Let It Be Sexual: How Health Care Transmission of AIDS in Africa was Ignored
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It is a widely accepted belief that human immunodeficiency virus (HIV) was spread throughout Africa primarily via heterosexual transmission. In 1988, the World Health Organization (WHO) estimated that 80% of HIV cases in Africa were due to heterosexual activity, while health care exposures were thought to be responsible for only 1.6% of cases. These estimates were likely influenced by the political climate of the time. The emphasis on heterosexual transmission of HIV provided support for pre-existing efforts to promote condoms as a means of reducing population growth in Africa, while health care transmission was downplayed for fear that people might avoid immunizations. By 1989, the heterosexual transmission hypothesis had been accepted as truth in HIV research, as well as in the popular media. However, a review of epidemiologic studies conducted in Africa prior to 1989 casts doubt on the proportion of HIV cases attributed to heterosexual activity and suggests that health care transmission may have been the principal route for the spread of HIV.

The authors examined all field studies of HIV risk factors conducted in Africa through 1988 that allowed the calculation of population attributable fractions (PAFs), an epidemiologic statistic indicating the percentage of disease cases that may be attributed to a particular exposure. Based on thirteen studies that used samples from the general population, the average PAFs were 48% for medical injections, 36% for prostitute contact, 27% for past or current sexually transmitted disease (STD), 16% for reporting more than one sexual partner, and 5% for blood transfusions. Nine studies of hospital patients indicated average PAFs of 45% for injections and 42% for blood transfusions, while PAFs for prostitute contact ranged from 6% to 83%. Overall, the available data indicate higher PAFs for health care exposures than for sexual risk factors. Further evidence comes from studies in which subjects were stratified according to their number of sexual partners. HIV infections did not appear to be concentrated in the groups that were most active sexually, as would be expected if HIV had been mainly spread through heterosexual contact. Similar findings were reported in numerous studies of prostitutes; there appears to be little or no association between HIV prevalence and the length of time spent in prostitution or the number of sexual partners per unit time.

Although this study presents a strong case for questioning the assumptions surrounding the spread of HIV in Africa, there are two issues that preclude determination of what the primary route of transmission actually was. First, the quality of the data is questionable. For example, there is a wide range of PAFs for most risk factors, and exposures were defined differently in each study. Second, confounding variables are a major problem since correlations exist among many medical and sexual risk factors and HIV infection. It is clear that variables such as number of sexual partners, prostitute contact, STDs, injections (for STD treatment), and HIV prevalence are associated with each other, so the PAF for any one risk factor is subject to confound by the others. Most studies in the 1980s did not collect the data necessary to resolve this issue, but the authors mention two studies that did find significantly reduced PAFs for STD after adjusting for injections. This suggests that medical treatments rather than sexual behaviour may account for much of the HIV risk associated with STDs. Certainly more research needs to be done in order to determine how HIV was transmitted in Africa, and the answer to this question will have important implications for HIV prevention programs and future management of the epidemic.


A Population-Based Study of Measles, Mumps, and Rubella Vaccination and Autism
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Vaccination programs are among the most effective primary prevention strategies in medicine. Since they are administered to predominantly healthy populations including children, concerns about their safety are often a source of alarm.

It has been suggested that the measles, mumps, and rubella (MMR) vaccine has a causal relationship to autism, particularly due to the temporal association between onset of symptoms and vaccination. The MMR vaccine consists of a live attenuated measles virus.

The awareness that wild-type measles can infect the central nervous system and possibly lead to post-infectious encephalomyelitis
has complicated matters. Madsen et al. (2002) reported results providing strong evidence contrary to this notion.

The Danish group conducted a retrospective cohort study of all children born in Denmark from January 1991 through December 1998, selected from the Danish Civil Registration System. MMR vaccination status was obtained from the Danish National Board of Health. Autism status of the children was obtained from the Danish Psychiatric Central Register. Of the 537,303 children in the cohort, 82.0% were vaccinated. The vaccinated versus the unvaccinated group were examined using a log-linear Poisson regression model with the outcome variables being incidence-rate ratios for autism and other autistic-spectrum disorders (fragile X, Angelman’s syndrome, tuberous sclerosis, and congenital rubella).

Overall, there was no increase in the risk of autism or other autistic-spectrum disorders among vaccinated versus unvaccinated children (adjusted relative risk of autism: 0.92, 95% CI: 0.68-1.24; adjusted relative risk of other autistic-spectrum disorders: 0.83, 95% CI: 0.65-1.07). Also, there was no association between the development of an autistic disorder and the age of vaccination (P=0.23) or the interval since vaccination (P=0.42). Adjustment of potential confounders resulted in similar estimates of risk.

This study yields a number of convincing arguments in opposition of a causal relationship between autism and MMR vaccination. Strengths of this study include the fact that the results were derived from a nationwide cohort study with complete follow-up data. Exposure data were collected prospectively, before the diagnosis of autism, and avoiding parental recall bias. Diagnosis of autism and MMR vaccination were recorded independently, rendering the possibility of differential misclassification of exposure and outcome unlikely. Despite a failure to adjust for a family history of autism - a factor that may have influenced their decision to have their children vaccinated – this high-powered study provides strong evidence against the hypothesis that MMR vaccination is associated with the development of autism in children.


