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Editorial Views

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The Ontogeny and Phylogeny of Medical Journals

THAT ONTOGENY recapitulates phylogeny is a truism which comes as no surprise to physicians. That the phenomenon may not be restricted solely to animate creatures may, however, come as a surprise. Take medical journals, for example. A glance at the shelves of a medical library, especially its historical section, reveals a curious fact: journals appear to grow. That they grow in girth is well recognized. But they also grow in height, in the dimensions of their pages. They do so not gradually, like a growing organism, but suddenly and spasmodically.

The earliest example of this hitherto unreported phenomenon can be seen in *Lancet*. *Lancet* started publication in 1823 with pages measuring 5 by 8¼ inches. In March of 1844 it suddenly appeared with 7¼ by 10½ inch pages, a size it has retained to the present. The same thing happened to the *Boston Medical and Surgical Journal*. It started in 1829 with small pages. In 1868, years before it transmogrified into the *New England Journal of Medicine*, it, too, suddenly shifted to the present, familiar 8 by 11 inch pages.

The frequency with which journals change with age from small to large is so great as to suggest the phenomenon is no mere mutagenic quirk affecting but one journal but instead represents a process of growth and development common to the whole phylum of *Medicojournaliensis*. Within the last decade this has become particularly evident. Indeed, essentially all major journals of clinical medicine today have pages approximately 8 by 11 inches in size even though almost all originally started with substantially smaller pages.

One exception to this trend has been the anesthetic literature. English-speaking and, with one exception, major foreign-language anesthesia journals have been and still are printed on small pages. With the present issue of ANESTHESIOLOGY this tradition is shattered. After much deliberation, and with all due respect for the sensitivities of its readers (to say nothing of the symmetry of their bookshelves), the decision was made some months ago, before the change in editorship, to move ANESTHESIOLOGY from the 6¾ by 10 inch league to the 8 by 11 inch league.

Lancet did not, when they announced the reasons for their changes in 1844, consider the possibility that they were dealing with an inherent ontological phenomenon. This can be forgiven because of the embryonic state of the phylogenology of medical journals at the time. Instead, the editors offered the prosaic, if hardly modest, explanation that the increase in page size was initiated to increase circulation and thereby, because of the manifest wisdom contained within each issue, to improve the quality of medical care throughout the British Empire. This salubrious change in the state of the world's health would be brought about, it was explained, because the increase in page size permitted the cost per copy to drop from eight pence to sixpence. The twopence saving would do the rest.

The editors of ANESTHESIOLOGY are loath to invoke ontogony (or phylogeny) as an explanation for the change in page size of ANESTHESIOLOGY. To do so might affront readers already affronted enough by the change. Nor can the editors explain their action on the same basis *Lancet* used in 1844. To tie the increase in page size to a lowering of the present subscription price of $15 per year (for 12 copies!) might or might not further accelerate the growth curve of subscribers, but to do so would

certainly establish ANESTHESIOLOGY as a major eleemosynary institution, and that is not one of the editorial objectives of ANESTHESIOLOGY.

No, the increase in page size of ANESTHESIOLOGY must realistically be ascribed purely and simply to economic factors. The larger page size will afford modest savings in the cost of printing the same amount of information. More important, the increase in page size will enable ANESTHESIOLOGY to retain its competitive edge for advertisers' dollars. Advertisers enjoy larger pages, the better to offer their messages. Advertisers not only like larger pages, however: in this day and age they have to have them to include all the fine print that federal regulations demand be printed for so many products of interest to anesthesiologists. The FDA requirement that pharmaceutical manufacturers essentially reproduce package inserts makes it almost impossible for the reader to grasp an advertiser's message if it is restricted to a 6¾ by 10 inch page.

Changing times require changing formats. But the reader can rest assured that though the form changes the substance will remain the same. ANESTHESIOLOGY will continue to present all that is new, all that is significant, and all that is valid in the art and science of anesthesiology. Perhaps we, like the editors of *Lancet*, can say in future years: "We now have ample reason to be satisfied at the resolution we adopted, and for congratulating ourselves on the soundness of the views [on page size] which we have entertained."

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Towards the Molecular Bases of Anesthetic Action

IN THE EARLY SIXTIES, Professor D. K. de Jongh could write of pharmacologists' concepts of the receptor[1]:

> To most modern pharmacologists the receptor is like a beautiful but remote lady. He has written her many a letter and quite often she has answered the letters. From these answers the pharmacologist has built himself an image of this fair lady. He cannot, however, truly claim ever to have seen her, although one day he may do so.

Today, acetylcholine receptors can be obtained, and purified in high yield, in the test tube. The existence of high concentrations of receptor in the specialized organs of certain electric fish, together with the use of certain components from snake venom that bind specifically with high affinity to the receptor, paved the way for this achievement. The pharmacologist can now test his old image against reality.

In our attempts to understand the bases for anesthetic action we are, however, still in the romantic age. The problem is in many ways more difficult: there is no receptor, and there is very little structural specificity to guide us. There are, however, a number of advantages: the agents themselves are extremely simple molecules and we therefore know a good deal about how they behave in different environments; we recognize that only the simplest physical forces are involved in anesthetic action; inhaled agents reach equilibrium readily with the brain so that we have a very good idea of the levels involved during anesthesia, and the dose–response curves are so steep that accurate values of anesthetic potency can be readily obtained.

The complicated nature of the central nervous system poses us an additional experimental problem; we may sidestep this problem biochemically with brain homogenates (a comparatively underutilized approach), or we may apply an electrophysiologic approach to simpler peripheral nervous systems, as was done in the classic work defining the synapse as the site most sensitive to anesthetic action. Happily, however, the advantages cited in the last paragraph make feasible an approach based on testing physical models against data obtained in the intact animal. In many ways the situation is analogous to that facing the early pharmacologists of whom Professor de Jongh wrote. They obtained defined conditions of drug concentration by perfusion of, for example, isolated neuromuscular junctions and, using this approach, built up a model of drug–receptor interactions that later proved to be quite accurate in certain particulars. Their model did not prove there were receptors, but it was consistent with that assumption. After a while a number of models, all requiring receptors but differing in detailed assumptions, appeared, and it often proved difficult to distinguish between them. Finally, isolation of the acetylcholine receptor resolved some of these questions.

The observations of Meyer and Overton led to the first, and most successful, model of anesthetic action, which bears their names. Many other models have been postulated, but when careful tests, using the widest possible set of experimental data, are made, the lipid-solubility hypothesis is vindicated. Dr. Robert Kaufman reviews this approach in this issue of ANESTHESIOLOGY. It is interesting to note how far this so-called physicochemical approach can be taken when an accurate data base is available for comparing the predictions of rival models. Nonetheless, a number of models pass the test unless a very critical choice of anesthetics is made;