

Meetings

Pharmacology of General Anesthetic Agents

At the recent symposium "Pharmacology of General Anesthetic Agents," which was held in conjunction with the meetings of the Federation of American Societies for Experimental Biology in Atlantic City on 17 April 1963, John W. Severinghaus (University of California) challenged present opinions when he suggested that general anesthetic agents exert no direct pulmonary effects, and that they are respiratory stimulants, presumably through action of the central nervous system, when given in concentrations providing light to moderate depth of anesthesia. Data supporting this thesis include the fact that the tachypnea associated with the administration of trichloroethylene or ethyl ether persists after vagotomy, that the pulmonary surfactant is not changed by anesthetics, and that the anesthetics are not known to alter tone in pulmonary blood vessels. Severinghaus pointed out that at the time of deepest sleep a normal individual's arterial carbon dioxide tension increases on an average of 9 mm-Hg and that one is therefore justified in regarding as a respiratory stimulant any anesthetic which maintains arterial $p\text{CO}_2$ below 50 mm-Hg. All of the anesthetic drugs studied by this group to date have produced this result when used in concentrations providing moderate depth of anesthesia. The general anesthetics do flatten the CO_2 response curve, but despite a marked reduction in the respiratory response to carbon dioxide, low or normal values for arterial $p\text{CO}_2$ have been found.

One possible site of action of the anesthetics, so far as respiration is concerned, may be an area described by Fink and co-workers in the rostral mid-brain of cats. Here an "awakeful stimulus" to respiration, unrelated to carbon dioxide, appears to exist; when the region is freed of inhibitory influences, tachypnea results and breathing is not influenced by CO_2 .

The alveolar-arterial $p\text{CO}_2$ gradient

in normal awake man is 1 mm-Hg. In most subjects and with most general anesthetics this gradient increases, occasionally reaching 15 mm-Hg or more. Severinghaus indicated that at least a partial explanation for this may be pooling of blood in dependent areas of the lung. He also suggested that the increased inspired oxygen associated with the administration of many general anesthetics may contribute to the gradient through relaxation of pulmonary vasculature and through partial restoration of perfusion to underventilated alveoli, a mechanism which would run counter to the normal control of ventilation-perfusion ratios.

At the same symposium, Henry L. Price (University of Pennsylvania) described the diverse effects of general anesthetics on the circulation. For example, ether decreases arterial pressure and increases cardiac output; thiopental decreases arterial pressure with little or no change in output; and halothane decreases both. Cyclopropane, on the other hand, increases arterial pressure with or without an elevation in cardiac output. Price reported on methods designed to study these hemodynamic actions in man and animals. Animal studies include perfusion of the dog head (isolated except for nerves from the remainder of the body), injection of solutions containing general anesthetic agents directly into pressor and depressor areas in the medulla, confinement of anesthetics to the pressoreceptor area of the carotid sinus, perfusion of the dilated heart, and placement of strips of aorta in solutions containing anesthetics. Experiments with human subjects illustrated the effect on hemodynamics of interruption of the sympathetic nerve supply to the heart by means of bilateral stellate ganglion blockade, and of increasing venous return and right atrial pressure by infusion or elevation of the lower extremities.

Cyclopropane appears to reduce the activity of medullary depressor mechanisms by a direct action, although the data of Wang and his associates

cast some doubt upon this. Such a finding would explain much of the circulatory response to cyclopropane, for the relatively unchecked pressor area would permit the release of norepinephrine from sympathetic endings. This humoral agent increases in the plasma linearly with increased concentration of the anesthetic. Medullary depressor area inhibition would explain the increase in forearm, splanchnic, and renal vascular resistance known to occur during administration of cyclopropane. To indicate the paradoxes evident as one studies the circulatory actions of anesthetics, Price reported that cyclopropane sensitized the pressoreceptors of the carotid sinus. Such an action alone should lead to reduction in arterial pressure rather than the hypertension so frequently observed.

Halothane decreases arterial pressure, total peripheral resistance, forearm, splanchnic, renal, and cerebral vascular resistance, and appears to sensitize the pressoreceptors. Findings associated with the generalized depression of circulatory functions include depression of the heart, a less responsive vasomotor center, and minimal mobilization of norepinephrine. A key issue that remains is whether perfusion of such tissues as the gastrointestinal tract, liver, heart, and brain is better during administration of cyclopropane or halothane.

