Meetings

Pituitary Hormones: International Colloquium

The zoological specificity of hypophysial hormones and their actions was the subject of a colloquium held 16–20 July 1968 in Paris under the auspices of the French National Center for Scientific Research and the National Museum of Natural History. The primary motivation for this meeting came from M. Fontaine, director and professor of comparative physiology at the museum, and Y.-A. Fontaine, whose own studies on this topic are extensive. Some of the major reports and shorter papers that comprised the colloquium are summarized below.

In a review of the chemistry of the major neurohypophysial (neural lobe) hormones, especially those from "lower" vertebrates (isotocin, mesotocin, and glumitocin), R. Acher (Paris) assessed the pharmacological evidence suggesting the presence of a mixture of mesotocin and oxytocin in the cobra (Pickering), of oxytocin in *Rana pipiens* (Munsick), and of oxytocin in the African lungfish (W. H. Sawyer). Acher did not find any chemical evidence for the presence of oxytocin in any of these species; in each case only mesotocin (along with arginine vasotocin) was found. The actions of neurohypophysial hormones were surveyed by H. Heller (Bristol), who emphasized the extreme sensitivity of some receptors (10^{-14} g of arginine vasotocin per milliliter is sufficient to promote contractions of the chicken oviduct). He also delineated the limited evidence for effects of these hormones in fishes, but did point out the increase in urine flow in fishes (including the Dipnoi) produced by isotocin and arginine vasotocin. Reported effects on gill function in fishes may be secondary to responses of the gill vascular supply, according to J. Maetz and J. C. Rankin (Villefranche). In aquatic amphibians, even more than in fishes, the functions of the neurohypophysial peptides remain unknown (P. Bentley, New York). The mechanism of action of these peptides was reviewed by S. Jard and F. Morel (Paris), who emphasized the importance of cyclic 3′,5′-adenosine monophosphate in mediating their effect on water transport. Of great interest was the report by K. Jost and J. Rudinger (Prague) that the disulfide bridge was not essential for biological activity of oxytocin and hence could not be directly involved in its mode of action.

C. H. Li (San Francisco) summarized the work of his laboratory on the chemistry and biological activities of adrenocorticotropic hormone (ACTH), melanocyte-stimulating hormone (MSH), and especially ovine beta- and gamma-lipotropins (LPH). Gamma-lipotropin, a polypeptide of 58 amino acids, appears to be a fragment of β-LPH, but no conditions have yet been found to convert the latter into the former. C. Mialhe and B. Koch (Strasbourg) reviewed their work on the comparative aspects of pituitary-adrenal interrelations, as exemplified by studies on stimulation of adrenal growth and steroidogenesis by mammalian ACTH, feedback inhibition of ACTH secretion by administered glucocorticoids, the effects of hypophysectomy on steroidogenesis, and the effects of inhibitors of steroid hydroxylation reactions in the adrenal of ACTH secretion. Particular emphasis was given to the finding of a number of workers (Phillips; deRoos and Gist) that reptilian adrenals fail to respond by steroidogenesis to ACTH administration, suggesting a significant degree of independence from pituitary control. Independence of thyroid function from pituitary control also was described for some amphibian species by Rosenkilde (Copenhagen).

In the sessions on growth hormones and prolactins, A. E. Wilhelmi and J. B. Mills (Atlanta) compared the details of growth hormone chemistry and suggested the existence of a monomer unit (molecular weight, approximately 22,000) for all mammalian species. The resemblances include a peptide containing 54 amino acids, 42 of which are in identical positions in porcine and human growth hormone, a similar "ground plan" of these two molecules, and general similarity at the COOH-terminals of all growth hormones (except for one less arginine in human growth hormone). The chemical basis for the biological differences and species specificities among the growth hormones appears much more subtle than originally thought. Some recent data from C. H. Li's laboratory concerned the helical nature of human growth hormone (50 percent α-helix) and demonstrated that both -S-S- bridges can be reduced and reacted with iodoacetamide with little effect on either the somatotropic (rat tibia) or prolactin-like (cropsac) activity. Earlier, however, Wilhelmi had indicated that the same treatment of porcine growth hormone resulted in complete loss of activity. E. Knobil (Pittsburgh) reviewed the species specificity problem with respect to growth hormones. The failure of the hypophysectomized guinea pig or its isolated diaphragm to respond to any growth hormone, including its own, remains enigmatic; the fact that growth in this animal is partially independent of the pituitary (30 percent of normal) may be explained by the proliferation of cells resembling those of the pars tuberalis in the sella turcica after hypophysectomy.

