THE CONTRIBUTION OF MDIBL TO COMPARATIVE PHYSIOLOGY

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At the 1st International Congress of Comparative Physiology and Biochemistry (August 27-31, 1984, Liège, Belgium), five senior investigators were invited to present reports on their work at MDIBL; other colleagues from the Laboratory gave short communications. This record, and the yearly reports of MDIBL investigators in the Bulletin attest to the fact that over more than 8 decades MDIBL has played a role in Comparative Physiology. A detailed account of the Laboratory's contribution to the understanding of renal function has been given by Bodil Schmidt-Nielsen (The Physiologist 26:261-266). We wish to point out here MDIBL'S involvement in two other fields:

Until some 10 years ago, the physiology underlying the formation of cerebrospinal fluid and aqueous humor was unknown. This has now been clarified due to experiments chiefly on the dogfish (*Squalus acanthias*) by demonstrating the primary role of HCO_3^- formation (Maren, T.H., Am. J. Physiol. 222:885-899, 1972). The basic work could not be done in mammals due to complications of sampling fluids and renal and respiratory function. However, after the initial work has been done in fish, it proved possible to design the proper experiments in mammals, where the identical mechanism was found (Vogh, B.T., and Maren, T.H. Am. J. Physiol. 228:673-683, 1975).

In recent years, the comparative physiology of the cornea has received considerable attention. The unique problem of maintaining corneal hydration (and hence the transparency of its stroma) differs in terrestrial mammals and in fish, where the cornea has to adapt to varied osmotic pressures between the aqueous humor and the environment. Studies on the basic problems, i.e. the pump functions of the epithelial layer, the properties of the stroma and corneal endothelium (Fischer, F.H., and Zadunaisky, J.A., Exp. Eye Res. 25:149-161, 1977; Ubels, J.L., and Edelhauser, H.F., Cur. Eye Res. 2:613-619, 1983) have contributed to the present understanding of the corneal physiology.

The above record of MDIBL might also be viewed as a challenge to maintain this standing in Comparative Physiology in the future. An appraisal of the role of the comparative approach in physiological studies may therefore be pertinent.

In his introductory remarks at the Congress, Prof. K.A. Munday (Univ. of Southhampton, England) outlined the aims of Comparative Physiology as follows: "Comparative Physiology proceeds from a collection of data in different species and phyla to an integrative view of biological phenomena." This comprehensive statement invites comments concerning the implications of the term "integrative view" which may find differing interpretations amongst the broad spectrum of physiologists. These different approaches reflect the basic questions underlying a concrete biological project (cf. Krebs, H.A. and Krebs, J.R. Comp. Biochem. Physiol. 67B:379-380, 1981), i.e., whether the aim is the clarification of physiological mechanisms or interest in its survival value.

1. Some would view integration as arising from an analysis of the interaction of different species and phyla with their environment, with the ultimate aim of tracing the evolution of a given physiological function. MDIBL is familiar

with such an approach, e.g., in the conceptual framework of Dahlgren's work (Dahlgren, U., and Kepner, W.A. Textbook of the Principles of Animal Histology. Macmillan, New York, 1908).

2. On the other hand those interested in physiological (including biochemical and biophysical) processes per se, would seek the integrative role in tracing those mechanisms which are broadly shared in living nature. Interest in the elucidation of physiological mechanisms characterized the contributions of MDIBL investigators at the Liège Congress. Such approach is a corrolary to the August Krogh principle: "For a large number of problems there will be some animal of choice...., on which it can be most conveniently studied (Krogh, A., Am. J. Physiol. 90:243-251, 1929). H.A. Krebs in his essay (J. Exp. Zool. 194:221-226, 1975) provides numerous examples where the application of Krogh's principle led to major progress in biological sciences.

