A study of hepatitis B infection in a Montana insititution for the mentally retarded
by Bradford Oldham Brooks

A thesis submitted in partial fulfillment of the requirements for the degree of MASTER OF SCIENCE in Microbiology
Montana State University

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Cohorting, Routine Admission Screening, Environmental Surface Testing, and Immune Competence testing were proposed in an endeavor to lower the prevalence of Hepatitis B at Boulder River School and Hospital.

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by

BRADFORD OLDHAM BROOKS

A thesis submitted in partial fulfillment
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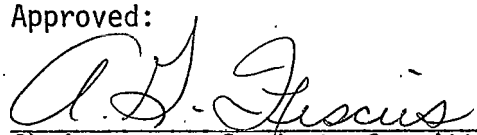
Approved:



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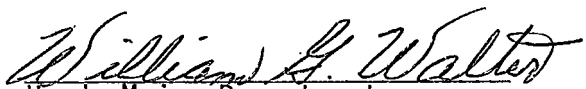

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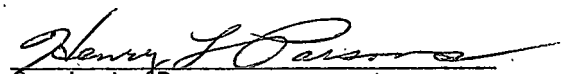

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ABSTRACT

A test population of 524 patients in residence at Boulder River School and Hospital was assayed for the prevalence of both anti-HB_s and HB_sAg. 16.8% of the test population were found to be positive for either of these markers indicating Hepatitis B infections are endemic to this institution. Correlations were observed between the prevalence of these markers and the following: Sex, Institutional Location, Degree of Ambulation, Feeding Skills, and Drinking from Faucets, Sinks and Bathtubs.

Cohorting, Routine Admission Screening, Environmental Surface Testing, and Immune Competence testing were proposed in an endeavor to lower the prevalence of Hepatitis B at Boulder River School and Hospital.

INTRODUCTION

Viral hepatitis has classically been a mysterious and intractable disease. It has long been recognized that symptoms arise from two distinct types of infection. Hepatitis A, also called infectious hepatitis, short incubation hepatitis, or MS-1 hepatitis, is thought to be transmitted primarily by fecal-oral contamination. Hepatitis B, also called serum hepatitis, long incubation hepatitis, or MS-2 hepatitis, is thought to be transmitted parenterally (1).

Until recently little else was known about viral hepatitis. A major breakthrough occurred in 1964 when Dr. Baruch S. Blumberg et al. (2) discovered a new antigen in the peripheral blood of an Australian Aborigine. This antigen was subsequently labeled the "Australia Antigen." It was thought to be implicated with lymphocytic leukemia, lepromatous leprosy, Hodgkins's disease, and Down's syndrome (3-6). In 1968, Prince et al. (7) observed a similar substance in the blood of patients with hepatitis B. Closer laboratory observation revealed that this substance and the "Australia Antigen" were identical. Further investigation has revealed the correlation of this antigen with hepatitis B infections (3, 5, 7-12).

This original antigen, now called the hepatitis B surface antigen (HB_sAg), served as the first serological marker for hepatitis B. It is both a means for diagnosing the presence of hepatitis B and an instrument with which to investigate the nature of the disease. HB_sAg is characterized as a small, spherical particle approximately 22 nm in

diameter. The predominant form is a spherical particle, although filaments 22nm in diameter and varying length are also observed. It is a protein substance containing some lipid components, but devoid of nucleic acids. It has a molecular weight of 3×10^6 and a buoyant density of 1.21. It is stable at 56°C overnight, resistant to treatment with proteolytic enzymes and withstands storage at -20°C for up to 20 years (13, 14).

All hepatitis B surface antigens (HB_sAg) have a common antigenic determinant designated *a* (15, 16). In addition, two pairs of mutually exclusive antigenic determinants (*d* and *y*, and *w* and *r*) have been described (16, 17). Therefore, there are four possible HB_sAg subtypes *adw*, *adr*, *ayw*, *ayr*. Subtypes of HB_sAg are useful mainly as epidemiological markers. Epidemiologically related cases of viral hepatitis type B have the same HB_sAg subtype (18, 19). The subtype of individuals, with acute or chronic hepatitis or those who are symptom-free carriers, almost always remains the same while they are HB_sAg positive (19, 20). There is an unequal geographical distribution of HB_sAg subtypes. In the U.S.A. the subtype observed in patients with chronic hepatitis and chronic symptom-free carriers is normally *ad*. Subtype *ay* is most often found in patients suffering attacks of acute hepatitis. This is readily seen among drug addicts (18, 21) and patients undergoing renal dialysis. Studies on the relation between subtype and liver abnormality have yielded inconclusive results (22).

