CONTINUING MEDICAL EDUCATION

AUSTRALIA ANTIGEN AND ITS SEXUAL TRANSMISSION

K V R Chari, M A Tutakne, K D Das and C B Mukherjee

Sexually transmitted diseases constitute one of the important communicable diseases in India next to malaria and tuberculosis.[1] These can be stated to be behavioural diseases, the behaviour depending upon social and cultural forces. The pattern of sexual behaviour has undergone remarkable changes due to rapid changes in the life-styles of some individuals adopting hazardous practices of sex. The inclusion of mouth and anus within the orbit of sexual activity in homosexuals has led to an increasing trend in sexually transmitted enteric diseases like hepatitis B, shigellosis, amoebiasis and giardiasis in western countries. The discovery of Australia antigen by Blumberg et al in 1965[2] opened up a new era in hepatitis research. Several studies in 1973 showed increased prevalence of Australia antigen in patients attending STD clinics,[3-7] but other studies[8-10] yielded conflicting results, leading to a doubt whether sexual transmission of Australia antigen is an important route of spread of infection in heterosexuals. In India, only a few studies dealing with sexual transmission of Australia antigen are available.

Historical Aspects

Blumberg et al called this antigen as the Australia antigen, because it was first discovered in the blood of an Australian aborigine.[2] It's association with serum hepatitis was confirmed by various workers differentiating infectious hepatitis from serum hepatitis.[11-14] Transmission of Australia antigen by blood transfusion was also established.[15-17]

From the Departments of Dermato-Venereology and Pathology, Armed Forces Medical College, Pune-411 040, India.

Address correspondence to : Lt. Col. K.V.R. Chari, Dermatologist, Military Hospital, Meerut Cantt-250 001, India.

Nature and Significance of Australia Antigen

Australia antigen is a lipoprotein and its specific gravity is less than 1.21.[18] Its concentration in infected serum has been estimated at about 10^{13} particles per ml.[19] Under an electron microscope, Australia antigen consists of three forms. The 'Dane' particles, regarded as the virus of hepatitis B, consists of a double shelled structure, the outer shell having a diameter of 42 nm containing HBsAg, and an inner core of 20 nm diameter containing hepatitis B core antigen (HBcAg).[20] Tubular forms and small round forms of about 20 nm diameter are also seen. Hepatitis B virus has three antigens known as the surface antigen (HBsAg), core antigen (HBcAg) and the 'e' antigen (HBeAg).[21]

HBsAg is found on the surface of all particles and its presence in the blood is a marker for the infection with hepatitis B virus. Australia antigen itself is now termed as hepatitis B surface antigen (HBsAg). HBsAg exhibits antigenic heterogenicity and four pheno types adw, ayw, adr and ayr are observed. These types are of value in the epidemiological studies. HBsAg appears in the serum about 4 weeks before the onset of symptoms, declining with the onset and usually disappearing in about six weeks thereafter. The antibody to HBsAg is called anti-HBs which persists in low titres until convalescence. HBcAg which is detected only in

the nuclei of infected hepatocytes, indicates high degree of infectivity. It appears at almost the same time as HBsAg but disappears more rapidly. Its antibody is called anti-HBc which indicates previous infection with serum hepatitis. If CMI is competent, the infection is eliminated, but in the case of impaired immune response, as in subclinical or mild hepatitis, persistent antigenaemia is likely to occur.

Incidence of Australia Antigen

The incidence of Australia antigen in developed countries is very low (USA 0.1%), while in developing countries it is very high.[14] Various studies done in India (Table I) showed that incidence varied from 0.6% to 4%. The wide variation in the incidence of Australia antigen is said to be due to the genetic susceptibility of various races,[35] geographical variations[27] and environmental factors.[11,29] India being a poor and tropical country, substandard hygiene may be responsible for the spread of the virus by the faeco-oral route.[29] Incidence of Australia antigen is high in professional blood donors.[33] In females, it is less than the males.[16,29] It is commoner in the younger age groups, as in them the infection tends to follow a mild clinical or subclinical course.[27,34,36]

Mode of Transmission of Hepatitis B

(a) Parenteral transmission

Parenteral transmission of Australia antigen through blood transfusions,[16] needles, blood sucking insects and by transplacental route[27] is well documented. In India however, Paul et al[29] did not find HBsAg in the cord blood of infected mothers.