Conceptually, the approach to Comparative Physiology, as outlined in point 2, is based on the assumption that basic mechanisms of physiological phenomena are similar in a broad variety of phyla; other, less efficient mechanisms, which may have developed would have been eliminated in the course of evolution. Hence it is a matter of careful selection by the experimenter which species should be chosen for the study of a given problem. The belief in the basic Unity of Physiology may be traced to I. Newton's statement (1686): "Natura enim simplex est" (Nature is pleased with simplicity) (Newton, I., Philosophiae naturalis principia mathematica, Vol. II, p. 160, Ed. Symmonds, London, 1803) and he implied in the preface to this treatise that the mathematical principles used to study the movement of celestial bodies, and the described forces of nature may also apply to other phenomena: "I wish we could derive the rest of phenomena of nature by the same kind of reasoning from mechanical principles; for I am induced by many reasons to suspect that they may all depend upon n forces by which particles of bodies, by some causes hitherto unknown, are either mutually impelled towards each other, or are repelled and recede from each other; .....but I hope that the principles here laid down will afford some light either to that or some truer method of philosophy" (Philosophiae ..., Vol. I, p. b2, Ed. Symonds, London 1803). The principle of Unity in Biochemistry (Kluyver, A.J. & Donker, H.J.L., Chemie d. Zelle u. Gewebe 13:134-190, 1926) has been accepted as a valuable heuristic tool in biochemical investigations. A student of transport physiology is impressed by the emerging knowledge that in all species and phyla studied so far, a broad diversity of physiological processes can be accounted for by the operation in polar epithelial cells of the sodium pump (and possibly some other "minor" ionic pumps), a handful of cotransport and exchange processes, and relatively few conductive pathways. Thus, the absorption and secretion of fluids, secretion of acids or alkaline solutions, concentration or dilution of fluids, all operate using the same limited number of basic components and diversity is rather an expression of quantitative aspects and spacial orientation.

It should be pointed out here that the converse of Krogh's Principle may also be valuable: Observations on physiological phenomena on any species on the evolutionary scale may be relevant also for the highly developed mammals. A case in point may be studies on the role of quaternary ammonium salts and allied organic bases in osmoregulatory processes. Studies on elasmobranchs, initiated at MDIBL by H. Smith and by R.P. Forster (c.f. Cohen, J.J., Krupp, M.A. and Chidsey, C.A., III, Am. J. Physiol. 194, 229-235, 1958) some 27 years ago, now find correlates in the physiology of the renal medulla (Balaban, R.,S. and Knepper, M.A., Am. J. Physiol. 245, C439-C444, 1983). Again, the same basic mechanisms are used in widely differing phyla in response to similar demands made on the cells, tissues and organisms.

The special value of the "right animal" emphasizes the importance of the comparative approach as a heuristic tool in the broad experimental strategy of studies of physiological phenomena. The search for the right animal is an important rationale for investigators leaving their well-equipped and organized laboratories at their home institutions, and coming to MDIBL in order to study the mechanisms of physiological phenomena in species not readily available year round.

Attention should now be drawn to problems concerning the choice of the "right" biological material for the given problem. A survey carried out at MDIBL in 1963 by Drs. H.G. Borei and H . Khouw concentrated on marine invertebrates and listed 69 species; the supply catalog of an Eastport company names 50 commercially available invertebrate sp. A list, on file at the MDIBL office indicates that, in addition to invertebrates, 17 marine and 3 fresh-water fish sp., as well as 4 amphibia, 1 turtle, 7 local birds and 2 local mammals (excluding conventional laboratory mammalian species) are available to investigators. The above data invite an inquiry into which biological material is especially abundant in the area of Frenchman's Bay and is available for experimentation. As to the use of available material: A search of the Bulletins from 1978-1983 shows that MDIBL investigators used 9 invertebrate species, 15 fish sp., 6 amphibian sp., and 4 other vertebrates; several species, 15 fish sp., 6 amphibian sp., and 4 other vertebrates; several species were particularly popular: Of 243 reports, the winter flounder (*Pseudopleuronectes americanus*) was the experimental animal in 52 studies; the skate (*Raja erinacea*) was favored in 41 reports, and the dogfish (*Squalus acanthias*) was clearly dominant (117 reports).

These data raise the question whether we sufficiently know and are making the best possible use of the "treasure house of nature" around MDIBL. Both Krogh and Krebs, and also A. V. Hill in his challenge to biochemists, (Biochim. Biophys. Acta. 4:4-11, 1950) emphasized that physiologists should seek help from zoologists in finding the most appropriate species for their studies. When envisaging the future for MDIBL, is this not a point to be considered?

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