For debate

Immunological functions of the human prepuce

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The demonisation of the human male prepuce has been an unscientific process, even though some research, on the surface, might seem to support it. In the late 19th century, when male circumcision came into vogue in medicine in the United States, there was near universal acceptance among American medical professionals that circumcision was an effective treatment for such "diseases" as masturbation, headache, insanity, epilepsy, paralysis, strabismus, rectal prolapse, hydrocephalus, and clubfoot.[1] Leading medical journals published thousands of case reports demonstrating these and other miraculous therapeutic benefits from preputial amputation. The notion that circumcision improves hygiene and prevents sexually transmitted diseases (STDs) originated at the same time in the context of the discourse over racial and moral hygiene. The peculiar American phenomenon of mass newborn (that is, involuntary) circumcision is a product of the cold war era. United States doctors readily embraced the concept of mass, involuntary circumcision just as they had embraced involuntary sterilisation and other eugenic measures—practices rejected by almost all other Western nations. Mass circumcision peaked in the 1970s, when almost 90% of male neonates in the United States were circumcised. Since then, the rate has declined, but circumcision industry spokesmen have added to the list of diseases that circumcision allegedly prevents and cures.

Historically, the most common reason given for circumcision has been that it prevents masturbation. Today, the most common reason given is that it inhibits the transmission of STDs, even though rigorously controlled studies have consistently shown that circumcised males are at greater risk for all major STDs than males whose penises are intact.[2–6] Circumcision advocates are now claiming that circumcision prevents AIDS.

A review of the scientific literature, however, reveals that the actual effect of circumcision is the destruction of the clinically demonstrated hygienic and immunological properties of the prepuce and intact penis.

The sphincter action of the preputial orifice functions like a one way valve, blocking the entry of contaminants while allowing the passage of urine.[7 8] Ectopic sebaceous glands concentrated near the frenulum produce smegma.[9–12] This natural emollient contains prostatic and seminal secretions, desquamated epithelial cells, and the mucin content of the urethral glands of Littré.[13 14] It protects and lubricates the glans and inner lamella of the prepuce, facilitating erection, preputial eversion, and penetration during sexual intercourse.

The inner prepuce contains apocrine glands,[15] which secrete cathepsin B, lysozyme, chymotrypsin, neutrophil elastase,[16] cytokine (a non-antibody protein that generates an immune response on contact with specific antigens),[17] and pheromones such as androsterone.[18] Lysozyme, which is also found in tears, human milk, and other body fluids, destroys bacterial cell walls.

The natural composition of preputial bacterial flora is age dependent and similar to that of the eyes, mouth, skin, and female genitals.[19] Washing the preputial sac was once thought to aid hygiene. Washing a stallion's preputial sack with soap, however, encourages the growth of pathogenic organisms.[20] Washing the human prepuce with soap is a common cause of balanoposthitis.[21]

Fussell *et al* have claimed that the prepuce is predisposed to colonisation by pathogenic bacteria, but they did not measure naturally occurring bacterial flora in living cohorts with undisturbed preputial microenvironments.[22] They measured bacterial rates in dead, amputated, chemically treated prepuces inoculated with virulent strains of pathogenic bacteria—conditions that represent no known biological or behavioural reality.

Animal experiments reveal that in the presence of hydrogen peroxide and halide or pseudohalides, soluble peroxidase in the prepuce has an antimicrobial activity.[23] Plasma cells in the mucosal lining of the bovine prepuce secrete immunoglobulin under the epidermis that diffuses across the epidermis into the preputial cavity. In response to pathogenic bacterial infection, preputial plasma cells increase.[24] Antibodies in breast milk supplement genital mucosal immunity in infants. Oligosaccharides in breast milk are ingested, then excreted in the urine, where they prevent *Escherichia coli* from adhering to the urinary tract and inner lining of the prepuce.[25] An 8 year prospective study that controlled for genitourinary abnormalities found no difference in the rate of upper urinary tract infections between circumcised and intact boys.[26]

There are no histological studies that validate the claim that the sclerotic keratinisation of the epithelium of the surgically externalised, desiccated glans penis, meatus, or scar of the circumcised penis creates a barrier against infection. The higher rate of STDs in circumcised males might well be the result of