Recent investigation has revealed that the HB_sAg is merely a fragment of an extremely complex antigen system. Dane et al. (23) first reported large particles 40-42 nm in diameter with a double wall and inner core resembling a viral neucleoid in the sera of patients with hepatitis B antigenemia. These particles (Dane particles) were found to have hepatitis B antigenic determinants on their surfaces. They also showed a distinct inner core approximately 27 nm in diameter. Dane et al. (24) proposed that these larger particles constitute the complete hepatitis B virion and that the other more abundant morphological forms (25) of serum HB_sAg particles denote excess virus coat protein. Dane's hypothesis was enchanced when Almeida (26) discovered a new antigen system in the 27 nm inner core of the Dane particle. Investigators have been able to detect and differentiate human antibody directed against surface antigenic components (HB_sAg) of the Dane particle and antibody directed against the core antigenic components of the Dane particle (HB_sAg) (27). Kaplan et al. (28) have demonstrated the DNA-polymerase activity is associated with the Dane core, lending further credence to Dane's original hypothesis.

Infection with hepatitis B is not always accompanied by overt clinical symptoms (29). Some apparently healthy carriers of the infection may be detected by assaying for the presence of HB_sAg in the patients' serum. A number of techniques have been developed and utilized to detect HB_sAg in the sera of infected patients. One sensitive

technique is that of radioimmunoassay (30). The solid phase sandwich radioimmunoassay developed by Ling and Overby (31) is both sensitive and specific, permitting a higher frequency of detection of HB_sAg (32).

An elevated incidence of HB_sAg chronic carriers has been found among the residents of certain institutions (33). Especially those institutions for the mentally retarded (4, 5, 34, 35). Boulder River School and Hospital, Boulder, Montana, is an institution of this type. It has been plagued with recurring outbreaks of hepatitis B since 1970. The risk of infection with hepatitis B that a patient encounters at Boulder River School and Hospital is not well defined. This risk needs to be more accurately assessed in a controlled survey, and the epidemiologic patterns of hepatitis B infections within this institution need to be investigated. Such a survey would contribute to a better understanding of the mechanisms of the transmission of the virus and its relation to environmental and genetic factors. Such a study could also be used to elucidate specific controls for hepatitis B at this institution.

MATERIALS AND METHODS

Sera

Serum samples were obtained from both residents and staff of the Boulder River School and Hospital (BRSH), an institution for the mentally retarded located in Boulder, Montana. Samples were stored at -20°C for various periods of time ranging from four weeks to 14 months. Ths sample drawing period extended from August 1974 to June 1975.

HB_sAg Assay

The technique used to detect hepatitis B surface antigen (HB_sAg) was radioimmunoassay, the Ausria-II 125 system produced by Abbott Laboratories. This is a solid phase radioimmunoassay employing an Antibody-Antigen-Antibody sandwich (31, 32, 37-40).

The procedure consisted of the addition of 0.2 ml of serum sample to wells containing anti-HB_s coated (guinea pig) beads. Beads and serum were then incubated for two hours at 45°C. Beads were washed with a total of 10.0 ml of sterile water using a cornwall syringe and an aspirating canula. 0.2 ml of ^{125}I-labeled antibody (antiHB_s) was added to the washed beads. The beads and the radiolabeled antibody were incubated for one hour at 45°C. The beads were washed as before and transferred to counting tubes. Samples were counted in a well-type gamma scintillation counter. The non-specific false positives that normally result from cross reactions in the sandwich technique of radioimmunoassay were circumvented by using a heterologous antibody system (Guinea Pig anti-HB_s coated beads and ^{125}I-labeled human anti-HB_s).

Negative human control in the Ausria-II system consisted of recalcified human plasma nonreactive for hepatitis B surface antigen (HB_sAg) or its corresponding antibody (anti-HB_s). 0.1% sodium azide was added as a preservative. Positive human control in this system consisted of human plasma reactive for hepatitis B surface antigen (HB_sAg) in a 0.01 M TRIS buffer containing 4% bovine serum albumin and 0.1% sodium azide as preservative. This control had been heat inactivated for 10 hours at 60°C. ^{125}I-anti-HB_s (human) in this system was supplied in a 0.005 M TRIS aminomethane buffer containing 50% calf serum, 2% normal human serum, 0.5% bovine serum albumin, and 0.1% sodium azide as preservative. Anti-HB_s (guinea pig) in this system was adsorbed onto the surface of polystyrene beads and used in that form.

