

anabolic steroids and vascular responses

R—The use of high doses of anabolic androgenic steroids is associated with impaired activity of the vascular nitric oxide pathway *in vitro*. In aortic segments from rabbits treated with nandrolone decanoate 10 mg/kg per week, Balfagón et al¹ reported significant decreases in endothelium-dependent vasodilation to acetylcholine and endothelium-independent vasodilation to exogenous nitric oxide or sodium nitroprusside. This study suggests that the effect of nandrolone to reduce the activity of the smooth-muscle component of the nitric oxide pathway (ie, the guanylate cyclase system). We present data from a study involving measurement of forearm blood flow (FBF) responses to brachial artery infusion of methacholine (MCh) and sodium nitroprusside (SNP).

Seven men (mean age, 22) were studied twice, 4 weeks apart. There were minor differences in the two sets of results in six of the subjects (figure, B) but, in one, vasodilation in response to the highest doses of SNP and MCh was 71% and 51%, respectively, lower in the second session compared with the first (figure, A). These values were at least two standard deviations outside the mean difference in paired measurements in the other six subjects, which prompted us to contact the subject.

The subject reported that he had been self-administering nandrolone decanoate for 4 months before the first test session (average of 250 mg per week, intramuscularly). However, for 21 days immediately preceding the initial infusion study, he had abstained from any drugs. After this session, he resumed steroid use (testosterone, 300 mg per week) up to and beyond the second infusion study. When we contacted the subject on follow-up, he had not taken anabolic steroids for 8 weeks and was invited to undertake a third infusion session. The SNP and MCh responses elicited during this test resembled those of the initial trial (figure A).

Our finding suggests that anabolic steroid use may induce changes in behaviour of the nitric oxide dilator system *in vivo*.

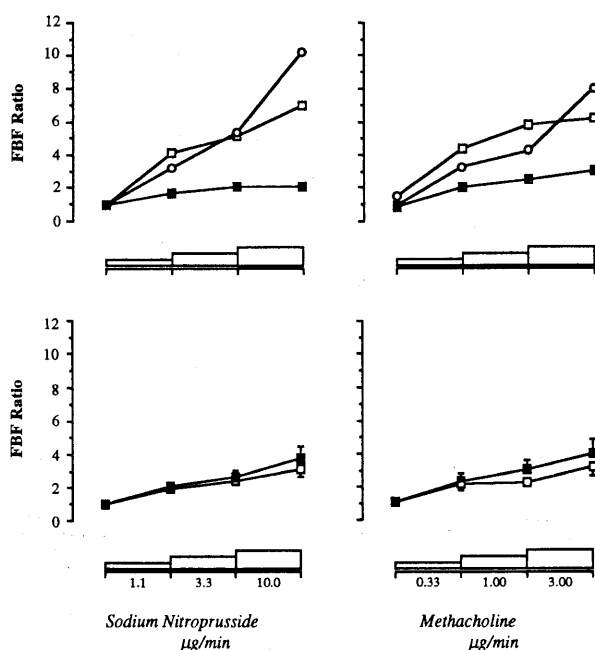


Figure 2: Dose-response curves for three doses of nitroprusside and methacholine

before (□) and after (■) 4 week period in anabolic steroid user (A) and six control subjects (B, mean [SE]). For steroid user, initial session occurred after 3 week abstinence and second session after 4 weeks of steroid administration. Response to each drug after 8 week abstinence is also shown (○). Blood flow response is expressed as ratio of infusion arm to non-infusion arm blood-flows normalised to similar ratio calculated during baseline.

Attenuated responses to both MCh and SNP might indicate that the defect lies distal to the endothelial component of the receptor-effect mechanism, probably within the smooth-muscle cells, a deduction similar to that reported in rabbits.¹ The mechanism responsible for steroid-induced effects on the nitric oxide dilator system is not known. However, hypertension and hypercholesterolaemia, both side-effects of chronic anabolic steroid abuse,^{2,3} are also associated with abnormalities in the nitric oxide pathway.^{4,5}

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Is cows' milk casein an allergen in latex-rubber gloves?

SIR—Surgical and other latex-rubber gloves are reported to cause immediate allergic reactions. At special risk are people with atopic disorders, health-care workers, and patients having many operations such as children with spina bifida.¹ Surgical gloves are made from ammoniated latex extracted from *Hevea brasiliensis*. Polyisoprene is the main constituent but latex rubber also contains about 1% of proteins. These seem to persist in variable amounts during glove manufacture and rubber proteins eluting into the skin and mucous membranes, or airborne contaminated glove powder, appear to be responsible for the variable symptoms in latex-allergic patients.²

We studied a 36-year-old female with atopic dermatitis and cows' milk allergy. When trying to protect her hands with rubber household gloves she immediately got pruritus and contact urticaria. Latex allergy was suspected but prick tests with natural latex rubber and eluates of several surgical and household gloves were negative, although wealing was seen on her hands with contact with a surgical latex rubber glove (Triflex, Baxter, USA) but not with a vinyl glove. Milk allergens were suspected because casein may be added to rubber during glove manufacture.³ We then did inhibition studies on the cows' milk radioallergosorbent test (RAST) and showed a distinct inhibition with the eluate of the surgical glove that had caused wealing. A lower milk-allergen activity was shown in another surgical glove but not in a third. Immunoelectrophoresis⁴ with rabbit anti-casein antibody confirmed the presence of casein in the first surgical glove and autoradiography showed specific IgE binding. The cows' milk allergy of the patient was verified by cows' milk RAST (28.1 kU/L; Pharmacia, Uppsala, Sweden), casein RAST (27.4 kU/L), and by positive prick tests to whole milk (ALK, Horsholm, Denmark), and casein (1 mg/mL).