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the loss of preputial immunoprotective structures. The loss of the protective, self lubricating, mobile, double layered prepuce exposes the glans and meatus to direct friction, abrasion, and trauma. Eyes without eyelids would not be cleaner. Neither is a glans without its prepuce. The surgically externalised and unprotected glans and meatus of the circumcised penis are constantly exposed to abrasion and dirt, making the circumcised penis less hygienic.[27] The circumcised penis is more prone to infection in the first years of life than the intact penis.[28–30]

The prepuce is a specific erogenous zone.[31] It contains a rich, complex network of nerves and an abundance of mucocutaneous end organs sensitive to motion, touch, temperature, and erogenous stimulation.[32–37] Both the inner and outer folds of the prepuce have a denser distribution of nerve networks than the rest of penile skin.[38] The rich innervation of the inner prepuce contrasts sharply with the limited sensory investment of the glans penis, which is characterised primarily by free nerve endings, which feel only deep pressure and pain.[39] The double layered prepuce provides the skin necessary to accommodate the expanded erect organ and to allow the penile skin to slide freely, smoothly, and pleasurably over the shaft and glans. One function of the prepuce is to facilitate smooth, gentle movement between the mucosal surfaces of the two partners during intercourse. The prepuce enables the penis to slip in and out of the vagina non-abrasively inside its own sheath of self lubricating, movable skin. The female is thus stimulated by moving pressure rather than by friction only, as when the male's prepuce is missing.

Circumcision radically desensitises the penis and immobilises whatever shaft skin remains.[40] The loss of preputial mobility, primary sensory structures, orgasm triggering nerve endings, and the inevitable desensitisation of the glans may necessitate more vigorous and prolonged thrusting to trigger orgasm. For this reason, a circumcised penis may be more likely than an intact penis to cause the breaks, tears, microfissures, abrasions, and lacerations in a vagina (or rectum) through which HIV in the thrusting partner's semen could enter the receiving partner's bloodstream.

The prepuce is also richly vascular.[37 41 42] The most vascular parts of the body are those least vulnerable to infection.

These factors may explain why circumcised American males are more likely than their genitally intact peers to engage in high risk sexual behaviours (such as anal intercourse and active and passive homosexual oral sex) that lead to HIV and other STD infections.[43]

Epithelial Langerhans cells (ELCs), a component of the immune system, help the body recognise and process antigens, directing them to lymphocytes or macrophages. Weiss *et al* noted an abundance of ELCs in the outer surface of the neonatal prepuce comparable with the general density of ELCs found in adult skin.[44] They suggest that the relative paucity of ELCs in the inner mucosal surface of the neonatal prepuce results in a reduced immune response to cutaneous antigens and recommend universal neonatal circumcision to prevent HIV infection. This recommendation is untenable because the prepuce of virtually all neonates is fused to the glans, sealing the undeveloped preputial pouch from external contact.[45 46] Furthermore, the newborn has just emerged from a sterile environment, where no ELCs are needed. There is no documentation of the comparable density of ELC in the mucous membranes of the surgically externalised glans penis, meatus, or the circumcision scar of the sexually active adult.[47]

Although a study of primates found that Langerhans-like cells in the lamina propria, not the epithelium, appeared to be infected with simian immunodeficiency virus,[48] it is unclear whether this observation can be extrapolated to the Langerhans cells in the epithelium of the human prepuce. If Langerhans cells are a factor, the ethical response would be to promote the use of condoms, not excise normal tissue laden with immunoprotective cells.

It was an American circumciser in 1986 who first hypothesised that circumcision prevents HIV infection.[49] In an attempt to verify this theory, others have published numerous epidemiological surveys, conducted primarily in Africa. A review of these surveys, however, does not support their assertion. Of the 36 published studies examining the relation between the circumcised penis and HIV infection, 15 found a negative correlation,[50–64] four found a positive correlation,[65–68] and 16 found no statistically significant difference.[2 69–83]

The studies that find a positive correlation are all population based. Most of the negative association studies are based on STD clinic data, have serious population bias, and must therefore be viewed with caution. For example, according to undisclosed criteria, Pépin *et al* counted 11% of their self reported circumcised cohort as intact.[70] Konde-Lule *et al* assumed all Muslims were circumcised,[77] an assumption that Urassa *et al* found to be true in only 68% to 92% of cases.[64]

