 l. which also contains a light rubber or neoprene bag of comparable capacity filled with air or the desired mixture for inhalation. Two or more such tanks can be used in sequence to switch from one to the other. In the absence of a carbon dioxide absorber, as shown in *Fig. 5*, the slope of the spirogram indicates the respiratory exchange ratio, provided the functional residual capacity of the subject does not change. By absorbing carbon dioxide on the expiratory side, oxygen consumption can be registered as in