Results of this assay were determined by relating net counts per minute of the unknown serum sample to net counts per minute of the negative control mean times the factor 2.1.

This factor has been selected in order to decrease the total number of non-repeatable positives (47). Serum samples whose net counts per minute were higher than the mean cutoff value established with the negative control mean were considered presumptively reactive for HB_sAg. The mean value for the positive control samples had to be at least five times the value of the negative control mean. Samples that were found to be presumptively positive were assayed a second time. Serum samples

whose counts per minute were repeatable above the established cutoff value were considered positive with respect to HB_sAg..

Chronic Carrier Determination

Chronic Carriers of the HB_sAg were determined by sequential testing of HB_sAg positive patients. Patients determined to be HB_sAg positive (31, 32, 37-40) were tested again at six months and again at one year. Those patients who were determined to be HB_sAg positive on all three occasions were considered to be chronic carriers of the HB_sAg.

Anti-HB_s Assay

Anti-HB_s detection in this study was accomplished through another sandwich type radioimmunoassay, the AUSAB system produced by Abbott Laboratories (31, 32, 41-44).

The procedure consisted of the addition of 0.2 ml of serum sample into a well containing antigen (HB_sAg) coated beads. Beads and serum were incubated for 18 hours at 25°C. Beads were washed in the wells with a total of 10.0 ml of sterile water using a cornwall syringe and an aspirating canula. 0.02 ml of ^{125}I-labeled antigen (HB_sAg was added to the wells. Beads and radiolabeled antigen were incubated for four hours at 25°C. Beads were washed with a total of 10.0 ml of sterile water as before and transferred to counting tubes. Samples were counted using a well-type gamma scintillation counter. Negative human control in this system consisted of recalcified normal human sera nonreactive for hepatitis B surface antigen (HB_sAg) or its corresponding antibody

(anti-HB_s). 0.1% sodium azide served as a preservative. ^{125}I-labeled HB_sAg was supplied in a 0.01 M TRIS aminemehtane buffer containing 20% recalcified normal human plasma, 1% bovine serum albumin and 0.1% sodium azide as preservative. All HB_sAg supplied in this system contained both *ad* and *ay* subtypes.

Results of this assay were determined by relating net counts per minute of the negative control mean times the factor 2.1. Samples whose net counts per minute were higher than the cutoff value established with the negative control mean were considered presumptively reative for anti-HB_s. Presumptively reative serum samples were retested to validate the presence of anti-HB_s in the specimen. Those samples found to be repeatedly reactive for anti-HB_s were considered to be positive with respect to anti-HB_s

Data Format

Medical histories were reviewed for each resident involved in the hepatitis B study at BRSH for the following information: 1. Age, 2. Sex, 3. BRSH location, 4. Duration of institutionalization, 5. Habits and Abilities. In the latter category, abilities pertains to information concerning the patient's relative skills in (1) Toilet Training, (2) Ambulation, (3) Feeding. Habits in this category pertains to behavior such as: 1. Playing in the toilet, 2. Playing in feces, 3. Playing in urine, 4. Placing foreign objects in mouth, 5. Eating/Sucking clothes, and 6. Drinking from toilets, sinks,

and bathtubs. These data were correlated to the presence of anti-HB_s, HB_sAg or both.

Statistical Treatment of Data

Statistical analysis of these data was carried out by making use of the ODDS-RATIO test, a commonly used epidemiological approach to data analysis (45, 46). Data were analyzed on a one-to-one basis as well as over a simultaneous confidence interval. Data analysis was reported using the one-to-one comparison. Maintaining an arbitrary p value of 0.05 as the minimal level of significance, all data were scrutinized for intrinsic differences. Comparisons having p values of ≤ 0.05 were considered to be significant and reported as such.

RESULTS

Upon the completion of radioimmunoassays for both HB_sAg and anti-HB_s among the 524 patients tested at BRSH, 66 patients were found to be positive for anti-HB_s and 22 patients were found to be HB_sAg positive. These data indicate that over 16% of the test population were infected with hepatitis B within the time frame of this study (Table I). In addition, four patients within the test population were found to be chronic carriers of the HB_sAg.