Casein in latex rubber gloves is, to our knowledge, a previously unrecognised source of allergy. As glove manufacturers' formulations are confidential, it is difficult to ascertain

how widely casein is used. Our finding of cows' milk allergens in two of the three examined latex gloves suggest that the presence of casein is not uncommon. As in latex-rubber allergy, minute amounts of casein eluting from gloves during surgery or medical examination could be a risk for a patient exquisitely sensitive to cows' milk casein. Milk proteins in napkin-rash ointment have caused anaphylaxis,⁵ and allergy to cows' milk casein is common, especially in children.

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Fertilising ability of testicular spermatozoa

SIR—Conventional thought is that spermatozoa must traverse the epididymis to gain fertilisation potential. However, we wondered whether testicular spermatozoa can achieve fertilisation, which would be relevant to men whose epididymo-vasostomy procedures have failed or because there is complete absence of the vas and epididymis.

A couple we have seen had a 15 year history of infertility due to obstructive azoospermia. On the right, the epididymis petered out towards the tail and there was no vas. On the left, only a short segment of proximal vas was present, and had been brought to the surface of the skin as a fistula after earlier surgery but the previously inserted cannula had fallen out and the patient remained azoospermic. The couple were included in our in-vitro fertilisation (IVF) programme but bilateral scrotal exploration failed to aspirate any spermatozoa because of gross distorted anatomy and fibrosis resulting from at least two previous operations. A small testicular biopsy was done and the specimen was placed in Medicult medium for 4 hours at 37°C in 5% CO₂ in air; a few non-progressive spermatozoa were identified after agitating the tissue with a pipette. The tissue was removed from the tube and the suspension was centrifuged for 15 minutes at 300g. The spermatozoa in the pellet were later injected into the cytoplasm (ICSI) of 13 metaphase II oocytes that had been retrieved after ovarian superovulation. 6 oocytes showed normal fertilisation with two pronuclei and later developed into cleaved embryos. 3 embryos of good grade were transferred into the uterus at the four-cell stage. Pregnancy was not achieved.

The concept that epididymal spermatozoa can fertilise, resulting in successful pregnancy after conventional IVF, is not new.¹ We have demonstrated that testicular spermatozoa can also fertilise, leading to embryo development, after ICSI. We presume this ability depends on the degree of sperm maturation within the testis. In our patient, histology revealed normal spermatogenesis with a Johnsen score of 8.6 (normal 9.1, abnormal below 8). We have achieved pregnancies after ICSI with lower than normal Johnsen scores.

We intend to obtain testicular tissue for diagnostic and

therapeutic purposes under local or sedation anaesthesia by using an electrically-powered mini-surgical drill percutaneously with sterile disposable biopsy probes. Such sampling would have relevance to the management of infertile couples in whom the man has an irremediable obstruction, more so if there is normal sperm development within the testis (eg, complete absence of vas, previous failed epididymo-vasostomy, and previous failed vasectomy reversal).

These new developments lead us to conclude that the limiting factors for successful pregnancy are not the quality of spermatozoa but rather oocyte quality and endometrial receptivity in the woman which are age-related, since we have now achieved pregnancies by IVF and ICSI with spermatozoa retrieved from the ejaculate, and by micro-epididymal sperm aspiration, and in the present case, fertilisation and early development with spermatozoa obtained from the testis.

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Surveillance case definition for AIDS in resource-poor countries

SIR—De Cock and colleagues (Aug 14, p 437) propose a new AIDS surveillance case definition for use in resource-poor countries. Serological testing for HIV is needed for this definition. Ideally, such definition should be evaluated in a resource-poor country. A drawback to such an evaluation, however, is the availability of a "gold standard" for advanced HIV disease. Indeed, laboratory facilities for CD4 lymphocyte counts or diagnosis of opportunistic infections or malignant diseases indicative of advanced HIV disease are often not available. We therefore evaluated the definition proposed by De Cock and colleagues on a patient population of 423 consecutive HIV seropositive inpatients and outpatients seen at three HIV treatment centres in Belgium.

A standard questionnaire was completed for each patient. All patients were examined and CD4 lymphocyte counts were done. The study population consisted of 329 (79%) males and 86 (21%) females, 78% of whom were of European origin; the remainder came from African (21%), Latin American (1%), and Asian countries (0.3%). 192 (46%) patients acquired HIV infection through homosexual contact, 187 (45%) through heterosexual contact, 8 (2%) through intravenous drug use, and 6 (1%) through transfusion of blood or blood products; in 22 (5%) patients the route of HIV infection was unknown. 114 (28%) had WHO clinical stage I disease, 119 (29%) stage II, 93 (22%) stage III, and 89 (21%) stage IV.¹ They had had the following opportunistic infections or diseases: *Pneumocystis carinii* pneumonia (21 patients), Kaposi's sarcoma (18), candida oesophagitis (13), *Mycobacterium tuberculosis* infection (15), cryptococcal meningitis (9), cerebral toxoplasmosis (9), chronic *Herpes simplex* infection (6), *M avium* complex infection (3), and cytomegalovirus infection (1).

Definition	Sensitivity	Specificity	Positive predictive value	Positive likelihood ratio
De Cock et al	42 (53/126)	90 (261/289)	65 (53/81)	4
Clinical WHO ²	26 (33/126)	93 (276/289)	72 (33/46)	6
WHO/CDC 1987 ³	56 (70/126)	93 (270/289)	79 (70/89)	8

Table: Evaluation of three AIDS surveillance case definitions in 423 HIV seropositive patients seen in three Belgian HIV/AIDS treatment centres

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