Although circumcision proponents in the United States cite these studies when debating routine circumcision,[84 85] African data are not applicable to developed nations.[86] Circumcision status in Africa has an important but poorly understood cultural significance that proponents of circumcision have ignored. Circumcised and intact males lead very different lives in the African regions investigated. Marck has shown that intact males in circumcising areas face severe discrimination in work, housing, marriage, and sexual relations. A significant percentage resort to prostitutes, increasing their risk of exposure to STDs.[87] Ignoring these facts, some AIDS researchers have recommended intervening into African cultures and promoting circumcision in circumcision-free regions.[88] Implementing this recommendation would invite disaster. In many parts of Africa, circumcision causes most tetanus infections.[89] The spread of tuberculosis through circumcision in developing countries is well documented.[90] The risk of severe complications and death following circumcision rituals in Africa is high.[91 92] The

common use of dirty instruments in group circumcisions only increases the risk of HIV transmission.[93] Although the risk of circumcision related complications is higher in Africa than in the United States, no level of risk is acceptable when a healthy, and often protesting, "patient" has not consented.

In addition to its long term immunological handicap, neonatal circumcision immediately compromises the immune system, making the circumcised male neonate vulnerable to infection, often with tragic consequences.[94 95] Even if the circumcisionists' studies were valid, the real and unavoidable risks of circumcision outweigh, both quantitatively and ethically, the alleged risks of intact genitalia. Amputation of the prepuce neither inhibits risky sexual behaviour nor confers immunity after exposure to pathogens. This is demonstrated by the fact that the United States has both the highest number of sexually active circumcised males and the highest rates of genital cancers, STDs, and AIDS of any first world nation.[96 97]

Mass involuntary circumcision has failed to achieve any of the public health benefits its advocates have claimed for it; but even if it had achieved them all, there can be no scientific or ethical justification for depriving anyone of sovereignty over his own sex organs. Neonatal circumcision violates bodily integrity and imposes on an unconsenting individual a diminished penis for life. In the wake of the Nuremberg trials, it is inappropriate and unethical for doctors to persist in performing or advocating involuntary penile reduction surgery on healthy, normal individuals. The totalitarian concept of involuntary prophylactic surgery espoused by circumcision advocates has no place in modern medicine or the civilised world. The key to decreasing the transmission of STDs is education, not amputation.

