The YEAR BOOK of

Endocrinology

1977

Editor
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Table of Contents

The material covered in this volume represents literature reviewed up to November, 1976.

Questions for Clinicians

1. What is some new evidence for an intracellular action of insulin? (p. 171)
2. What condition is associated with an insulin-receptor disorder? (p. 189)
3. What besides beta cell adenomas may account for hyperproinsulinemia? (p. 193)
4. What catastrophic condition may *Pseudomonas aeruginosa* cause in diabetics? (p. 197)
5. How does Hb A_{Ic} relate to diabetes? (pp. 199–202)
6. Are kidney transplants in diabetics subject to diabetic nephropathy? (p. 204)
7. Is insulin absorbed better subcutaneously than intramuscularly? (p. 207)
8. Which is more susceptible to damage from pancreatitis – the alpha cell or the beta cell? (p. 212)
9. In what condition is hyperkalemia associated with hyperglycemia? (p. 213)
10. What easily missed problem may occur in the joints of juvenile diabetics? (p. 217)
11. What substance is very useful for control of calcium metabolism in patients with chronic renal failure? (p. 73)
12. What is likely to become an important source of 1α, 25-dihydroxycholecalciferol? (p. 77)
13. What is a severe dermal complication of the deranged calcium and phosphate metabolism of chronic renal failure? (p. 78)
14. What essential metabolite appears to be lacking in both hypoparathyroidism and pseudohypoparathyroidism? (pp. 83 and 85)
15. What may be an uncommon complication of maternal hypoparathyroidism? (p. 86)
16. How does magnesium deficiency cause hypocalcemia? (p. 90)
17. What may accentuate the effect of calcitonin in treatment of hypercalcemia? (p. 97)
18. What may be a skeletal complication of smoking? (p. 99)

Introduction

How to Edit a Year Book

This editor has discovered, on trips to and from airports and at meetings, that many of his colleagues are curious about what is involved in producing annually a volume like the Year Book of Endocrinology. His response has been highly variable, ranging from a self-deprecatory dismissal to a lecture on the enormous talent that is required to do the job properly. In casting about to pick a topic for this year's Introduction, the editor thought it worthwhile to set the record straight in a reasonably dispassionate manner. Then future inquiries can be referred to what is detailed below.

By far the most difficult task in editing a Year Book is getting asked. In the present case, the editor knew nothing of the process; the invitation came as a complete surprise and he was too diffident to ask the publisher, now long retired, how the decision was made.

Once the job is accepted and the initial terror of public exposure as a fraud subsides, it turns out that the mechanics of editing are surprisingly easy. The publishers are extraordinarily helpful. They supply, in the form of whole journals, tear-outs or reprints, essentially all the endocrinology literature of the English language journals and most of that of the Scandinavian, French, German, Spanish, Italian, Swiss and Dutch. Unfortunately neither they nor the editor have access to the eastern European literature except that which gets published in western journals. There may be easy access to Oriental journals, but no concerted effort to translate them is made. Selection of foreign (I am sorry that "foreign" is such an *alien* word in medicine) language articles is eased somewhat by the fact that the editor's knowledge of French is good, of German, fair, and of English summaries, excellent.

The material arrives in packages and boxes at preset dates throughout the year. The editor looks through this

mass (he has never made the effort to determine how many articles are processed per year). He does *not* attempt to read every article, holding the unalterable opinion that there is a great deal of "junk" in medical literature. Those articles selected for further scrutiny are retained, those destined for Dr. Will Ryan's assessment are turned over to him and much of the remainder is returned to the publishers to be sent to other YEAR BOOK editors, if pertinent. The candidate articles, those which have survived the first cut, are scrutinized carefully and a final selection made. The articles selected are returned to the publishers who send them to professional abstracters. These individuals in general perform an excellent job. When their work is completed, the abstract is proofread and it, together with the original article, is returned to the editor. He checks to see that the abstract includes points of emphasis that he had indicated in the original article as well as the inclusion of tables or figures that he had selected. He also double-checks that the abstract makes sense. He then arranges the articles in an order which provides chapters and sections and, finally, dictates what he believes to be trenchant, insightful and witty comments. He proofreads the typewritten comments, sends the completed material back to the publishers, checks the galley proofs and then collapses.

