Diabetes insipidus in Man

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Drug Dosage
The authors and publisher have exerted every effort to ensure that drug selection and dosage set forth in this text are in accord with current recommendations and practice at the time of publication. However, in view of ongoing research, changes in government regulations, and the constant flow of information relating to drug therapy and drug reactions, the reader is urged to check the package insert for each drug for any change in indications and dosage and for added warnings and precautions. This is particularly important when the recommended agent is a new and/or infrequently employed drug.

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This book is the first attempt to provide a comprehensive clinical overview of the disease diabetes insipidus. It is remarkable that this disease which was distinguished from diabetes mellitus by the famous ‘taste test’ of Willis [1] as early as 1664, and has contributed greatly to advances in medical science, has not previously been the subject of an extensive review. A few historical landmarks illustrate the impact of basic research on understanding neurohypophyseal endocrinology. The studies of Bernard [2] that discrete lesions in the hypothalamus produced an effect on the kidney (1849) was an original demonstration of the role of the nervous system in control of peripheral organ function. It was subsequently
shown that lesions in the hypothalamus, in the median eminence, or in
the posterior pituitary might produce disorders of diabetes insipidus and
the neurohypophysis was, for a time, thought to be a 3-part organ [3]. It
was eventually shown the 3 parts were all a single gland originating in the
hypothalamus and ending in the posterior lobe. The concept of neurosecretion
and axon flow of neuropeptides was based on this organ as described
in the classic studies of Scharrer and Scharrer [4] and the signal
contribution of Bargmann and Scharrer [5] who proved conclusively that
section of the pituitary stalk resulted in accumulation of neurosecretory
material on the brain side of the section. Bargmann’s studies used the
chrome-hematoxylin-phloxine stain which Gomori [6] had used on pancreas
and identified the classic neurohypophyseal system. More recently
use of antibodies for immunohistology was described and again studies
of the neurohypophysis became the model for identification of peptide
hormones within nerve cells [7]. These studies have led to the identification
of a vast innervation of the nervous system by peptidergic neurons

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and the physiologic significance of these multiple interventions is only
beginning to be unraveled.
Possibly because of the large size of the magnocellular neurons, the
discrete anatomic location, and the ease of demonstrating a physiologic
effect (antidiuresis, pressor activity, uterine contraction, or milk ejection)
the cells were a ready target for neurophysiologists and have
provided the most detailed correlation of nerve cellular electrical activity
with physiologic effect [8]. In studies of biosynthesis, vasopressin was
hypothesized to be synthesized as a prohormone [9] before the more
widely known description of synthesis of insulin as proinsulin. The prohormone
has now been conclusively documented by the isolation of the
gene which produces vasopressin, neurophysin and the glycopeptide of
the posterior pituitary.
Therapy of diabetes insipidus has been equally illustrative. Extracts
of the posterior pituitary were shown to have antidiuretic activity in
patients with diabetes insipidus in 1913 [10,11] and were further demonstrated
to produce antidiuresis in normal subjects. These reports were
one of the first uses of replacement hormone therapy which became
known in the early 1900s as ‘organotherapy’. In more recent years
L-desamino-8-D-arginine-vasopressin (DDAVP) has been used to treat
this disorder. DDAVP is a model of the ability of molecular pharmacology
to specifically tailor a drug which will enhance the desired
effects and decrease the undesired effects [12].
These few highlights are not meant to be a comprehensive review of the history of the neurohypophysis and the references cited are of necessity highly selective. Nonetheless, they do illustrate the critical role that the study of the posterior pituitary has played in medical history. It is on this background that the editors convened an international congress in Paris, France, in January 1984, to provide a clinical and scientific update of the major disease of the posterior pituitary, diabetes insipidus.

We acknowledge the support of Ferring AB, Malmö, Sweden, and of USV Pharmaceuticals of Revlon Health Care, USA, who sponsored the symposium. The excellent organization by the secretary of the congress, Sophie Battarel, made the symposium possible.

Les Gets, January 1984
P. Czemichow
A.G. Robinson

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1 Willis, T.: Cerebri anatome: cui accessit nervorum descriptio et usus (Flesher, London 1664).