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1 Hodges F. A short history of the institutionalization of involuntary sexual mutilation in the United States. In: Denniston GC, Milos MF, eds. *Sexual mutilations: a human tragedy.* New York: Plenum, 1997:17–40.
2 Laumann EO, Masi CM, Zuckerman EW. Circumcision in the United States: prevalence, prophylactic effects, and sexual practice. *JAMA* 1997;**277**:1052–7.
3 Donovan B, Bassett I, Bodsworth NJ. Male circumcision and common sexually transmissible diseases in a developed nation setting. *Genitourin Med* 1994;**70**:317–20.
4 Smith GL, Greenup R, Takafuji ET. Circumcision as a risk factor for urethritis in racial groups. *Am J Public Health* 1987;**77**:452–4.
5 Cook LS, Koutsky LA, Holmes KK. Clinical presentation of genital warts among circumcised and uncircumcised heterosexual men attending an urban STD clinic. *Genitourin Med* 1993;**69**:262–4.
6 Bassett I, Donovan B, Bodsworth NJ, *et al*. Herpes simplex virus type 2 infection of heterosexual men attending a sexual health centre. *Med J Aust* 1994;**160**:697–700.
7 Jefferson G. The peripenic muscle; some observations on the anatomy of phimosis. *Surg Gynecol Obstet* 1916;**23**:177–81.
8 Lakshmanan S, Parkash S. Human prepuce—some aspects of structure and function. *Indian J Surg* 1980;**42**:134–7.
9 Delbanco E. Über das gehäufte Auftreten von Talgdrüsen an der Innenfläche des Präputium. *Monatshefte für praktische Dermatologie* 1904;**38**:536–8.
10 Hyman AB, Brownstein MH. Tyson's "glands": ectopic sebaceous glands and papillomatosis penis. *Arch Dermat* 1969;**99**:31–7.
11 Piccinno R, Carrel C-F, Menni S, *et al.* Preputial ectopic sebaceous glands mimicking molluscum contagiosum. *Acta Derm Venereol* 1990;**70**:344–5.
12 Krompecher St. Die Histologie der Absonderung des Smegma Praeputii. *Anatomischer Anzeiger* 1932;**75**:170–6.
13 Koning M, Streekferk JG. Kleine Kwalen in de Huisartsgeneeskunde; Smegma en Fysiologische Fimose. *Ned Tijdschr Geeneskd* 1995;**139**:1632–4.
14 Parkash S, Rao R, Venkatesan K, *et al.* Sub-preputial wetness—its nature. *Ann Nat Med Sci* 1982;**18**:109–12.
15 Ahmed A, Jones AW. Apocrine cystadenoma: a report of two cases occurring on the prepuce. *Br J Derm* 1969;**81**:899–901.
16 Frohlich E, Schaumburg-Lever G, Klessen C. Immunelectron microscopic localization of cathepsin B in human exocrine glands. *J Cutan Pathol* 1993;**20**:54–60.
17 Ahmed AA, Nordlind K, Schultzberg M, *et al.* Immunohistochemical localization of IL-1 alpha-, IL-1 beta-, IL-6- and TNF-alpha-like immunoreactivities in human apocrine glands. *Arch Dermatol Res* 1995;**287**:764–6.
18 Cohn BA. In search of human skin pheromones. *Arch Derm* 1994;**130**:1048–51.
19 Neubert U, Lentze I. Die Bakterielle Flora des Präputialraumes. *Hautarzt* 1979;**30**:149–53.
20 Bowen JM, Tobin N, Simpson RB, *et al.* Effects of washing on the bacterial flora of the stallion's penis. *J Reprod Fert (Suppl)* 1982;**32**:41–5.
21 Birley HDL, Walker MM, Luzzie GA, *et al.* Clinical features and management of recurrent balanitis; association with atopy and genital washing. *Genitourin Med* 1993;**69**:400–3.
22 Fussell EN, Kaack MB, Cherry R, *et al*. Adherence of bacteria to human foreskins. *J Urol* 1988;**140**:997–1001.
23 Prabir K. Tissue distribution of constitutive and induced soluble peroxidase in rat: purification and characterization from lacrimal gland. *Eur J Biochem* 1992;**206**:59–67.