In performing his functions, the editor must set, implicitly at least, certain goals, although he may find it difficult to judge with what success he meets them. Above all he feels that he should include those aspects of medicine which should interest a *clinical* endocrinologist. He tries to make his selections international; indeed, other things being equal, he holds a bias in favor of articles published outside the United States. He does not slavishly honor priorities of authorship and attempts to stay removed from the sometimes vicious controversies surrounding them. He tries to select the best work along with a sprinkling of inferior performances to be used as object lessons. He attempts to monitor selections so that a measure of continuity is built into the completed text. He sometimes provides an "instant symposium" in an area of particular interest. He keeps current a file of articles that had become candidates but were not finally selected. He increasingly refers to these candidate

articles in his comments to provide a better bibliography for those who would use the YEAR BOOK to gain access to the literature in a specific area. Further, with the increasing costs of publication, it has been necessary to reduce modestly the total number of articles abstracted; therefore, the luxury of an instant symposium is less often available. Instead the editor will try to compress the symposium into a comment on a single article. The editor makes the assumption that his personal taste in the endocrinologic literature reflects that of most of his colleagues. Having no particular subspecialty interest in endocrinology, he saw himself from the inception of his function (1964–65 YEAR BOOK, p. 5) as "an endocrinologic 'man in the street.'" Lastly, he has felt it not only his prerogative but also his responsibility to reveal in his comments his view of medicine, his family and the world. He agrees with those who insist that total objectivity in editorial functioning is impossible. He operates from the general tenet that therapeutic medicine (as distinct from preventive or social medicine) is a process by which a physician helps a damaged person to repair himself, knowing that for most disorders the reparative forces of the patient are far more powerful than those of the physician. The editor does not try to foment controversy but he does not hesitate to take a stand on controversial issues.

There are hazards in editing a YEAR BOOK. The opportunities to be wrong are plentiful. The editor occasionally encounters resentment because of the omission of someone's favorite article and, infrequently, the editor is favored by hostile letters ranging from the caustic to the vituperative because of comments seen as unfavorable or unfair. He has yet to be physically assaulted.

Advantages? Well, "It's a good way to keep up with the literature." It provides an extraordinary and continuing opportunity to voice an opinion on just about anything. And, finally, it is one of the areas that permits the editor and his wife to work together. She types the dictated comments and her task is often difficult. Sometimes his voice is overwhelmed by background music, sometimes she is dismayed by his verbosity or frivolity. A few days ago she said, wearily, "Maybe you ought to make more of those comments that say, 'A good study. Look ahead!'" The editor closes with a

quote of the last sentence to his first Introduction, "The editor wishes to express deep gratitude to his wife, without whose help this YEAR BOOK certainly *could* have been completed – but it wouldn't have been much fun."

THEODORE B. SCHWARTZ, M.D.

The Hypothalamus and the Anterior Pituitary

General

Phytoestrogens: Adverse Effects on Reproduction in California Quail are described by A. Starker Leopold, Michael Erwin (Univ. of California, Berkeley), John Oh (Univ. of California, Hopland) and Bruce Browning[1] (California Dept. of Fish and Game, Sacramento). The California quail breeds irregularly in the more arid parts of its range but vigorously when rainfall is generous, the rains nourishing a rich carpet of forbs that supply greens and seeds for quail consumption. The breeding success of arid-land quail has been linked to the hepatic storage of vitamin A obtained from green foods. Phytoestrogens in subterranean clover inhibit breeding in domestic sheep and also might regulate quail breeding.

