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Prostacyclin and cyclic AMP synthesis by the penis of the diabetic rabbit

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Introduction: Diabetes mellitus (DM) is a major risk factor for the development of erectile dysfunction. To investigate the role of DM in the pathogenesis of erectile dysfunction we developed a rabbit model in which we investigated whether DM elicits deleterious effects on two variables involved in the erectile process; prostacyclin (PGI_2) and cAMP.
Materials and methods: Non-ketotic DM was induced in New Zealand white rabbits using alloxan. After 6 months, six diabetic and six age-matched control rabbits were killed and their penises excised. All diabetic rabbits had a plasma glucose > 20 mmol/L compared to controls (mean = 6·6 mmol/L). The corpus cavernosum was dissected out and cut into disks approximately 2 mm thick. The disks were then incubated at 37°C in the presence of a range of stimulators of PGI_2 and cAMP synthesis. Tissue cAMP and PGI_2 (as 6-oxo-$PGF_1\alpha$) release were measured by radioimmunoassay.
Results: PGI_2 release in response to acetylcholine (Ach) and adrenaline (adren) but not arachidonate (AA) was significantly reduced in the penis of rabbits with DM compared to controls. Cyclic AMP synthesis in response to forskolin (FK) and PGE_1 was also significantly reduced in the diabetic penises.

pg 6-oxo $PGF_{1\alpha}$ / mg tissue / min, mean (SD)						pmol cAMP / mg tissue / min, mean (SD)			
Ach (10^{-6}mol/L)		adren (10^{-6}mol/L)		AA (10^{-6}mol/L)		FK (10^{-7}mol/L)		PGE_1 (10^{-7}mol/L)	
C	D	C	D	C	D	C	D	C	D
28 (3)	8 (1)*	24 (4)	10 (2)*	35 (3)	33 (3)	20 (2)	14 (1)*	18 (2)	13 (1)*

C = control D = diabetc * $P < 0.01$

Conclusions: These data show that: 1) receptor-linked PGI_2 and cAMP synthesis is markedly impaired in the penis of the diabetic rabbit, which in turn may contribute to erectile dysfunction as the PGI_2-cAMP axis mediates relaxation of vascular smooth muscle and 2) the rabbit constitutes a useful model for assessing the impact of DM on the biochemical systems that control erection.

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Primary retro-peritoneal teratoma in men; treated with chemotherapy followed by excision of the residual mass

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Introduction: Primary retro-peritoneal teratomas are rare and usually present as a large abdominal mass. Although in some the primary tumour may arise from the testis and then regress, others are thought to arise from vestigial testicular remnants within the retro-peritoneum. The results of primary surgical treatment of these tumours has been disappointing. These tumours are sensitive to contemporary chemotherapy regimens although a residual mass is often present following this.
Patients and methods: A consecutive series of 14 men with primary retro-peritoneal teratoma (mean age 33 years, range 24–64) were referred to our unit. Four had atrophic testes that had been removed but revealed no primary tumour. Ultrasonography of the testes was normal in the remaining 10, four of whom had also had testicular biopsies that had revealed no malignancy or carcinoma *in situ*. In all cases, CT revealed a retro-peritoneal mass and tumour markers (AFP and/or hCG) were elevated in 12. Initially, each patient was treated with an intensive platinum-vincristine methotrexate-bleomycin/carboplatin-etoposide regimen and the response monitored by tumour marker assays. Following chemotherapy each patient had abdominal and thoracic CT scans.
Results: A residual retro-peritoneal mass was present in each case and metastatic disease was evident within the retrocrural nodes in three and the lung in two patients. Thoraco-abdominal extra-peritoneal exploration and excision of the primary tumour and metastases was performed in each case. The mean blood loss was 2·5 L (range 1·5–5·1). The median in-patient stay was 7 days and none of the patients had paralytic ileus. Histological examination of the resected specimen revealed active tumour in 12 cases and necrotic tissue in two. The mean follow-up period was 15 months. One patient had died as a result of a brain metastasis, the remaining patients are in remission.
Conclusions: Historically, the outlook for primary retro-peritoneal teratomas has been dismal, often because of late presentation and a low index of suspicion in making this diagnosis. However, early treatment with contemporary chemotherapy regimens followed by complete surgical excision of the residual primary and metastases can lead to prolonged remission.