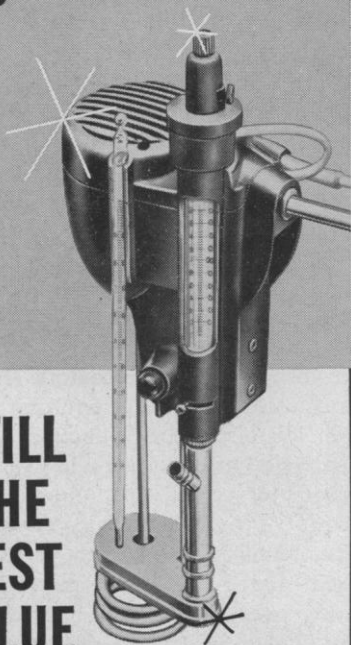
Leroy D. Vandam (Harvard University) reviewed the present knowledge of the effects of general anesthetics on metabolism. He commented upon the lack of information on such essential items as total metabolism of oxygen and of metabolism of the heart, liver, and kidneys. Robert Epstein (Columbia University) presented data on the uptake, distribution, and elimination of inert gases.

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Stereology Congress

The problem of reaching or testing inferences about three-dimensional properties from observations made in plane sections occurs in many natural sciences. It is the specific concern of the International Society for Stereology, an organization formed in 1961 largely through the efforts of H. Elias (Chicago Medical School), H. Haug (University of Erlangen), and A. Hennig (Univers-

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ity of Munich). The new society has just held its first congress (Vienna, Austria, 18–20 April 1963) a 2½-day meeting in the course of which more than 40 technical papers were delivered. About half the papers were immediately concerned with anatomy and histology, and the bulk of the remainder dealt with either metallurgical or mathematical topics. Abstracts and preliminary manuscripts received in time were published in a proceedings volume distributed to members at the meeting; simultaneous translation in English and German was available throughout the technical sessions; and despite dreadful overcrowding of the program no parallel sessions were held. The subject matter ranged from geometrical probability to the interpretation of electron microphotographs of brain and nerve tissue.

Both the society and its congress seem of particular interest as experiments in communication. At the moment the society has 128 members, of whom 55 were registered at the congress. Throughout most of the technical session the audience included more than 40 of these. These figures reflect a very high level of membership participation, but of course it remains to be seen whether this level can be maintained as the society grows. The usual escape from the intellectually deadening atmosphere of the large society convention is the small “by-invitation-only” symposium, dedicated to intensive discussion of a single subject. There are advantages in this scheme, but there are also advantages in the normal society organization which we are perhaps sacrificing unnecessarily. Small scientific “craftunions” purposely cutting across the “industrial-union” rationale of the major professional societies might provide communication channels combining the advantages of continuing organization with those of the small ad hoc symposium.

The range of subject matter was so great and the opportunity for informal discussion so limited by language difficulty and excessive crowding of the program that specific interdisciplinary collaboration was hardly to be expected. Probably the principal effect on most of us was a rather general intellectual stimulation. It is exciting, for instance, to speculate about the possibility that the descriptive techniques and vocabulary of structural petrology might find application in the study of the orientation of cells and fibers in nerve tissues, and that, similarly, the behavior of

geological materials in the plastic flow leading to isoclinal folding might find parallels in the development of convolutions in brain tissues. Interactions of this sort—and most participants experienced one or more of them—are immensely satisfying. They probably would have been more numerous had there been more opportunity for informal, off-the-floor discussion.

At the close of the technical session the organizing committee was relieved of its functions and the first business meeting of the new society elected a full set of officers, with H. Elias as its first president. The second meeting, scheduled for spring of 1966, will be held on the campus of the University of Florida, at Gainesville. F. Rhines, (University of Florida Metallurgical Research Laboratory) is in charge of program and meeting arrangements.

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Genetics: Molecular Structure and Function

A symposium on molecular studies on the structure and function of genes was a highlight of the 8th annual meeting of the Genetics Society of Canada, held at Ottawa 18 to 20 March. Topics as diverse as cereal-crop breeding and cytogenetics, genetics of vegetable crops, mutation, radiation genetics, medical genetics, genetics of swine, poultry genetics, *Drosophila* genetics, and the genetics of microorganisms were discussed.

The annual invitational lecture, delivered by Bruce Wallace (Cornell University), dealt with the genetic structure of *Drosophila* populations. He discussed the bearing of his studies upon evolutionary theory. His data indicate that mutation may not be as harmful as is often thought, for heterozygotes are, on the whole, adaptively superior to both kinds of homozygotes.

I. Takahashi (Central Experimental Farm, Ottawa) discussed his work on the DNA of bacteriophages ϕBS1 and ϕBS2 . Although this DNA appears to have a typical double-helix structure, the bases include uracil rather than thymine, a characteristic usually associated with RNA. Also, glucose is attached to the cytosines and guanines. M. Ycas (State University of New York) spoke on “Reading the gene” and em-