24 Flower PJ, Ladds PW, Thomas AD, *et al*. An immunopathologic study of the bovine prepuce. *Vet Pathol* 1983;**20**:189–202.
25 Coppa GV, Gabrielli O, Giorgi P, *et al*. Preliminary study of breastfeeding and bacterial adhesion to uroepithelial cells. *Lancet* 1990;**335**:569–71.
26 Mueller ER, Steinhardt G, Naseer S. The incidence of genitourinary abnormalities in circumcised and uncircumcised boys presenting with an initial urinary tract infection by 6 months of age. *Pediatrics (Suppl)* 1997;**100**:580.
27 Van Howe RS. Variability in penile appearance and penile findings: a prospective study. *Br J Urol* 1997;**80**:776–82.
28 Fergusson DM, Lawton JM, Shannon FT. Neonatal circumcision and penile problems: an 80 year longitudinal study. *Pediatrics* 1988;**81**:537–41.
29 Enzenauer RW, Dotson CR, Leonard T Jr, *et al*. Increased incidence of neonatal staphylococcal pyoderma in males. *Mil Med* 1984;**149**:408–10.
30 Enzenauer RW, Dotson CR, Leonard T, *et al.* Male predominance in persistent staphylococcal colonization and infection of the newborn. *Hawaii Med J* 1985;**44**:389–90, 392, 394–6.
31 Winkelmann RK. The erogenous zones: their nerve supply and its significance. *Proc Staff Meet Mayo Clin* 1959;**34**:39–47.
32 Dogiel AS. Die Nervenendigungen in der Haut der äusseren Genitalorgane des Menschen. *Archiv für Mikroskopische Anatomie* 1893;**41**:585–612.
33 Winkelmann RK. The cutaneous innervation of human newborn prepuce. *J Invest Dermat* 1956;**26**:53–67.
34 De Girolamo A, Cecio A. Contributo alla conoscenza dell'innervazione sensitiva del prepuzio nell'uomo. *Boll Soc Ital Biol Sper* 1968;**44**:1521–2.
35 Ohmori D. Über die Entwicklung der Innervation der Genitalapparate als peripheren Aufnahmeapparat der Genitalen Reflexe. *Zeitschrift für Anatomie und Entwicklungsgeschichte* 1924;**70**:347–410.
36 Bazett HC, McGlone B, Williams RG, *et al.* Depth, distribution and probable identification in the prepuce of sensory end-organs concerned in sensations of temperature and touch; thermometric conductivity. *Arch Neurol Psychiat* 1932;**27**:489–517.
37 Taylor JR, Lockwood AP,Taylor AJ. The prepuce: specialized mucosa of the penis and its loss to circumcision. *Br J Urol* 1996;**77**:291–5.
38 Bourlond A, Winkelmann RK. L'innervation du prépuce chez le nouveau-né. *Arch Belg Derm Syph* 1965;**21**:139–53.
39 Halata Z, Munger BL. The neuroanatomical basis for the protopathic sensibility of the human glans penis. *Brain Res* 1986;**371**:205–30.
40 Lander MM. The human prepuce. In: Denniston GC, Milos MF, eds. *Sexual mutilations: a human tragedy*. New York: Plenum, 1997:79–81.
41 Juskiewenski S, Vaysse Ph, Moscovici J, *et al*. A study of the arterial blood supply to the penis. *Anat Clin* 1982;**4**:101–7.
42 Hinman F Jr. The blood supply to preputial island flaps. *J Urol* 1991;**145**:1232–5.
43 Van Howe RS, Cold CJ. Advantages and disadvantages of neonatal circumcision. *JAMA* 1997;**278**:203.
44 Weiss GN, Sanders SM, Westbrook KC. The distribution and density of langerhans cells in the human prepuce: site of a diminished immune response? *Israel J Med Sci* 1993;**29**:42–3.
45 Kayaba H, Tamura H, Kitajima S, *et al*. Analysis of shape and retractability of the prepuce in 603 Japanese boys. *J Urol* 1996;**156**:1813–5.