(b) Non-parenteral transmission

Studies in closed institutions,[11,36] in families,[38] and in hospital staff[39] showed increased incidence of Australia antigen, suggesting non-parenteral transmission. Other non-parenteral routes such as air-borne spread,[39] faeco-oral route,[40] through urine,[41] saliva,[42,44] semen,[43,44] menstrual fluid[45] and vaginal

Table I. Incidence of Australia antigen in India.

Place	Number of sera Tested	Percent positive	Method
1. Calcutta	199	Nil	I.D.
2. (a) Delhi blood donors	952	0.1	I.D.
(b) ——do——	876	2.7	IEOP
(c) Armed Forces Blood Transfusion centre New Delhi			
(i) Voluntary blood donors	680	2.65	
(ii) Professional blood donors	176	2.58	IEOP
(d) AIIMS New Delhi professional donors	1024	3.91	IEOP
(e) Delhi			
(i) Voluntary	876	1.6	
(ii) Professional blood donors	—	2.73	IEOP
3. Bombay Blood Group Reference centre			
(a) Healthy	200	1.0	I.D.
(b) Professional	—	4.0	I.D.
4. South India	253	2.8	I.D.
5. Chandigarh			
(a) Voluntary male blood donors	1001	2.2	
(b) Healthy females	460	0.43	IEOP
(c) Cord blood	68	0	
6. Madras			
(a) Blood donors	123	1.62	IEOP
		9.79	RPHA
(b) Hospital personnel	123	4.59	IEOP
		16.53	RPHA
7. Aurangabad	625	4.00	IEOP
8. Pune	420	1.4	I.D.
9. Vellore			
(a) Voluntary blood donors	531	0.75	
(b) Professional blood donors	—	3.8	IEOP
10. Trivandrum			
(a) Voluntary blood donors	475	1.8	
(b) Professional blood donors	575	2.4	IEOP
(c) Pregnant women	400	3.0	
(d) Staff & students of Medical College Trivandrum	150	0.6	

secretions[46] have been suggested. However, presence of HBsAg in menstrual fluid has not been accepted by many.[3-5,38]

(c) Australia antigen and sexual transmission

Some studies on the incidence of Australia antigen in families indicated spread of the infection between couples.[38] Tanno et al[42] reported that 4 patients developed the disease after an attack of acute hepatitis in their spouses. Both had Australia antigen in their urine and saliva. Wright[17] recorded transmission of HBsAg in two hepatitis patients who had had sexual contact six months before their illness, with asymptomatic carriers of HBsAg. Moslley[48] found that 18% spouses of acute viral hepatitis patients contracted the infection, but none of the other family members. Koff et al[19] found that out of the 13 spouses of 81 household contacts of acute viral hepatitis patients, 2 spouses developed acute viral hepatitis and one developed antibody. In a survey at Pune, out of 19 couples in 12 families, 10 had infection in both spouses, and in the remaining 9, only one partner had infection. Demonstration of the Australia antigen in the saliva, semen and menstrual blood showed that sexual transmission might play a possible role in the transmission of serum hepatitis. But since the concentration of the antigen in semen (ratio in semen as compared to serum being in the range of 1/250 to 1/25,000) was low, it was not possible to say to what extent, the saliva and semen would be infectious.[43]