Age Correlation with Anti-HB_s and HB_sAg

Standard epidemiological age groupings were analyzed in order to determine if there is, in this institution, a correlation between the age of a patient and the presence of either anti-HB_s or HB_sAg. The results (Tables II, III) reveal that the older age groups in the institution have higher levels of anti-HB_s prevalence than age groups 15 years of age and younger. Age groups 40-44 years and 20-24 years were observed to have the highest levels of anti-HB_s prevalence. It was interesting that the 20-24 year age group contained 38% of the 66 anti-HB_s positive patients identified in this study.

The prevalence of HB_sAg positives also was higher in the 40-44 year age group. The 25-29 year age group was also observed to have higher levels of HB_sAg prevalence than the younger age groups analyzed. The 25-29 year age group contained 27.3% of the 22 HB_sAg positive patients identified in the test population. It was noted that no anti-HB_s positives and only one HB_sAg positive patient were found in age groups below 10 years of age. Of the chronic carriers of HB_sAg

Table I. Results of Anti-HB_s and HB_sAg Radioimmunoassays

Group	No.	% of Total Patients
Patients	524	100
Anti-HB_s(+)	66	12.6
HB_sAg(+)	22	4.2
Patients (+) for both HB_sAg and Anti-HB_s	4	.7
Chronic carriers of HB_sAg	4	.7
Patients (+) for either Anti-HB_s or HB_sAg	84	16.8

Table II. Anti-HB_s Association with Age Groupings

Age Group (years)	Anti-HB_s(+)	%	Chronic Carrier (HB_sAg)
1	0/0	0.0	0
1-4	0/10	0.0	0
5-9	0/26	0.0[b]	0
10-14	4/55	7.3	0
15-19	10/98	16.2[b]	0
20-24	25/129	19.4[a]	3
25-29	14/92	15.2[a]	1
30-34	5/55	9.1	0
35-39	4/26	15.4	0
40-44	3/12	25.0	0
45	1/23	4.3	0

[a,b,c]Percentages that differ in superscript are significantly different using the Odds-Ratio test (45, 46) $p \leq 0.05$.

Table III. HB_sAg Association with Age Groupings

Age Group (years)	HB_sAg (+)	%*	Chronic Carrier (HB_sAg)
1	0/0	0.0	0
1-4	0/10	0.0	0
5-9	1/26	3.8	0
10-14	2/53	3.8	0
15-19	1/98	1.1	0
20-24	5/129	3.9	3
25-29	6/92	6.5	1
30-34	2/55	3.8	0
35-39	1/26	3.8	0
40-44	1/12	8.3	0
45	0/23	0.0	0

*Percentage not having superscripts were not found to be significant using the Odds-Ratio test (45, 46).

identified in this study, three were located in the 20-24 age group and one was located in the 25-29 year age group.

Sex Correlation with Anti-HB_s and HB_sAg

The sex of patients was analyzed in order to determine if there is, in this institution, a correlation between the sex of a patient and the presence of either anti-HB_s or HB_sAg. The results Tables IV, V) reveal that there is a higher level of prevalence in both anti-HB_s and HB_sAg in the male segment of the test population. 15.9% of the males were found to be anti-HB_s positive as compared to 7.4% of the females. HB_sAg also followed a male predominance pattern with 5.5% of the males in the test population identified as positive compared with 2.3% of the females identified as HB_sAg positive. It was noted that 74.3% of the 66 anti-HB_s positives identified were male and 77.3% of the 22 HB_sAg positives were male. Chronic carriers of HB_sAg were male predominant 3:1. These data implicate a strong male predominance in the prevalence of both anti-HB_s and HB_sAg among the patients of BRSH.

Duration of Institutionalization Correlation with Anti-HB_s and HB_sAg

The length of a patient's institutionalization was observed in order to determine if there is in this institution, a correlation between a patient's length of stay and the presence of either anti-HB_s or HB_sAg. The results (Tables VI, VII) reveal that the prevalence of anti-$HB_s$is highest in the 10-14 years and 30-39 years duration groups.

