**Letters**

Letters to the Editor should be typed double-spaced (including references) with conventional margins. The overall length is limited to five manuscript pages, including not more than one figure or one table.

---

**"Hook-Effect" In a Patient with a Gonadotropin-Secreting Tumor**

To the Editor:

Two-site or "sandwich" immunoradiometric assays (IRMA) offer theoretical advantages over competitive immunoassay systems for sensitivity, precision, and rapid incubation. However, practical realization of these advantages has been limited by the phenomenon of the "high-dose hook effect," in which high concentrations of an analyte give similar responses to those of much-lower concentrations. Here we report a patient with excessive secretion of lutropin (LH) and follitropin (FSH), which was masked by spuriously low assay values for the gonadotropins.

In June 1988, a 25-year-old woman was referred to the Department of Neurosurgery for bitemporal visual field impairments due to a large intracranial suprasellar tumor. Her previous medical history included ovarioectomies in 1982 and 1983 due to increasing cystic tumors in both ovaries. Since then, she had been on constant estrogen replacement therapy (1.25 mg of conjugated estrogens per day). She was otherwise asymptomatic, and the suprasellar tumor was removed by cranial surgery.

The pre-operative assessment of the endocrine pituitary function revealed increased basal values for LH and FSH combined with a paradoxical decrease in LH concentration after stimulation with gonadotropin (GnRH, 0.1 mg intravenously). Concentrations of other pituitary hormones were normal in the basal and stimulated states. The estradiol concentration was 283 ng/L. We determined LH and FSH with "MAIA-clone" kits supplied by Serono, Freiburg, F.R.G., according to the manufacturer's instructions. The kits are IRMAs with two monoclonal antibodies that recognize the respective epitopes of both hormones. Standard curves are linear up to 200 and 150 int. units/L, respectively. Values exceeding this range are identified and samples must be diluted and the assay repeated. In the kit instructions the manufacturer indicates the possibility of a high-dose hook effect for LH and FSH above a concentration range of 400 and 1000 int. units/L, respectively.

Figure 1 illustrates LH and FSH concentrations in the patient's serum, diluted and undiluted. Although the FSH values of the undiluted specimens are registered as being outside the standard curve, the measured LH values are decreasing. Only the diluted specimens show clearly that the true concentrations are 15 to 20 times higher than values for the undiluted ones. After GnRH administration these values increase considerably.

The initially determined results for basal and stimulated LH and FSH concerned us, because they revealed a quite unusual situation. The increased basal values could be explained by the functional menopause after bilateral ovarectomy and estrogen replacement treatment. However, the paradoxical decrease in LH hinted at a method-dependent hook effect. When we repeated the determination with 20-fold diluted samples, the results for the basal and stimulated LH and FSH values revealed excessive gonadotropin secretion. These laboratory findings, together with the clinical symptoms, confirmed the diagnosis of a gonadotropin-producing tumor of the pituitary gland. Retrospectively, we can speculate that the patient's bilateral cystic ovarian tumors were already a pathological consequence of the endogenous gonadotropin excess induced by the pituitary adenoma; however, hormone data from the time of ovarectomy are not available.

The hook effect is gaining importance as more and more monoclonal antibodies are being used in modern test systems designed as "sandwich" assays. Various theories as to the causes of the hook effect and various methods to avoid it have been developed (surveyed in 1). In general, this artifact can be prevented by decreasing the sample volume or by modifying the one-step assays to a two-step procedure (2).

The possibility of a method-dependent hook effect must be considered carefully, because this methodological problem might contribute to a delayed diagnosis, with hazardous clinical consequences.

References


Nicolaus Dahlmann
Karl A. Brensing
Dietrich Klingmüller
Frank Bidlingmaier

Instit. für Klinische Biochemie
Universität Bonn
Stegmann-Freud-Straße 25
5300 Bonn 1, F.R.G.

Cord Serum Thyrotropin and Birth Weight in a Normal Japanese Population

To the Editor:

Orinda et al. (1) described an inverse relationship between thyrotropin (TSH) concentration in cord blood and birth weight of normal newborn infants in Kenya. They suggested that the high TSH in babies with low birth weight...