Clitoral surgery and sexual outcome in intersex conditions

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Parents who are confronted with a newborn baby with ambiguous genitalia are overwhelmed because they have probably never before heard of such a condition. They need good information about surgical procedures and the effect of the operation on body image, self-concept, and gender identity of their daughter during childhood and her sexual life in adolescence and adulthood. Professionals treating these patients also lack this essential information. There are not many studies about the sexual outcome of genital surgery in women born with ambiguous genitalia. Patients are not motivated to participate in research because of fear of stigmatisation and often refuse physical examinations because of previous traumatic experiences and shame.

In this week’s *Lancet*, Catherine Minto and colleagues report on sexual outcome after clitoral surgery in individuals with intersex conditions and ambiguous genitalia. The subsamples are small and only 44 of the 81 patients returned the questionnaires, but the study still provides important information.

The 18 women who had had clitoral surgery had higher rates of non-sensuality and of failure to achieve orgasm than did the ten who had not had surgery. Minto and colleagues conclude that sexual function can be compromised by clitoral surgery, but are hesitant to advise against such surgery—they advocate an ethical debate about the use of such surgery and stress the need for good information about the potential risks on sexual functioning.

Sexual functioning can also be compromised by other factors, such as sexual shyness due to a negative genital body-image. Mureau and colleagues have shown that hypospadiac boys and adult men report inhibitions when seeking sexual contacts because of dissatisfaction with penile appearance. So the higher rates of non-sensuality in the group who had clitoral surgery in Minto’s study can also be explained by dissatisfaction of the women with the appearance of their genitals, which is supported by the finding that difficulties with sensuality correlated with communication difficulties and avoidance. Dissatisfaction with genital appearance could also explain the high frequency (11/39) of not being sexually active.

Minto and colleagues examined sexual functioning only within a relationship. Sexual shyness could make it difficult for women with an intersex condition to enjoy their sexuality. They might be afraid of rejection by their partner and they might feel self-conscious about their body. These factors do not mean that they lack the ability to reach an orgasm by self-stimulation. In a previous study of ten women with congenital adrenal hyperplasia, seven used self-stimulation and were satisfied with their libido; however, only four of the ten had been in love or had been capable of experiencing erotic feelings. In Minto’s study, 11 of the 39 women were not sexually active and thus not questioned about sexual functioning. Assessment of sexual satisfaction by self-stimulation would have been interesting.

Sexual functioning can also be hindered by problems about gender behaviour. Most women born with ambiguous genitils are masculine in behaviour. Masculine gender behaviour in childhood excludes such women from the social world of their sexmates. In adolescence and adulthood, this behaviour can continue and lead to problems in making sexual contacts.

Sexual functioning can also be impaired by problems with vaginal penetration or insensitivity of the vagina. Minto and colleagues examined only the effect of clitoral surgery, not the effect of vaginoplasty. Several women had small vaginas (1.5–2.5 cm); one woman had no vagina. Also, several women had had more than one vaginoplasty, which might have led to scar tissue in the vagina. Clinical experience shows that intersex women are often dissatisfied with their neovagina, by contrast with male-to-female trans-sexuals.

All 28 sexually active individuals in the Minto study, irrespective of whether or not they had had clitoral surgery, had a sexual problem. Thus the investigators advocate that women with an intersex condition and ambiguous genitalia need sexual counselling from adult age onwards. But I feel this counselling should start from pre-adolescence. At that age most girls with an intersex condition need to be informed about their condition because of starting hormone-replacement therapy and often vaginoplasty. These adolescent girls are inclined to avoid all sexual or romantic contacts, with the result that in adulthood they have no experience in dating and are sexually shy.

Current surgery and medical treatment are not necessarily the best solution for a better outcome in intersex women. But any changes in the policy of sex-assignment might overrule the question of the necessity for genital surgery in some groups of individuals born with ambiguous genitalia. In the Sophia Children’s Hospital in Rotterdam, sex-assignments in newborn babies with ambiguous genitalia are, since about 1995, usually male, except for girls with congenital adrenal hyperplasia and for undervirilised boys with partial androgen insensitivity syndrome. There is international consensus by the joint ESPE/LWPES working-group on congenital adrenal hyperplasia about the policy of genital surgery in affected girls. Although this protocol is clear about the age for surgery (between 2 and 12 months of age, and from adolescence onwards), it is not clear for the degree of virilisation. There is an unclear area between minimal clitoromegaly (no indication) and Prader 5 (indication for a one-stage complete repair with vaginoplasty and clitoral and labial surgery). Formulating criteria for genital surgery is not easy.