The most conclusive proof of sexual transmission followed studies on homosexual populations. Based on the observation that Australia antigen positive homosexuals never had any injections, Vahrmann[50] suggested venereal transmission of the antigen from mucous membrane to mucous membrane or from abrasions exuding infected serum. Fulford, et al[3] studied 974 patients attending the STD clinics and found that the incidence of HBsAg and its antibody was 10 times greater in their sera compared to the blood donors. Jeffries et al[5] found 10 times more incidence of Australia antigen in homosexuals than in controls and heterosexuals, and concluded that homosexuals constituted the high risk group. The frequency of drug abuse was low and possible transmission with insects was excluded. Heathcoate and Sherlock[4] surveyed 69 patient contacts of acute hepatitis B and found sexual or domestic contacts in 40%. Szmuness et al[6] found 51% incidence of HBsAg in the homosexuals compared to 20.4% in the heterosexuals. Lim et al[7] found that 30% homosexuals and bisexual men were antibody positive compared to 5% heterosexual men. Simmons et al[51] found 77% male homosexuals to be hepatitis 'e' antigen positive and they are of subtype 'ad' compared to subtype 'ay' in heterosexual partners. Coleman et al[52] found 5.2% positivity of HBsAg or its antibody in 600 male homosexuals. Dietzman et al[53] recorded 5.8% HBsAg and 34% its antibody in 144 homosexuals compared to 0.9% HBsAg and 3.6% antibody in 111 heterosexuals and healthy controls. These studies suggest that increased incidence of Australia antigen depends upon the pattern of sexual behaviour, such as large number of sexual partners, long duration of homosexuality, predominantly ano-rectal intercourse, oro-genital sexual contact, and the practice of swallowing semen. Skinhoj et al[54] outlined that homosexual subpopulation represents the reservoir of infection. One third of these patients were found to have chronic active hepatitis, 1/5 of them had chronic persistent hepatitis but were symptom-free. Simmons[55] deduced that high-risk-groups who carry HBV include homosexuals, drug abusers, prostitutes, patients with previous liver disorders and tatooed patients. Reiner et al[56] found that asymptomatic bleeding points on the rectal mucosa in homosexuals in chronic carriers of HBsAg, created a setting for de facto parenteral transmission when there was a contact with oral

or urethral mucosa. Dutta and Sachdeva[57] studied sexual transmission of viral hepatitis B and its carrier state in patients with STD and found that hepatitis B infection was not related to sexual contacts in India and thus his studies did not suggest sexual mode of transmission of the virus. In a study at Pune by the author, no significant increase in the incidence of Australia antigen was found in STD cases (unpublished data).

Studies in Prostitutes

Prostitutes constitute high-risk-groups to contract STD and Australia antigen, and can be taken as a suitable group to assess promiscuity. Studies on prostitutes however, gave conflicting results.

Adam et al[8] studied 272 prostitutes and 162 women controls and found that the incidence of the antigen was 5% in prostitutes and 9% in women controls, and that for the antibody 20% was in prostitutes and 12% in controls. Papaevangelou et al[9] found HBsAg in 4.4% prostitutes and 3.4% in controls at Athens, while on the other hand, anti-HBs was found in 56.7% prostitutes but in 24.5% controls. Frosner et al[10] found no significant difference in the incidence of Australia antigen in the prostitutes and controls, but found 31% antibody positivity in the prostitutes compared to 10% in the female blood donors and nuns in a convent. The incidence of antibody increased with age.[8-10] In a study by the author at Pune on 75 prostitutes, no case was positive for Australia antigen compared to 0.69% incidence in 145 female controls (unpublished data).

Studies on homosexuals, heterosexuals and prostitutes thus, indicate that even though prevalence of Australia antigen is more in homosexuals, it cannot be firmly said that Australia antigen can be transmitted by the vaginal route.