Table IV. Anti-HB_s Association with Sex

Sex	Anti-HB_s(+)	%	Chronic Carrier (HB_sAg)
Male	49/307	15.9[a]	3
Female	17/216	7.4[b]	1
Unknown	0/1	0.0[c]	0

[a,b,c]Percentages that differ in superscript are significantly different using the Odds-Ratio test (45, 46) $p \leq 0.05$.

Table V. HB_sAg Association with Sex

Sex	$HB_sAg(+)$	%	Chronic Carrier (HB_sAg)
Male	17/307	5.5^a	3
Female	5/216	2.3^b	1
Unknown	0/1	0.0^c	0

^{a,b,c}Percentages that differ in superscript are significantly different using the Odds-Ratio test (45, 46) $p \leq 0.05$.

Table VI. Anti-HB_s Association with Duration of Institutionalization

Duration (years)	Anti-HB_s(+)	%	Chronic Carrier (HB_sAg)
1	0/2	0.0	0
1-4	5/41	12.2	0
5-9	13/175	7.4[a]	1
10-14	24/116	20.6[b]	3
15-19	16/113	14.2	0
20-24	3/30	10.0	0
25-29	2/24	8.3	0
30-39	3/18	16.6	0
40-49	0/5	0.0	0

[a,b]Percentages that differ in superscript are significantly different using the Odds-Ratio test (45, 46) $p \leq 0.05$.

Table VII. HB_sAg Association with Duration of Institutionalization

Duration (years)	$HB_sAg(+)$	%*	Chronic Carrier (HB_sAg)
1	0/2	0.0	0
1-4	1/41	2.4	0
5-9	6/175	3.4	1
10-14	6/116	5.2	3
15-19	5/113	4.4	0
20-24	0/30	0.0	0
25-29	1/24	4.2	0
30-39	2/18	11.1	0
40-49	1/5	20.0	0

*Percentages that have no superscript do not differ enough to be significant ($p \leq 0.05$) using the Odds-Ratio test (45, 46).

It was noted that 61% of the 66 anti-HB_s positives were in duration groups between 5 and 15 years. The HB_sAg prevalence levels present a more equal distribution among the duration groups indicating that higher levels of HB_sAg prevalence may not be associated with longer durations of institutionalization. These data implicate a very limited degree of association between a patient's length of stay at BRSH and the presence of either anti-HB_s or HB_sAg. Of the four chronic carriers of the HB_sAg identified, one was located in the 5-9 years group and three were located in the 10-14 years group.

Each year of admission of each patient was also analyzed for the occurrence of specifically "hot" years in which the prevalence of either anti-HB_s or HB_sAg reached significantly high levels. This approach provided a consistent and equal distribution throughout the range of years of admission.

Institutional Location Correlation with Anti-HB_s and HB_sAg

The institutional location of patients was analyzed in order to determine if there is, in this institution, a correlation between a patient's location and the presence of anti-HB_s and HB_sAg. The results (Tables VIII, IX) reveal a higher prevalence of both anti-HB_s and HB_sAg in the male segregated cottages than the rest of the population. This observation further supports the sex correlation results observed earlier. To allow for this observed sexual predisposition at BRSH,

Table VIII. Anti-HB_s Association with Location

Location (cottage)		Anti-HB_s(+)	%	Chronic Carrier (HB_sAg)
3	(male)	8/36	22.0	0
4	(male)	15/34	44.0[a]	1
5	(female)	2/24	8.3	0
6a	(male)	6/31	19.4[b]	0
6b	(female)	2/20	10.0	1
10	(male)	4/30	13.3[b]	1
11	(female)	1/32	3.1	0
12	(male)	6/17	35.3	0
13	(female)	1/24	4.2	0
14	(co-ed)	1/18	5.5	0
15	(co-ed)	2/18	11.0	0
16ab	(co-ed)	1/32	3.1	0
16c	(co-ed)	3/53	5.7	1
104c	(male)	0/8	0.0[b]	0

[a,b]Percentages that differ in superscript are significantly different using the Odds-Ratio test (45, 46) $p \leq 0.05$.