46 Gairdner D. The fate of the foreskin: a study of circumcision. *BMJ* 1949;**2**:1433–7.
47 Berman B, Chen VL, France, DS, *et al.* Anatomical mapping of epidermal Langerhans cell densities in adults. *Br J Derm* 1983;**109**:553–8.
48 Spira IA, Marx PA, Patterson BK, *et al.* Cellular targets of infection and route of viral dissemination after intravaginal inoculations of simian immunodeficiency virus into rhesus macaques. *J Exp Med* 1996;**183**:215–25.
49 Fink AJ. A possible explanation for heterosexual male infections with AIDS. *N Engl J Med* 1986;**315**:1167.
50 Bwaya JJ, Omari AM, Mutere AN, *et al.* Long distance truck-drivers: 1. Prevalence of sexually transmitted diseases (STDs). *East Afr Med J* 1991;**68**:425–9.
51 Bwayo J, Plummer F, Omari M, *et al.* Human immunodeficiency virus infection in long-distance truck drivers in East Africa. *Arch Intern Med* 1994;**154**:1291–6.
52 Kreiss JK, Hopkins SG. The association between circumcision status and human immunodeficiency virus infection among homosexual men. *J Infect Dis* 1993;**168**:1404–8.
53 Cameron DW, Simonsen JN, D'Costa LJ, *et al.* Female to male transmission of human immunodeficiency virus type 1: risk factors for seroconversion in men. *Lancet* 1989;**2**: 403–7.
54 Greenblatt RM, Lukehart SA, Plummer FA, *et al.* Genital ulceration as a risk factor for human immunodeficiency virus infection. *AIDS* 1988;**2**:47–50.
55 Diallo MO, Ackah AN, Lafontaine M-F, *et al.* HIV-1 and HIV-2 infections in men attending sexually transmitted disease clinics in Abidjan, Cote d'Ivoire. *AIDS* 1992;**6**: 581–5.
56 Simonsen JN, Cameron DW, Gakinya MN, *et al.* Human immunodeficiency virus infection among men with sexually transmitted diseases. *N Engl J Med* 1988;**319**:274–8.
57 Tyndall MW, Ronald AR, Agoki E, *et al.* Increased risk of infection with human immunodeficiency virus type 1 among uncircumcised men presenting with genital ulcer disease in Kenya. *Clin Infect Dis* 1996;**23**:449–53.
58 Nasio JM, Nagelkerke NJD, Mwatha A, *et al.* Genital ulcer disease among STD clinic attenders in Nairobi: association with HIV-1 and circumcision status. *Int J STD AIDS* 1996; **7**:410–4.
59 Mehendale SM, Shepherd ME, Divekar AD, *et al.* Evidence for high prevalence and rapid transmission of HIV among individuals attending STD clinics in Pune, India. *Indian J Med Res* 1996;**104**:327–35.
60 Sassan-Morokro M, Greenberg AE, Coulibaly IM, *et al.* High rates of sexual contact with female sex workers, sexually transmitted diseases, and condom neglect among HIV infected and uninfected men with tuberculosis in Abidjan, Cote d'Ivoire. *J Acquir Immune Defic Syndr Hum Retrovirol* 1996;**11**:183–7.
61 Hunter DJ, Maggwa BN, Mati JKG, *et al.* Sexual behavior, sexually transmitted diseases, male circumcision and risk of HIV infection among women in Nairobi, Kenya. *AIDS* 1994;**8**:93–9.
62 Seed J, Allen S, Thierry M, *et al.* Male circumcision, sexually transmitted disease, and risk of HIV. *J Acquir Immune Defic Syndr Hum Retrovirol* 1995;**8**:83–90.
63 Malamba SS, Wagner H-U, Maude G, *et al.* Risk factors for HIV-1 infection in adults inn a rural Ugandan community: a case-control study. *AIDS* 1994;**8**:253–7.
64 Urassa M, Todd J, Boerma JT, *et al.* Male circumcision and susceptibility to HIV infection among men in Tanzania. *AIDS* 1997;**11**:73–80. [study 4]
65 Barongo LR, Borgdorff MW, Mosha FF, *et al.* The epidemiology of HIV-1 infection in urban areas, roadside settlements and rural villages in Mwanza Region, Tanzania. *AIDS* 1992;**6**:1521–8.
66 Grosskurth H, Mosha F, Todd J, *et al.* A community trial of the impact of improved sexually transmitted disease treatment on the HIV epidemic in rural Tanzania: 2. Baseline survey results. *AIDS* 1995;**9**:927–34.
67 Chao A, Bulterys M, Musanganire F, *et al.* Risk factors associated with prevalent HIV-1 infection among pregnant women in Rwanda. National University of Rwanda-Johns Hopkins University AIDS Research Team. *Int J Epidemiol* 1994;**23**:371–80.
68 Urassa M, Todd J, Boerma JT, *et al.* Male circumcision and susceptibility to HIV infection among men in Tanzania. *AIDS* 1997;**11**:73–80. [study 1]