Incidence of Australia Antigen in Different types of Sexually Transmitted Diseases

Since the study of Australia antigen evoked the study of different STDs, the distribution of Australia antigen in various sexually transmitted diseases was studied by various workers Papaevangelou et al[9] found no statistical difference between the incidence of syphilis and Australia antigen and its antibody in prostitutes. Vranckx[58] found Australia antigen in 9.1% of syphilis patients. Lenka et al[59] found 21.73% incidence of Australia antigen in syphilis. Joshi and Jundre[60] found 5.2% syphilis cases positive for Australia antigen or antibody. Kelkar[61] found no significant difference. Kacaki et al[62] found increased antigenaemia in acute gonorrhoea. In a study at Pune by the author, no significant difference was found with relation to the type of STD. However, the significance of the incidence of Australia antigen in different types of STD is not known.

Concluding Remarks

Detailed review of the incidence of Australia antigen in sexually transmitted diseases suggests that while studies in homosexuals as a group in western countries showed increased incidence of antigen, studies of heterosexuals and prostitutes on the contrary, indicated that it cannot be firmly said that Australian antigen is transmitted by the vaginal route. In India, even though promiscuity is on the increase, homosexuality with anal or oro-genital intercourse is not very common, accounting for low incidence in the sexually active population. The culturally conditioned behaviour of women in India makes sexual transmission of Australia antigen unlikely.

References

1. WHO (1967) Third report on the world health situation, in : Text book of Preventive and Social Medicine, Sixth Ed, Editors, Park JE and Park K : Banarasi Das Bhanot Publishers, Jabalpur, 1977; p 487.
2. Blumberg BS, Alter HJ and Visnich S : New antigen in leukemic sera, JAMA, 1965; 191 : 541-546.
3. Fulford KWM, Dane DS, Catterall RO et al : Australia antigen and antibody among patients attending a clinic for STD, Lancet, 1973; 1 : 1470-1473.