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A conservative approach to bilateral testicular germ cell carcinoma

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Introduction: Bilateral germ cell tumours account for approximately 3% of all testicular malignancies. Bilateral orchidectomy is recommended as the therapy of choice, resulting not only in a lifelong dependency on androgen substitution but also in infertility. We examined whether another more conservative therapy exists which does not compromise the quality of life.
Patients and methods: From 1991 to 1995, 50 patients were treated for malignant germ cell tumour in our department. Bilateral malignancy developed in three patients (6%). One tumour occurred simultaneously and two tumours developed sequentially after 22 and 48 months. After pre-operative ultrasonographic localization of the tumour, the following operative technique was carried out: 1) Doppler ultrasonographic localization of blood vessels; 2) Cold ischaemia; 3) Enucleation of the tumour; 4) Biopsies of the remaining tumour margin and one biopsy distant from the tumour cavity; 5) Irrigation with distilled water; 6) Post-operative irradiation of the remaining testicle with a dose of 18 Gy.
Results: The follow-up was 48 months, 36 months and 6 months, respectively. Retroperitoneal progress, distant metastasis or a local recidive were not detected. The testosterone values were normal.
Conclusions: These results confirm that bilateral testicular germ cell tumours can be treated by organ-sparing surgery and that this clinically sufficient method preserves endogenous testosterone production. The disease-free follow-up underlines that carcinoma *in situ* can be treated by radiotherapy. A definitive statement is only possible after 10 years, because of the slow development of carcinoma *in situ* to a clinically manifest tumour. Careful controls should be performed every 3 months for 2 years and monitoring of LH and testosterone is necessary until normal values are documented.

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Human vas: a model for the α1a adrenoceptor

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Introduction: α adrenoceptor sub-types have been characterized by molecular cloning, radio-ligand binding and functional studies. Human vas smooth muscle contraction has been shown to be α1-mediated. Vas deferens is the most readily available human tissue that will allow reproducible experimentation on the α1 adrenoceptor sub-type.
Methods: Segments (1 cm) of vas obtained from routine vasectomy were placed in Krebs' solution, gassed with 5% CO_2 and 95% O_2 and maintained at 37°C. Tissues were set up at 1 g tension to equilibrate. Dose responses to phenylephrine alone and with antagonists, prazosin, WB4101, 5-methyl-urapidil, abanoquil, Tamsulosin, rauwolscine and chlorethylchloride (CEC) were obtained.
Results: Prazosin, WB4101, 5-methyl urapidil and Tamsulosin acted as competitive antagonists, yielding pA2 values of 8·8, 9·2, 8·8 and 10 (pKB). Rauwolscine and abanoquil produced little effect and failed to alter responses significantly. Incubation of tissues with CEC (10^{-4} mol/L for 20 min) did reduce maximum response to phenylephrine, but by only 32%.

Conclusions: The high affinity of 5-methyl urapidil, WB4101 and Tamsulosin, together with the relative failure of CEC to antagonise responses, indicates that the predominant α1-adrenoceptor mediating contraction of human vas is the pharmacologically defined α1a-adrenoceptor. These data are also consistent with those described for the cloned α1c-adrenoceptor, thereby supporting the hypothesis that the two receptors are identical. The human vas deferens therefore represents a readily accessible preparation for functional studies of the human α1a-adrenoceptor.

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The incidence of cystic fibrosis gene mutations in patients with congenital bilateral absence of the vas deferens (CBAVD) in Scotland

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Introduction: Congenital bilateral absence of the vas deferens (CBAVD) is an important cause of obstructive azoospermia. It is frequently associated with mutations of the cystic fibrosis transmembrane conductance regulator (CFTR) gene and is considered to be a genital-tissue specific form of cystic fibrosis. These mutations on the long arm of chromosome 7 include most commonly the mutation Delta F508. Many further pathogenic mutations have been identified and the number of mutations identified is increasing.
Patients and methods: We examined a series of 30 patients with CBAVD presenting with infertility for CFTR gene mutations. All of these patients were healthy and without clinical signs of cystic fibrosis.
Results: Eighteen patients (60%) were heterozygous for the Delta F508 mutation. Five of these showed other known mutations on the second allele (R117H × 3, G551D, P67L), while in 13 no second mutation was found. One further patient was homozygous for R117H. Two other patients were heterozygous for N1303K and G551D without mutation on the other allele.
Conclusions: In summary, 70% of our patients showed CFTR gene mutations while only 30% had no identifiable abnormality. This is one of the highest prevalences reported. Our results confirm that CBAVD is genetically linked with the cystic fibrosis genes in most patients. It is likely that unidentified cystic fibrosis gene abnormalities account for the remainder of patients. Thus, genetic counselling including partner testing is strongly recommended for all patients with CBAVD before considering *in vitro* fertilization methods.