69 Hira SK, Kamanga J, Macuacua R, *et al.* Genital ulcers and male circumcision as risk factors for acquiring HIV-1 in Zambia. *J Infect Dis* 1990;**161**:584–5.
70 Pépin J, Quigley M, Todd J, *et al.* Association between HIV-2 infection and genital ulcer diseases among male sexually transmitted disease patients in The Gambia. *AIDS* 1992;**6**:489–93.
71 Bollinger RC, Brookmeyer RS, Mehendale SM, *et al.* Risk factors and clinical presentation of acute primary HIV infection in India. *JAMA* 1997;**278**:2085–9.
72 Chiasson MA, Stoneburner RL, Hildebrandt DS, *et al.* Heterosexual transmission of HIV-1 associated with the use of smokable freebase cocaine (crack). *AIDS* 1991;**5**:1121–6.
73 Carael M, Van De Perre, PH, Lepage PH, *et al.* Human immunodeficiency virus transmission among heterosexual couples in central Africa. *AIDS* 1988;**2**:201–5.
74 Moss GB, Clemetson D, D'Costa L, *et al.* Association of cervical ectopy with heterosexual transmission of human immunodeficiency virus: results of a study of couples in Nairobi, Kenya. *J Infect Dis* 1991;**164**:588–91.
75 Allen S, Lindan C, Serufilira A, *et al.* Human immunodeficiency virus infection in urban Rwanda: demographic and behavioral correlates in a representative sample of childbearing women. *JAMA* 1991;**266**:1657–63.
76 Seidlin M, Vogler M, Lee E, *et al.* Heterosexual transmission of HIV in a cohort of couples in New York City. *AIDS* 1993;7:1247–54.
77 Konde-Lule JK, Berkley SF, Downing R. Knowledge, attitudes and practices concerning AIDS in Ugandans. *AIDS* 1989;**3**:513–8.
78 Van de Perre P, Clumeck N, Steens M, *et al.* Seroepidemiological study on sexually transmitted diseases and hepatitis B in African promiscuous heterosexuals in relation to HTLV-III infection. *Eur J Epidemiol* 1987;**3**:14–8.
79 Quigley M, Munguti K, Grosskurth H, *et al.* Sexual behaviour patterns and other risk factors for HIV infection in rural Tanzania: a case-control study. *AIDS* 1997;**11**:237–48.
80 Urassa M, Todd J, Boerma JT, *et al.* Male circumcision and susceptibility to HIV infection among men in Tanzania. *AIDS* 1997;**11**:73–80. [study 2]
81 Urassa M, Todd J, Boerma JT, *et al.* Male circumcision and susceptibility to HIV infection among men in Tanzania. *AIDS* 1997;**11**:73–80. [study 3]
82 Urassa M, Todd J, Boerma JT, *et al.* Male circumcision and susceptibility to HIV infection among men in Tanzania. *AIDS* 1997;**11**:73–80. [study 5]
83 Hudson CP, Hennis AJM, Kataaha P, *et al.* Risk factors for the spread of AIDS in rural Africa, hepatitis B and syphilis in southwestern Uganda. *AIDS* 1988;**2**:255–60.
84 Schoen EJ. Benefits of newborn circumcision: is Europe ignoring medical evidence? *Arch Dis Child* 1997;77:258–60.
85 Weiss GN. Prophylactic neonatal surgery and infectious diseases. *Pediatr Infect Dis J* 1997;**16**:727–34.
86 Storms MR. AAFP fact sheet on neonatal circumcision: a need for updating. *Am Fam Physician* 1996;**54**:1216, 1218.
87 Marck J. Aspects of male circumcision in sub-equatorial African culture history. *Health Transition Review* 1997;**7**: 337–59.
88 Moses S, Bradley JE, Nagelkerke NJD, *et al.* Geographical patterns of male circumcision practice in Africa: association with HIV seroprevalence *Int J Epidemiol* 1990;**19**: 693–7.
89 Sow PS, Diop BM, Barry HL, *et al.* Tétanus et pratiques traditionnelles à Dakar (à propos de 141 cas). *Dakar Med* 1993;**38**:55–9.
90 Hardy DB. Cultural practices contributing to the transmission of human immunodeficiency virus in Africa. *Rev Infect Dis* 1987;**9**:1109–19.
91 Annobil SH, Al-Hilfi A, Kazi T. Primary tuberculosis of the penis in an infant. *Tubercle* 1990;**71**:229–30.
92 Crowley IP, Kesner KM. Ritual circumcision (umkhwetha) among the Xhosa of the Ciskei. *Br J Urol* 1990;**66**:318–21.
93 Phillips K, Ruttman T, Viljoen J. Flying doctors, saving costs. *S Afr Med J* 1996;**86**:1557–8.
94 Bliss DP Jr, Healey PJ, Waldhausen JHT. Necrotizing fasciitis after Plastibell circumcision. *J Pediatr* 1997;**131**:459–62.
95 Williams N, Kapila L. Complications of circumcision. *Br J Surg* 1993;**80**:1231–6.
96 Hitchcock R. Comentary on: Benefits of newborn circumcision: is Europe ignoring medical evidence? *Arch Dis Child* 1997;**77**:260.
97 Wise J. HIV epidemic is far worse than thought. *BMJ* 1997; **315**:1486.