4. Heathcoate J and Sherlock S : Spread of acute hepatitis B in London, Lancet, 1973; 1 : 1468-1470.
5. Jeffries DJ, James WH, Jeffries FJ et al : Australia (hepatitis associated) antigen in patients attending venereal disease clinic, Brit Med J, 1973; 2 : 455-456.
6. Szmuness W, Much MI, Prince AM et al : On the role of sexual behaviour in the spread of hepatitis B infection, Ann Int Med, 1975; 83 : 489-495.
7. Lim KS, Tamwong V, Fulford KWM et al : Role of sexual and non-sexual practices in transmission of hepatitis B, Brit J Vener Dis, 1977; 53 : 190-192.
8. Adam E, Hollenger FB and Melnick JL : Type B hepatitis antigen and antibody among prostitutes and nuns. Study of possible venereal transmission, J Infect Dis, 1974; 129 : 317-321.
9. Papaevangelou G, Trichopoulas D and Kremastenou T : Prevalence of hepatitis B antigen and antibody in prostitutes, Brit Med J, 1974; 2 : 256-258.
10. Frosner GG, Buchholz HM, Gertz HJ : Prevalence of hepatitis B antibody in prostitutes, Amer J Epidemiol, 1975; 102 : 241-250.
11. Sutnick AI, London WT, Grestley BJ et al : Anicteric hepatitis associated with Australia antigen. Occurrence in patients with Down's syndrome, JAMA, 1968; 205 : 670-674.
12. Hirschmann RJ, Schulman NR, Barker LF et al : Virus like particles in sera of patients with infectious and serum hepatitis, JAMA, 1969; 208 : 1667-1670.
13. Krugman S and Giles J : New light on old disease, JAMA, 1970; 212 : 1019-1029.
14. Blumberg BS, Sutnick AI, London WT et al : The discovery of Australia antigen and its relation to the viral hepatitis, Perspect Virol, 1971; 7 : 223-240.
15. Allen JG, Altopalo C and Sayman WA : Serum hepatitis from transfusion of blood, Epidemiological study, JAMA, 1962; 180 : 1079-1085.
16. Okochi K and Murakami S : Observation of Australia antigen in Japanese, Voxsang, 1968; 15 : 374-385.
17. Barker LF, Shulmann NR and Murray R : Transmission of serum hepatitis, JAMA, 1970; 211 : 1509-1512.
18. Alter HJ and Blumberg BS : Further studies on new human iso-precipitin system (Australia antigen), Blood, 1966; 27 : 297-309.
19. Almeida JD and Waterson AP : Immune complexes in hepatitis, Lancet, 1969; 11 : 983-986.
20. Dane DS, Cameron IG and Briggs M : Virus like particles in serum of a patient with Australia antigen associated hepatitis, Lancet, 1970; 1 : 695-698.
21. Catterall RD : Some observations on epidemiology and transmission of hepatitis B, Brit J Vener Dis, 1978; 54 : 335-340.
22. Hill WD, Pattanayak S and Arora DD : Detection of Australia antigen in human viral hepatitis, Ind J Med Res, 1970; 58 : 1172-1176.
23. Sama SK, Anand S, Malaviya AN et al : Australia SH antigen in normal population and patients of viral hepatitis in Delhi, Ind J Med Res, 1971; 59 : 64-67.
24. Wali JD, Sama SK, Bajaj R et al : A study of hepatitis associated antigen carrier-Paper presented in 13th Annual conference of Indian Society of Gastro-enterology at Goa, 1972; (Quoted by 29).
25. Dutta RN, Mohammed GS: Incidence of Australia antigen in voluntary and professional blood donors and also in cases of viral hepatitis, Ind J Med Res, 1972; 60 : 1774-1778.
26. Pastakia B, Sashianand Gandhi GS and Sama SK: Hepatitis B antigen in professional blood donors at AIIMS hospital, Ind J Med Res, 1975; 62 : 1195-1198.
27. Sama SK, Sarla PK and Gora KL : Hepatitis associated antigen against blood donors in Delhi by counter electrophoresis, Ind J Med Res, 1973; 61 : 405-410.
28. Bombay blood group research centre, ICMR, GS Seth Medical College, Bombay, Yearly Report, 1971; 41.
29. Paul SR, Dutta DV, Choudhry S et al : SH Ag amongst patients with liver diseases and voluntary blood donors—a prospective study, Ind J Med Res, 1973; 61 : 1784-1798.
30. Thyagarajan SP, Subramaniam S, Sundravelu T et al : Hepatitis B surface antigen carriers among hospital personnel, J Assoc Phy Ind, 1981; 29 : 941-945.
31. Kotwal SP and Kelkar SS : Hepatitis B antigen in endemic hepatitis at Aurangabad, Ind J Med Sciences, 1973; 27 : 856-860.
32. Kelkar SS, Niphadkar KB and Khare PM : Titres of Australia antigen in healthy carriers, leprosy, cirrhosis liver and acute hepatitis, Ind J Med Res, 1973; 61 : 684-688.