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Action down the Y

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Introduction: Two years ago at the BAUS Annual Meeting we reported microdeletions on the long arm of the Y chromosome associated with azoo- or oligozoospermia. We identified a gene (YRRM) which was male-specific and highly conserved. Subsequently, a second gene has been identified by an American team, in the same area (DAZ gene). Both of these genes are mainly located towards the end of the long arm of the Y. We now wish to report a new area of deletion nearer to the centromere (Jolar area).
Results: We have identified deletions in this area in four of 117 patients with oligo- or azoospermia. Altogether there were seven of 117 patients with deletions in the YRRM/DAZ area and thus a total of 11 of 117 patients (9·4%) with microdeletions. We did not detect these deletions in fertile comparison populations.
Conclusion: This work suggests that microdeletions in the Y chromosome are a major factor in men with azoo- or severe oligozoospermia. As each man has only one Y chromosome, these microdeletions may be passed on if such men father male children using the newer IVF technologies. Genetic defects associated with male infertility are at least as common as chromosomal abnormalities in this context. Men considering intracytoplasmic sperm injection as a solution to severe male subfertility should be given information about these defects and their likely inheritance.

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Epididymectomy is useful in the management of post-vasectomy scrotal pain

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Introduction: Scrotal pain following vasectomy is an uncommon problem. Its treatment is mainly conservative and aimed at symptomatic relief. Epididymectomy has been described as a treatment but its effectiveness is unclear.
Patients and method: Fifteen patients (mean age 38·47 years, range 31–52) undergoing epididymectomy were identified and their clinical notes were reviewed. Details of presenting complaints, physical signs, findings from ultrasonographs and histology were evaluated against the outcome following epididymectomy.
Results: Fifteen patients underwent 18 epididymectomies (three bilateral and 12 single). All patients complained of severe scrotal pain; additional symptoms included groin pain (n = 1) and erectile dysfunction (n = 2), both dating from the vasectomy. All patients had uneventful vasectomy with no immediate post-operative complications. The time elapsed from vasectomy to the onset of pain was variable, ranging from immediate to 11 years, with a mean of 36·5 months. The mean duration of scrotal pain before epididymectomy was 2·4 years (range, 4 months to 18 years). Clinical diagnosis of pain related to vasectomy was made in all cases, with findings of swollen tender epididymis (n = 14) and painful testis (n = 1). Assessment by ultrasonography of the scrotum confirmed the clinical impression except in four cases (three normal scans and one showing an epididymal cyst). Thirteen patients had good symptomatic relief following epididymectomy. The two patients with persistent symptoms included one with testicular pain on examination and the other with an epididymal cyst on ultrasonography. Histological examination revealed dilatation and inflammation of the epididymis, and/or the presence of sperm granuloma in all cases except for the case of epididymal cyst noted by ultrasonography.
Conclusions: In selected patients, epididymectomy is a reliable and effective treatment for post-vasectomy pain, regardless of the time before the onset of symptoms and the duration of symptoms.

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Open *versus* closed epididymal sperm retrieval in men with secondarily obstructed vasal systems

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Introduction: We sought to evaluate and compare sperm quality and suitability for intracytoplasmic sperm injection (ICSI) in open and percutaneous epididymal aspiration in men with obstructive azoospermia and to determine the relevance of epididymal morphology to successful sperm retrieval.
Patients and methods: A series of 20 men undergoing vasectomy reversal were evaluated by percutaneous (PESA) and open epididymal sperm aspiration (MESA) before reversal surgery. Two samples were taken with PESA, one with the needle *in situ* (PESA1) and the second on withdrawing the needle (PESA2). Epididymal morphology was graded as normal, distended and grossly distended. Five men undergoing vasectomy served as a control non-obstructed group for percutaneous aspiration. Aspiration was considered successful if sperm suitable for ICSI were retrieved.
Results: In the obstructed group, 15 men had successful PESA and 13 of these also had successful MESA. PESA was successful bilaterally eight times compared to MESA on five occasions. Two men with successful PESA had negative MESA. PESA2 was five times more successful than PESA1. PESA had an 84% success rate in distended or grossly distended epididymi compared to 14% in non-distended systems. Only one PESA in the non-obstructed group was suitable for ICSI.
Conclusions: PESA is a viable alternative to MESA in patients with obstructive azoospermia, particularly when associated with clinically distended epididymi.