Leaf samples of plants eaten by quail were analyzed for phytoestrogens and four isoflavones were identified in several samples, including biochanin A, genistein, daidzein and formononetin and coumestrol. Subclover extract fed to penned quail resulted in later and lesser egg production (table). The extract contained high amounts of biochanin A and genistein and a medium amount of formononetin. Analyses of wild quail crop samples showed evidence of formononetin and genistein in foods eaten during a dry year when breeding was poor and the near absence of these compounds during a wet year when quail breeding was excellent. Large amounts of greens and insects were consumed in the wet year and only modest amounts of stunted plants were eaten in the dry year.

The presence or absence of phytoestrogens in the foliage of annual plants may be a coordinating factor in quail reproduction with the prospective available food resource. A luxu-

(1) Science 191:98–100, Jan. 9, 1976.

EFFECTS OF DIET ON EGG PRODUCTION

Diet	Feeding period (month/day)	Onset of egg laying	Eggs per pair (No.)
Turkey starter*	10 March to 6 June	8 April	62
Low energy, low protein†	3 March to 30 June	8 May	28
Turkey starter plus subclover extract‡	3 March to 30 June	2 June	12

*Containing 26% crude protein.
†Low-protein diet contained 15% crude protein.
‡Containing biochanin A, genistein and formononetin.

riant forb growth produces abundant seeds to nourish the young quail in the next year. The seed crop in a dry year would probably be inadequate to support a large crop of young.

[Greetings from your annual (but not yet superannuated) commentator. I'm beginning to feel like one of our perennial tulip bulbs. Let's hope that this year's bulb will not be dim. . . .

This first article is not exactly what one would call "clinical endocrinology," but I couldn't resist including it as an elegant example of endocrinologic ecology. In a dry year there are more phytoestrogens and more quail infertility so that fewer birds have a better chance of surviving on the scant food supply. In a wet year, the converse is true. It almost, but not quite, makes me feel more kindly toward "the pill."

It is a striking demonstration of *conservation* in its truest sense. The feedback is *anticipatory* and prevents waste while preserving balance.—T.B.S.] ◄

β-Lipotropin as a Prohormone for the Morphinomimetic Peptides Endorphins and Enkephalins. Recently the isolation of novel oligopeptides of whole brain or hypothalamus-neurohypophysis origin, endowed with biologic characteristics similar to those of opium alkaloids in bioassays and stereospecific binding assays, has been described. β-Lipotropin (β-LPH) is a homomeric 91-residue polypeptide isolated from the pituitary of a variety of species, the physiologic significance of which has been obscure. Larry H. Lazarus, Nicholas Ling and Roger Guillemin[2] (Salk Inst., La Jolla, Calif.) determined the morphinomimetic activity of several synthesized fragments of β-LPH and analogues. Bioassays used the myenteric plexus-longitudinal muscle of the guinea pig ileum, and binding to synaptosomal opiate

(2) Proc. Natl. Acad. Sci. U.S.A. 73:2156–2159, June, 1976.

receptors was examined. Synthetic peptides were prepared by a solid-phase method.

Even at high doses, β-LPH had no morphinomimetic activity in bioassays. Incubation of β-LPH with an aqueous extract of rat brain generated opioid activity, which was increased by naloxone. In the opiate receptor binding assay, competing activity displacing ^{3}H-etorphine was observed after incubation of β-LPH with aqueous brain extract, but intact β-LPH had no significant activity. In both assays, prolonged incubation with the brain extract led to disappearance of the activity. The peptides competed with etorphine in the synaptosomal binding assay in a manner paralleling the effects of levorphanol or normorphine. Some of the β-LPH fragments tested had definite opioid activity. The active fragments included the tetrapeptides H-Tyr-Gly-Gly-Phe-OH and H-Tyr-Gly-Gly-Phe-Met-NH_2.

Incubation of β-LPH with aqueous brain extracts at neutral pH generates peptides with morphinomimetic activity. The likely biogenesis of the neurotropic peptides is reminiscent of that of the angiotensins. It will be of major physiologic importance to characterize, locate and study the regulation of the several enzymes involved in the multiple cleavages of β-lipotropin that yield the neurotropic peptides.