H. A. Bern and C. S. Nicoll (Berkeley) considered the biological specificity of prolactins and emphasized that fish prolactins, like tetrapod prolactins, can induce waterdrive in efts and sustain hypophysectomized euryhaline teleosts in fresh water, but, unlike tetrapod prolactins, are not able to induce typical cropsac and mammary gland responses. The reality of the "partial" prolactins of fishes was emphasized by these workers, as well as by J. N. Ball and D. M. Ensor (Sheffield), who also delineated precisely the sodium-conserving activity of prolactins in teleosts. Ball and Ensor have developed a biological assay for prolactins, based on the linear dose-response curve obtained from measurements of sodium ion in blood in hypophysectomized *Poecilia* injected with prolactins (of teleost, frog, or mammal origin). The adrenocorticotropic effect of prolactins in some teleosts—*Gambusia* (Chambolle) and *Fundulus kansae* (Fleming)—but not in others—*Poecilia* and *Fundulus heteroclitus* (Ball)—was also noted. Other effects of prolactin, including its role with corticosteroids in brood-pouch maintenance in male sea horses (Boisseau), its ability to cause release of thyroid-stimulating hormone (TSH) in eels (Olivereau), and its contribution to brood-patch formation in quail (Gourdji and Tixier-Vidal) were considered.

Fewer chemical data are available

for the group of pituitary glycoprotein hormones, TSH, luteinizing hormone (LH or ICSH), and follicle-stimulating hormone (FSH), than for any of the other pituitary hormones, and questions can still be raised concerning the purity of present preparations. The complete review of the chemistry of mammalian thyrotropins (TSH) by P. G. Condliffe (Paris and Bethesda) and by J. G. Pierce and his collaborators (Los Angeles) was thus very useful. With a few exceptions (concerning the possible presence of tryptophan and glucose in bovine TSH) the analytical data from the two laboratories were in reasonable agreement, but the two speakers currently hold different views concerning the important question of whether the native TSH molecule (with a molecular weight of approximately 25,000) consists of subunits. The findings of Condliffe concerning the behavior of reduced carboxymethylated TSH during gel filtration suggest that TSH may be analogous to LH in that more than one peptide chain may be present (see below); however, the end-group and sedimentation-equilibrium data of Pierce and co-workers point toward a single peptide chain with a molecular weight of 25,000. Analyses of the fractions obtained by gel filtration should solve the apparent discrepancy. Double-diffusion studies showed various degrees of immunoreactivity among thyrotropins of different mammalian species, but none was found between LH and TSH by this technique. However, with their radioimmunoassay system, G. Rosselin, P. Freychet, and J. Dolais (Paris) stated that some common immunological sites are shared by gonadotropins and TSH, as reported by others.

Y.-A. Fontaine (Paris) considered the zoological specificity of thyrotropins, reporting the inability of hypophysial extracts from eels to stimulate mouse thyroid gland or sheep isolated thyroid cells, whereas both mammalian (bovine) and eel material can stimulate the trout thyroid. However, if fish TSH (carp) is used in very large quantities, mammalian thyroids will respond, but the activity on mammals is about 1/300 that observed on the trout. Lungfish material affects both mouse and trout thyroids much as does bovine TSH. An inherent thyrotropic activity (that is, heterothyrotropic) of mammalian gonadotropins in fish is apparent.

M. Jutisz and P. de la Llosa (Paris) reviewed their work on the separation of two subunits in the gonadotropin LH by urea, guanidine, or acid (*p*H 3), and their recombination into an active molecule, an achievement which has also been reported by Papkoff and Samy. Luteinizing hormone is beginning to yield some significant sequence data (Ward, Papkoff), but these were not discussed. Some disagreement still exists among workers on mammalian LH's even with respect to composition, with considerable discrepancies noted in the values for carbohydrate content.

A. V. Nalbandov (Urbana) expressed his belief that in higher vertebrates FSH and LH were either released together (revival of an old idea) or formed a complex in the blood which acted on the target tissues. The need for more than mammalian FSH and LH to promote ovarian maturation in the chicken points either to a possible essential third gonadotropin, serving as a factor maturing the follicle, in the chicken pituitary, or to a recognized chicken gonadotropin which has this function as well. The activities of gonadotropins from and in other vertebrate groups were considered at some length. A particularly interesting report on the purification and properties of a gonadotropin from carp was given by E. Burzawa-Gerard (Paris). This material, which gives excellent responses in several biological assays in lower vertebrates, does not elicit any responses in standard tests for mammalian gonadotropins such as the Parlow and Steelman-Pohley assays. Its composition is significantly different from that of any known mammalian gonadotropin.

I. I. Geschwind (Davis) marshaled the evidence for the existence of four major families of hormones: the neurohypophysial hormones, the ACTH-MSH-LPH complex, the glycoprotein hormones, and growth hormone–prolactin. Except for the first group, neither the amino acid sequence of any nonmammalian pituitary hormone, nor of any glycoprotein hormone or prolactin, has been elucidated, and therefore it would be premature to attempt to develop lines of molecular evolution for these hormones. The proceedings of the colloquium will be published by the French National Center for Scientific Research.

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