[1, 2]. It is, however, a common observation in those patients that the response of plasma testosterone to the application of hCG is diminished, a condition termed "latent androgen deficiency" [3].

The mechanism causing this diminished response is unknown. It is assumed that normal Leydig cell function depends on pulsatile stimulation by the hypophyseal LH-secretion. Therefore we studied this pattern in men with sexual impotence. In 10 patients and 10 healthy men of the same age, blood samples were taken at 20-min intervals over a period of 8 hours. The test persons were lying in bed during the observation period. The blood samples were centrifuged, stored at −20°, and assayed for LH by RIA.

Similar basal LH-values (1.2–5 mU/ml) were observed in both groups. An average of 3 (2–4) LH-peaks appeared during the observation period. They had a relative height of 2.3 to 5.5 above the basal levels in both groups.

Thus a specific pattern of LH-secretion could not be demonstrated in the patients. It is unlikely that diminished stimulation of the Leydig cells by the hypophysis causes the finding of "latent androgen deficiency" in sexual impotence.

References

156. HCG-induced hyperthyroidism in a patient with testicular cancer

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In patients with gestational trophoblastic neoplasia, an association between high human chorionic gonadotropin (hCG) levels and hyperthyroidism is well established. However, no reports of the same association in males with hCG-secreting tumors of the genital tract have been published.

We report a case of hCG-induced hyperthyroidism in a patient with a malignant testicular tumor. A 28-year-old male was referred to our clinic after orchectomy for a testicular tumor. A malignant trophoblastic teratoma was found histologically. On admission the patient presented with bulky disease (stage IVCL3, Royal Marsden Hospital Staging Classification), was severely ill and cachectic, but there were no unequivocal clinical signs of thyroid dysfunction except for cachexia due to the malignant disease. The thyroid gland was not palpable, and the patient had not had previous medication. Thyroid hormone serum concentrations were determined as part of the routine laboratory tests on admission.

Before initiation of chemotherapy, extremely high serum hCG concentrations of 1080,000 U/l were measured and high serum thyroxine (T4) levels of 15.5 µg/dl (normal range 4.5–13) and an increased effective thyroxine ratio (ETR) of 1.28 (normal range 0.87–1.13) were found. TSH secretion was completely suppressed [basal TSH: 1.2 µU/ml; stimulated (30 min after 200 µg TRH i.v.) TSH: 1.3 µU/ml]. The Tc-pertechnetate thyroid scan showed an organ of normal size with normal tracer uptake. The immunological tests (thyroglobulin antibodies, microsomal antibodies, TSH-receptor antibodies) were all negative.

After chemotherapy with vinblastine, bleomycin and cis-platinum a marked decrease in serum hCG levels was observed; 12 days after the onset of chemotherapy, serum hCG concentrations were 84,000 U/l and serum T4 (9.8 µg/dl) and ETR (1.08) had returned to the normal range. In addition, the TRH-test normalized (TSH 0 min: 1.8 µU/ml; 30 min: 4.3 µU/ml). Serial determination of T4 and ETR during the following months of chemotherapy showed normal values and a gradual decline in serum hCG levels (the patient is still under chemotherapy).

Examination of 3 additional patients with malignant trophoblastic teratoma and very high serum hCG levels (400,000, 700,000 and 800,000 U/l) revealed normal thyroid function.

The presented case report is suggestive of hCG-induced hyperthyroidism in a patient with testicular cancer, since the elevated thyroid hormone serum concentrations and the suppressed TSH secre-
tion normalized after chemotherapy without specific antithyroid medication and in correlation with decreasing serum hCG levels. Obviously only extremely high hCG levels (over 100,000 U/l) seem to be able to induce thyrotoxicosis since the other patients with high hCG levels showed normal thyroid function.

157. Acidic choriogonadotropins obtained from patients with testicular tumors are not uniform in biologic and structural properties

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As we have shown earlier [1,2] patients with testicular cancer may produce variants of choriogonadotropin (hCG) which differ from placental hCG by very low isoelectric points (<3.9) in the following denominated hCGav.

hCGav populations were isolated from the urine of 9 patients by ultrafiltration, ion-exchange chromatography (DEAE- and SP-Tris-acryl-M), chromatography on Biogel AcA 44, and preparative isoelectric focusing (IEF) in the pH range 3–6. Receptor binding activity was determined with a radioligand receptor assay using rat testis homogenate. Biologic activity was assayed by means of the stimulation of testosterone biosynthesis of purified mouse Leydig cells. In some cases the amount of substance available allowed quantitation of the sialic acid content with the thiobarbituric acid method.

In all cases so far investigated, the hCGav were microheterogeneous in IEF. The isoelectric points (pi) of the predominant hCGav bands ranged from 3.4–4.2, whereas the 6 main bands of placental hCG showed pi's form 4.1–4.7. Incubation of hCGav with neuraminidase (EC 3.2.1.18) was used to determine the contribution of sialic acid to the negative charge of the hCGav; in one case (U.R.) the desialylated form showed a pi-value of 9.4, appeared to be a single band in IEF and thus was not discernible from placental hCG. In another case (B.J.) even prolonged incubation caused only a shift of the whole band pattern (pi 3.5–4.5) into the region of pi 5.0 indicating that in addition to sialic acid other residues were responsible for the strong negative charge of these hCGav. This result also corresponds to the relatively low sialic acid content (2.3–7.1%) of the 4 fractions of B.J. In contrast to placental hCG where isolated bands exhibit a higher biologic activity the lower their pi is, single hCGav bands isolated from a certain patient in most cases show increasing biologic activity with increasing pi. The biologic activity of hCGav varied within a large range: one group displayed biologic activities of 600–3,000 IU/mg, an intermediate group those ranging between 4,000 and 8,000 IU/mg, and a third had biologic activities in the range of purified placental hCG (12,000 IU/mg) or even higher. Concerning receptor binding activities, we also found variations over a broad range. Receptor binding activity and biologic activity seem to be correlated.

When compared to placental hCG, the molecular weight of the hCGav subunits was increased in some cases. However, subunits with smaller and higher apparent molecular weights may occur within the same patient.

Determination of the N-terminal amino acids of hCGav showed end groups different from those known from placental hCG as well as the known N-termini.

Conclusion: The results show the large heterogeneity of the biologic and structural properties of the acidic variants of choriogonadotropin synthesized by human testicular tumors.

References