► [Astonishing! It is somehow fitting that an article on lipotropin was the first selection made by this editor at the beginning of his tenure (1964–1965 YEAR BOOK, p. 7). We said then "How important it may be, in physiologic control of metabolism or other pathologic states, remains hypothetical." Thirteen years later we learn that it is a prohormone. Endorphins and enkephalins are fragments of the β-lipotropin molecule. They, among others, have been shown to be far more potent analgesics than morphine or heroin. What part do they play in the body's economy? Are they involved in the genesis of manic-depressive psychosis? Of sleep? Of schizophrenia? Of orgasm? We think so. Are we on the threshold of defining emotion in neurobiochemical terms? We think not. Man remains more than the chemicals of which he is composed (to coin a sentence). To think otherwise is, in our view, a reductionist hope of those whose drive to understand man and nature drives them to simplistic conceptions.

Incidentally, "synaptosomal" opiate receptors refers to in vitro preparations of nerve endings (see the 1976 YEAR BOOK, p. 12).

If you feel bombarded by words like "endorphin" and "enkephalin," how does "bombesin" grab you? Look below.—T.B.S.] ◄

Distribution of a Bombesin-Like Peptide in Human Gastrointestinal Tract was investigated by J. M. Polak, S. R. Bloom, S. Hobbs, E. Solcia and A. G. E. Pearse.[3] For one

(3) Lancet 1:1109–1110, May 22, 1976.

group of amphibian skin peptides, the bombesin family, no mammalian counterpart has been identified. Bombesin has powerful effects on mammalian gastric acid secretion, pancreatic secretion, intestinal myoelectric activity and smooth muscle contractility. Evidence suggests presence of bombesin-like material in the intestinal mucosa and an increased plasma concentration after food ingestion.

Fresh specimens of human gastrointestinal mucosa, including pancreas, were obtained at operation and freeze-dried for indirect immunofluorescence staining with antibodies to pure bombesin. Cells specifically stained with bombesin antibodies were seen in all areas of the gastrointestinal mucosa studied, predominantly in the basal parts of the glands; they were more numerous in the duodenal mucosa. "Bombesin cells" were not seen in sections of pancreas. The cells apparently were not identical with the gastrointestinal enterochromaffin cells. Immunofluorescence staining was abolished by preincubation with the bombesin, tyrosine nonapeptide of bombesin, but not by vasoactive intestinal peptide, somatostatin, substance P or gastrin, even in very high concentrations.

Bombesin may be important in controlling gastric acid secretion. Its pathophysiology in such conditions as duodenal ulceration and its importance in control of pancreatic secretion need investigation. Work is under way on the effect of pancreatic dysfunction on cells producing bombesin-like substance. The pharmacology of amphibian skin peptides promises to lead to discovery of a new mammalian hormonal system.

► [New hormones are surfacing like mosquito larvae in a sylvan pool, a strained analogy but forgivable because bombesin was first found in frog skin. Here we see that this tetradecapeptide is found in specific cells in intestinal mucosa. Deschodt-Lanckman et al. (J. Clin. Invest. 58:891, 1976) studied the effect of bombesin and some analogues on rat pancreatic fragments. They found that these peptides stimulated amylase secretion and calcium efflux, actions very similar to cholecystokinin-pancreozymin (CCK-PZ). Basso and associates (Gut 16:994, 1975) infused bombesin in man and found similar effects with great augmentation in amylase and trypsin secretion. These workers could not be certain whether bombesin functioned by stimulating CCK-PZ secretions or by stimulating its activity directly. An answer comes from Conturek et al. (J. Physiol. 257:663, 1976), who found that bombesin exerted its pancreatic effects not directly, but by stimulating the secretion of CCK-PZ.

Why all these interlocking controls of intestinal function? It looks like endocrinologic overkill, but I suspect in time it will make sense.—T.B.S.]