Table IX. HB_sAg Association with Location

Location (cottage)		$HB_sAg(+)$	%*	Chronic Carrier (HB_sAg)
3	(male)	4/36	11.1	0
4	(male)	4/34	11.8	1
5	(female)	1/24	4.2	0
6a	(male)	0/31	0.0	0
6b	(female)	1/20	5.0	1
10	(male)	1/30	3.3	1
11	(female)	0/32	0.0	0
12	(male)	0/17	0.0	0
13	(female)	0/24	0.0	0
14	(co-ed)	1/18	5.5	0
15	(co-ed)	2/18	11.0	0
16ab	(co-ed)	0/32	0.0	0
16c	(co-ed)	3/53	5.7	1
104c	(male)	1/8	12.5	0

*Percentages that have no superscript do not differ enough to be significant ($p \leq 0.05$) using the Odds-Ratio test (45, 46).

cottages were separated into male segregated, female segregated, and co-ed living groups. Each group was analyzed for its' possible correlation with the presence of either anti-HB_s or HB_sAg. Even after allowing for this predisposition, differences in the levels of prevalence of both anti-HB_s and HB_sAg were found to each group. Anti-HB_s prevalence was found to reach higher levels in cottages 4 and 12 than in the rest of the male segregated cottages. Cottages 5 and 6b had higher levels of anti-HB_s prevalence than the rest of the female segregated cottages. Levels of anti-HB_s prevalence were observed to be higher in cottage 15 than in the rest of the co-ed cottages. HB_sAg prevalence levels were found to be higher in cottages 3 and 4 than in the rest of the male segregated cottages. Cottages 5 and 6b were observed to have higher levels of HB_sAg prevalence than the rest of the female segregated cottages. Cottage 15 was found to have a higher level of HB_sAg prevalence than the rest of the co-ed cottages. Chronic carriers of the HB_sAg identified in this study were located in cottages 4, 6b, 10, and 16c.

Another segment of the test population is located outside of the institutional grounds (Tables X, XI). This segment consists of those patients who have for one reason or another been placed in Nursing Homes, Foster Homes, Other Institutions, Home Placement, or have been completely discharged. Also included in this segment are those members of the test population who have died during the time span of this study.

Table X. Anti-HB_s Association with Location

Location[a]	Anti-HB_s(+)	%*	Chronic Carrier (HB_sAg)
NHP	5/64	7.8	0
FHP	6/49	12.0	0
OI	0/4	0.0	0
HP	2/14	14.2	0
DIS	1/10	10.0	0
EX	0/6	0.0	0

[a]NHP=Nursing Home Placement
FHP=Foster Home Placement
OI= Placement in Other Institutions
HP= Home Placement
DIS=Discharged
EX= Died during the study period

*Percentages that have no superscript do not differ enough to be significant ($P \leq 0.05$) using the Odds-Ratio test (45, 46).

Table XI. HB_sAg Association with Location

Location[a]	$HB_sAG(+)$	%*	Chronic Carrier (HB_sAg)
NHP	2/64	9.1	0
FHP	1/49	2.1	0
OI	0/4	0.0	0
HP	0/14	0.0	0
DIS	1/10	0.0	0
EX	0/6	0.0	0

[a]NHP=Nursing Home Placement
FHP=Foster Home Placement
OI= Placement in Other Institutions
HP= Home Placement
DIS=Discharged
EX= Died during study period

*Percentages that have no superscript do not differ enough to be significant ($p \leq 0.05$) using the Odds-Ratio test (45, 46).

Since in nearly every instance, placement outside the institution involves a co-ed living group, this group was not analyzed with allowance for the sexual predisposition as the cottage living groups were. In this segment, highest levels of anti-HB_s prevalence were observed in the Foster Home Placement and Home Placement groups. The highest levels of HB_sAg prevalence were found in the Nursing Home Placement and Discharged groups. There were no HB_sAg chronic carriers in this segment of the test population.

Habits and Abilities Correlation with Anti-HB_s and HB_sAg

Selected habits and abilities of patients in BRSH were analyzed in order to determine if there is, in this institution, a correlation between these habits and abilities and the presence of either anti-HB_s or HB_sAg. The results (Tables XII, XIII) reveal a number of interesting associations within the segments of this correlation.