Froukje M E Slijper

Gender Team, Erasmus MC/Sophia Children’s Hospital, 3000 DR Rotterdam, Netherlands

(e-mail: slijper@dds.nl)

S-adenosylmethionine in plasma to test for Pneumocystis carinii pneumonia

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Pneumocystis carinii is a fungal opportunist, the cause of a severe and often fatal pneumonia in susceptible immunocompromised individuals. The incidence of *P carinii* pneumonia (PCP) has fallen as a result of combination antiretroviral therapy and use of specific chemoprophylaxis, but PCP remains common in the developed world1 and in Africa2 in patients who are unaware of their HIV-1 serostatus or are denied state-of-the-art medical care.

It is a matter of debate whether PCP without diagnostic confirmation should be empirically treated. A high likelihood of PCP among HIV-1-infected patients with CD4 cell-counts below 200/µL, hypoxia, and diffuse interstitial infiltrates favours empirical treatment. However, because of the inadequate specificity of clinical signs and the risk of toxicity with treatment (3 weeks of high-dose cotrimoxazole, with corticosteroids in patients with moderate-to-severe respiratory failure), confirmation of PCP is essential.

A lower-respiratory-tract specimen is usually required because few organisms are present in upper airways. Induced sputum or bronchoalveolar lavage with immunofluorescent antibody-detection3 are sensitive but invasive and discomfoting tests for the patient. Serodiagnosis, lung-function testing, and nuclear and high-resolution CT are of limited use. A rapid, specific, and non-invasive test for PCP has therefore been wanted. PCR tests of *P carinii* DNA have been investigated over the past decade and offer a high sensitivity, including in samples with a small number of organisms such as oral washes.4 However, subclinical PCR colonisation rather than active infection is being increasingly recognised and may limit the diagnostic value of PCR tests.5

Therefore the report in today’s *Lancet* by Michael Skelly and colleagues that plasma concentrations of the metabolite S-adenosylmethionine can be used to diagnose and monitor treatment of PCP is interesting. During an attempt (still unfulfilled) to establish a continuous culture system for *Pneumocystis* spp, these investigators were the first to observe that S-adenosylmethionine enhances axenic growth of the organism. In a rat model they then showed that *P carinii* has a specific transport system for S-adenosylmethionine and that this metabolite is depleted during infection.6 These findings are extended in the latest report to human PCP. 15 patients with confirmed or suspected HIV-associated PCP had an undetectable plasma concentration of S-adenosylmethionine, by contrast with the control group of 36 patients with other conditions, such as bacterial pneumonia, in whom S-adenosylmethionine was found. Further, four patients with PCP had a rapid rise of S-adenosylmethionine concentrations 7 days after starting effective treatment. These promising results need confirmation, and Skelly’s study has limitations, including the small sample size, the fact that only half the cases had confirmed PCP, and that only a few HIV-1 patients at risk of PCP (CD4 count below 200/µL) were included in the control group. Larger prospective investigations of the diagnostic value of plasma S-adenosylmethionine in patients at risk of PCP are needed.

A possible limitation to the use of a blood-based test is the risk of overlooking concomitant pulmonary infection or cancer. 20% of AIDS-associated cases of PCP occur as coinfections with bacterial pneumonia or tuberculosis.7 With the increasing recognition of PCP in Africa, particularly among infants, development of a simple accessible test based on secretions from the upper respiratory tract is still needed.

A more likely use of the findings on S-adenosylmethionine is the prospect of investigating and monitoring response to treatment. Although organisms may be detected by microscopy in more than half of patients with PCP at the end of treatment, little is known of the kinetics and viability of *P carinii* during treatment. Respiratory failure is common during the first weeks of therapy and it may be clinically difficult to discern whether this is because of treatment failure or protracted acute respiratory distress syndrome with no viable organisms. The rapid rise in S-adenosylmethionine concentrations after therapy suggests that this marker is correlated to the burden and viability of *P carinii*, and offer a promising method to monitor and investigate the course of treatment.

Jannik Helweg-Larsen Copenhagen HIV Programme, Department of Infectious Diseases, Hvidovre Hospital, 2650 Hvidovre, Copenhagen, Denmark (e-mail: jhelweg@cpphv.dk)

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