Perfectionism in Anorexia Aervosa: A 6-24-month Follow-up Study
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A study was conducted to determine the influences of body dissatisfaction on girls between the ages of nine and twelve. Weight related attitudes of parents, friends and media as well as the BMI were the four factors that were measured. Internalization of the socially accepted ideal body promoted by these sources was thought to play a central role in the development of body dissatisfaction. The study comprised of 356 females whose perceptions were evaluated based on several measures: Sociocultural Attitudes Towards Appearance Questionnaire (Heinberg, Thompson and Stormer, 1995), Body Esteem Scale (Mendelson and White, 1982), Body Shape Perceptions and Preferences (Collins, 1991), Perception of Weight (Wardle and Marsland, 1990), Maternal and Peer Weight/ Eating Related Concerns and Behaviour (Conner, Martin, Silverdale and Grogan, 1996), and Media Exposure. It was found that while body dissatisfaction was associated with a higher BMI, it was not restricted to overweight girls. Media exposure and
parental guidance shaped the girls’ perceptions of the ideal body image, however, peer weight related attitudes had the greatest impact. Perhaps future interventions should target the influences of media, peers and parents on the development of body dissatisfaction in young women.


RNA Interference Targeting Fas Protects Mice from Fulminant Hepatitis
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Hepatocytes are very susceptible to Fas-mediated apoptosis, which occurs in various hepatic injuries including viruses, autoimmunity and transplant rejection. This study tests the therapeutic potential of RNA interference (RNAi) to treat or prevent liver diseases by using small interfering RNA (siRNA) duplexes that inhibit Fas expression on mouse hepatocytes in vivo.

Synthetic Fas siRNA duplexes were created that specifically and stably reduced Fas mRNA and Fas protein in hepatocytes by 81-86% compared to saline or GFP siRNA when injected intravenously. When treated in vitro with either an agonistic Fas-specific antibody or concanavalin A (ConA)-stimulated hepatic mononuclear cells (both induce apoptosis), hepatocytes from mice treated with Fas siRNA were resistant to cytolyis while those from mock treated or untreated mice were not.

Mice were then given ConA by intravenous injection. Those pretreated with saline or GFP siRNA showed hepatocyte necrosis and inflammatory infiltration, while those pretreated with Fas siRNA had only mild hepatocyte swelling. This liver pathology was reflected in the measurements of serum transaminases. Next, to imitate chronic liver injury, a reduced dose of ConA was given in six weekly injections, with Fas siRNA administered 24 hr after the 2nd and 4th injections. All mock and GFP siRNA treated mice developed bridging fibrosis, whereas no hepatic fibrosis or necrosis was observed in Fas siRNA treated mice. Also, in Fas siRNA treated mice, indicators of active fibrosis (hepatic hydroxyproline and serum procollagen type III) were present in reduced levels.

Lastly, mice were injected intraperitoneally with an agonistic Fas-specific antibody to mimic an aggressive hepatitis model. All control mice died within 3 days, whereas 33 of the 40 mice pretreated with Fas siRNA survived the 10 days of observation, showing that Fas silencing during the acute insult can prevent death from fulminant hepatitis. Thus, siRNA-directed Fas silencing may be of therapeutic value for preventing and treating acute and chronic liver injury.


Vitamin D Receptor as an Intestinal Bile Acid Sensor
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Epidemiological studies have demonstrated that vitamin D \([1,25(OH)_2D_3]\) exerts protective effects in the development of colorectal cancer. In the report by Makishima et al., vitamin D receptor (VDR), a member of the nuclear hormone receptor superfamily of ligand-activated transcription factors, mediates the detoxification of a potent hepatic and enteric carcinogen, lithocholic acid (LCA). LCA is a toxic secondary bile acid metabolite formed in the intestine by the bacterial \(7\alpha\)-dehydroxylation of chenodeoxycholic acid, the main bile acid that emulsifies dietary fats.

In this report, it was shown that both LCA and vitamin D bind to and activate VDR in the small intestine and liver of mice. This activation results in \(de novo\) expression of the detoxifying enzyme CYP3A, a member of the P450 class of monoxygenase enzymes that is active in small intestine and liver. CYP3A expression was induced directly by the binding of VDR and its heterodimerization partner retinoid X receptor (RXR) to DNA at specific VDR-response elements in the promoter of the CYP3A gene.

These DNA-binding studies were carried out in vitro. To definitively demonstrate a role for VDR, and more specifically vitamin D, in the induction of CYP3A activity in vivo, mice were treated with \(1\alpha\)(OH)\(D_3\), and a synthetic and highly specific VDR agonist, EB1089. The researchers show that in vivo the CYP3A genes are induced to robust levels in both murine liver and intestine. The group speculates that this may be a mechanism of the enteric system in response to potentially harmful chemicals, and they argue that the activation of P450 enzymes mediated by VDR may be one of the ways by which vitamin D exerts protective effects from the development of colorectal cancer.

Certainly, this work draws an interesting molecular link between vitamin D and the metabolism of hepato- and enterotoxic compounds; however, as the researchers correctly describe, much more work is needed to clarify the role that diet, bile acids, and vitamin D have in the pathogenesis of colorectal cancer. Indeed, these same experiments should be carried out in a murine model of colorectal cancer to examine whether or not this intriguing regulatory circuit affects the development of this type of cancer.