33. Peter GH, Jacobjohn T, Shanmugam RV et al : Australia antigen in blood donors in Vellore, Ind J Med Res, 1973; 61 : 378-382.
34. Shanmugam J, Balakrishnan V, Venugopalan P et al : Prevalence of hepatitis B surface antigen in blood donors and pregnant women from Southern Kerala, Ind J Med Res, 1978; 68 : 91-96.
35. Blumberg BS, Sutnick AI and London WT : Australia antigen as hepatitis virus, Amer J Med, 1978; 48 : 1-3.
36. Szmuness W and Prince AM: The epidemiology of serum hepatitis (SH) infection, A controlled study in 2 closed institutions, Amer J Epidemiol, 1971; 94 : 585-595.
37. Papaevangelou G, Hoofnagle J and Kremastinou J : Transplacental transmission of hepatitis B virus by symptom-free chronic carrier mothers, Lancet, 1974; 2 : 746-748.
38. Hersh T, Melnick J, Goyal RK et al : Nonparentral transmission of viral hepatitis type B, New Eng J Med, 1971; 285 : 1363-1364.
39. Almeida JD, Chisholm GD, Kulatilake AE et al : Possible airborne spread of serum hepatitis virus within a haemodialysis unit, Lancet, 1971; 2 : 849-850.
40. Grob PJ and Jemelka H : Faecal SH (Australia) antigen in acute hepatitis, Lancet, 1971; 1 : 206-208.
41. Apostovlov K, Bauer DJ, Selvay JWT et al : Australia antigen in urine, Lancet, 1971; 1 : 1274-1275.
42. Tanno H, Fay O and Ron Coroni M : Virus B hepatitis in saliva, Lancet, 1972; 2 : 822-823.
43. Heathcoate J, Cammeron CH and Dane DS : Hepatitis B antigen in saliva and semen, Lancet, 1974; 1 : 71-73.
44. Linnemann CC and Goldberg : Hepatitis B antigen in saliva and semen, Lacet, 1974; 1 : 320.
45. Mazzur S : Menstrual blood as a vehicle for Australia antigen transmission, Lancet, 1973; 1 : 749.
46. Darani M and Gerber M : Hepatitis B antigen in vaginal secretions, Lancet, 1974; 1 : 1008.
47. Wright RA : Hepatitis B and hepatitis B surface antigen carrier—An out-break related to sexual contact, JAMA 1975 ; 232 : 717-721.
48. Mosllcy JW : The epidemiology of viral hepatitis-an overview, Amer J Med Sci, 1975; 270 : 253-270.
49. Koff RS, Slavin MM, Commelly LJD et al : Contagiousness of acute hepatitis B secondary attack rates in house-hold contacts, Gastroenterology, 1977; 727 : 297-300.
50. Vahrmann J : Transmission of hepatitis, Lancet, 1970; 11 : 774.
51. Simmons PD, Islam MN, Knott S et al : Antigen among male homosexual patients, Brit Med J, 1977; 2 : 1458.
52. Coleman JC, Waught M and Bayton R : Hepatitis B antigen and antibody in male homosexual population, Brit J Vener Dis, 1977; 53 : 132-134.
53. Dietzman DE, Harnisch JP, Key CG et al : Hepatitis B surface antigen (HBsAg) and antibody to HBsAg—Prevalence in homo and heterosexual men, JAMA, 1977; 238 : 2625-2626.
54. Skinhoj P, Hoybye G, Hentzer B et al : Chronic hepatitis B infection in male homosexuals, J Clin Path, 1979; 32 : 783-785.
55. Simmons PD : Follow up of patients with hepatitis B surface antigen, Brit J Vener Dis, 1979; 55 : 116-117.
56. Reiner NE, Judson FN, Bond WW et al : Asymptomatic rectal mucosal lesions and hepatitis B surface antigen at sites of sexual contact in homosexual men with persistent hepatitis B virus infection, Ann Int Med, 1982; 96 : 170-173.
57. Dutta AK and Sachdeva SM : Sexual transmission of viral hepatitis B and its carrier state in patients with sexually transmitted diseases (STD), J Assoc Phys Ind, 1982; 30 : 861-864.
58. Vranckx R : Hepatitis B antigen and serological evidence of syphilis, Lancet, 1975; 1 : 1193.
59. Lenka MR, Ghosh E, and Panja SK : Prevalence of Australia antigen (HBsAg) in STD, Ind J Dermatol Venereol Leprol, 1981; 47 : 208-211.
60. Joshi BN and Shailaja Jundre : Prevalence of hepatitis B antigen/antibody in patients of syphilis, Ind J Dermatol Venereol Leprol, 1980; 46 : 335-337.
61. Kelkar SS, Phaltankar : Sexual transmission of hepatitis B virus, JAMA, 1982; 30 : 90-100.
62. Kacaki J, Schuurs AHWM and Walters G : Hepatitis antigen in venereal diseases, Lancet, 1975; 11 : 363-364.