When the external genitalia of these two fetuses were examined, the urethral orifice was still on the under-surface of the penis, while in fetuses of crown-rump length of 8 cm it had approached the tip of the glans. The mean plasma testosterone concentration of the 6 fetuses with crown-rump length of 8 cm was 302 ng/100 ml, range 252–379 ng/100 ml. In fetuses of crown-rump length of 10 cm or longer, the urethral orifice appeared to be in the normal adult position. These results confirmed those of Glenister (1954).

Discussion

When the fetal plasma testosterone levels and the position of the urinary meatus are correlated it can be suggested that the transposition of the orifice to the tip of the penis is associated with rising levels of testosterone. On a fetus of 8 to 10 cm in crown-rump length when there is a reactive proliferation at the anterior extremity of the urethral plate (Glenister, 1954), the levels of testosterone are high and steady and drop well after the completion of the male external genitalia.

These findings do not prove that the positioning of the urinary meatus is dependent on fetal androgen levels in the human, as the high testosterone concentration and the transposition of the meatus may just be a coincidence in timing, but evidence from animal experiments using both anti-androgens and antiserum against testosterone suggests more than a close association.

Neumann *et al.* (1969), using the androgen antagonist cyproterone acetate in dog fetuses, found that the first sign of an androgen deficiency was the presence of hypospadias, while Goldman *et al.* (1972), who injected antiserum to testosterone into pregnant rats from 13 to 20 days of gestation, found that the male offspring had hypospadias. Thus it can be suggested in man that because high levels of testosterone are present in the fetus at the time of urethral formation, some cases of glandular hypospadias are caused by an androgen deficit. It is realized that this hypothesis may only apply to a small number of cases as a cause of hypospadias. It may well be that there is a lack of tissue response to normal levels of testosterone. Nevertheless, in the human this correlation of the high and rising androgen levels with the development of the urethra is reinforced by the available animal evidence.

Summary

Animal experiments strongly point to testosterone being implicated in the differentiation of the fetal male external genitalia. Plasma testosterone levels in human male fetuses are significantly higher than

those found in female fetuses just at the time of urethral formation in the male fetuses, suggesting that testosterone in the human may be implicated in the differentiation of the male external genitalia and that its lack may be important in some cases of glandular hypospadias.

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Iodide sialadenitis in childhood

Intravenous pyelography is frequently used in the investigation of renal disease in childhood. This is generally a safe procedure, though anaphylactic reactions may follow the intravenous injection of iodide (Tucker and Di Bagno, 1956). A rare occurrence, however, is painful swelling of sub-mandibular or parotid glands known as iodide sialadenitis. This has been reported previously in adults but not hitherto in children (Nakadar and Harris-Jones, 1971; Sussman and Miller, 1956).

Case report

An 8-year old girl presented with a 6-month history of intermittent right loin pain, dysuria, pyrexia, and vomiting. She was noted to be pale but examination was otherwise negative. Routine analysis of her urine showed no abnormality and culture was sterile. In view of her history she was admitted for further investigations. These showed Hb 12.9 g/100 ml, WBC 9200/mm³, erythrocyte sedimentation rate 15 mm/1st hour, urea 28 mg/100 ml, creatinine 0.6 mg/100 ml, uric acid 4.2 mg/100 ml. Serum electrolytes and plasma proteins were normal and her urine remained sterile.

An intravenous pyelogram was performed using 20 ml Conray 280 (a total dose of 5.6 g iodine). The child vomited during the injection of contrast but showed no immediate anaphylactic reactions. There was prompt excretion of contrast from both kidneys which showed normal pyelograms. 24 hours after the investigation the child complained of right-sided facial pain and developed a unilateral, localized swelling of the right parotid gland but was afebrile. There was local tenderness with erythema, unilateral conjunctivitis, photophobia, and lacrimation. Iodide allergy with sialadenitis was diagnosed and diphenhydramine hydrochloride 50 mg, 3 times daily, was started and the swelling subsided within 3 days. Mumps antibody titres showed negative results (mumps S+V antibody, titres 1/8 in both acute and convalescent sera).

Comment

In addition to renal clearance, inorganic iodide is removed from plasma by the breasts, the thyroid, the stomach, and the salivary glands (Mason, Harden, and Alexander, 1966). Though the salivary glands trap substantial amounts of iodide, this accumulation is independent of thyroid function (Fellinger *et al.* 1956; Gabrielsen and Kretschmar, 1956).

Iodide sialadenitis, a painful swelling of the salivary glands, has been reported after infusion pyelography in a uraemic adult (Nakadar and Harris-Jones, 1971). This was associated with a conspicuous rise in plasma inorganic iodide, but these workers also showed the presence of similarly raised levels in reversible renal failure with no clinical evidence of salivary gland enlargement. Furthermore, the plasma inorganic iodide remained raised until the ureteric obstruction responsible for the renal failure was relieved. Though the pathogenesis of iodide sialadenitis is uncertain, it seems, therefore, to depend upon individual sensitivity and not upon the absolute level of inorganic iodide. This was not measured in our patient, but with normal renal function and after a standard amount of contrast medium, a prolonged rise in plasma inorganic iodide seems unlikely.

A review of published reports revealed only 6 cases of iodide sialadenitis, 5 were adults with apparently normal renal function and one case was in a uraemic adult. The condition followed either oral or intravenous iodide. The glandular swelling occurred typically within 48-96 hours of iodide administration and clinical resolution was complete by the 7th day, as in our patient. In the 6 reported cases, the adenitis was either unilateral or bilateral and involved the submandibular or parotid glands, though 1 patient experienced abdominal pain with vomiting and coexistent pancreatitis was diagnosed. However, in none of these cases was

mumps excluded by appropriate serological investigation.

Tucker and Di Bagno (1956) reviewed 2000 cases given intravenous iodide for pyelography but found no case of parotitis within this group.

Despite the relative infrequency of this form of salivary gland enlargement, iodide sialadenitis should be considered in the differential diagnosis of acute submandibular or parotid swelling in childhood. A history of recent intravenous pyelography suggests the diagnosis, but in this context it should be remembered that iodide-containing proprietary cough mixtures can be freely purchased by parents, unknown to their family doctor. A careful drug history should be obtained, therefore, in all cases of acute salivary gland enlargement where the clinical features or history seem atypical.

Summary

An 8-year-old child developed an acute swelling of the right parotid gland after intravenous pyelography. The possible relation of this sialadenitis to iodide sensitization is discussed.

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Bilateral renal venous thrombosis Recovery after peritoneal dialysis

Renal venous thrombosis is a well-recognized entity of early infancy, 60% of cases occurring in babies under the age of 2 months. The thrombosis originates in the small intrarenal veins (Johnston,