Among the Toilet Training observations, the segment of patients that were completely toilet trained had the highest levels of anti-HB_s prevalence. The "partially" toilet trained segment was intermediate in its levels of anti-HB_s prevalence, with the segment of patients with no toilet training having the lowest levels of anti-HB_s prevalence. HB_sAg prevalence did not follow the previous anti-HB_s pattern. The higher levels of HB_sAg prevalence were found in both the "completely" toilet trained segment and that segment of patients

Table XII. Anti-HB_S Association with Habits and Abilities

Habits/Abilities	Anti-HB_S(+)	%	Chronic Carrier (HB_SAg)
Toilet Training			
complete	29/160	18.1	1
partial	15/102	14.7	1
none	7/103	6.8	2
Ambulation			
yes	46/285	16.1[a]	4
no	3/63	4.8[b]	0
Feeding Skills			
complete	18/77	23.8[a]	2
partial	29/226	10.9[b]	1
none	2/52	9.6[b]	1
Plays in Toilet	2/16	12.5	0
Plays in Feces	3/56	5/4[a]	2
Plays in Urine	2/17	11.8	2
Foreign Objects in Mouth	9/72	12.5[a]	0
Clothes in Mouth	0/20	0.0[a]	0
Drinks from Faucets, Sinks, and Tubs	13/44	29.5[b]	2

[a,b]Percentages that differ in superscript are significantly different using the Odds-Ratio test (45, 46) $p \leq 0.05$

Table XIII. HB_sAg Association with Habits and Abilities

Habits/Abilities	$HB_sAG(+)$	%	Chronic Carrier (HB_sAg)
Toilet Training			
complete	8/160	5.0	1
partial	3/102	2.9	1
none	6/103	5.8	2
Ambulation			
yes	16/285	5.6	4
no	1/63	1.6	0
Feeding Skills			
complete	3/77	3.9	2
partial	12/226	5.3	1
none	2/52	3.8	1
Plays in Toilet	0/16	0.0	0
Plays in Feces	4/56	7.1	2
Plays in Urine	3/17	17.6^a	2
Foreign Objects in Mouth	1/72	1.4^b	0
Clothes in Mouth	0/20	0.0	0
Drinks from Faucets, Sinks, and Tubs	4/44	9.1	2

^{a,b}Percentages that differ in superscript are significantly different using the Odds-Ratio test (45, 46) $p \leq 0.05$.

having no toilet training skills, as compared with the lower levels of prevalence found in that segment of patients classified as being "partially" toilet trained.

Observations on the ambulatory ability of patients revealed the highest levels of both anti-HB_s and HB_sAg prevalence were to be found in that segment of patients that were classified as being ambulatory. Those patients classified as non-ambulatory had lower levels of anti-HB_s and HB_sAg prevalence.

Observations on the feeding skills of patients revealed that the highest levels of anti-HB_s prevalence were to be found among those patients possessing "complete" feeding skills as opposed to those patients possessing "partial" feeding skills and no feeding skills. HB_sAg prevalence patterns did not follow the anti-HB_s prevalence patterns seen above. The highest levels of HB_sAg prevalence were found among these patients possessing "complete" feeding skills and those patients possessing no feeding skills.

Observations of selected patient habits yielded complex associations with the presence of anti-HB_s and HB_sAg. Analysis of those patients known to play in the toilet on a regular basis showed a relatively high level of anti-HB_s. Patients known to play in urine and place foreign objects in their mouths also had relatively high levels of anti-HB_s prevalence. The highest levels of anti-HB_s prevalence were found in patients known to drink from faucets, sinks, and bathtubs

within the institution. The highest HB_sAg levels of prevalence were found among those patients known to play in urine on a regular basis. Those patients who drink from the faucets, sinks, and bathtubs of the institution also were found to have elevated levels of HB_sAg prevalence. The rest of the categories in this segment were observed to have low levels.

Admitting Diagnosis Correlation with Anti-HB_s and HB_sAg

The admitting diagnosis of each patient was analyzed in order to determine if there is, in this institution, a correlation between the admitting diagnosis assigned each patient and the presence of either anti-HB_s or HB_sAg. The results (Tables XIV, XV) reveal that several of the diagnosis groups show relatively high levels of both anti-HB_s and HB_sAg prevalence. Relatively high levels of anti-HB_s prevalence were observed in groups IV, V and VI. Groups I, VII, VIII and the undiagnosed patients were found to have intermediate levels of anti-HB_s prevalence. Relatively low levels of anti-HB_s prevalence were observed in groups II and III. HB_sAg prevalence was also found to be elevated in some diagnosis groups. However, the elevated levels of HB_sAg did not closely follow those previously observed for anti-HB_s in the same diagnosis classifications. Relatively high levels of HB_sAg prevalence were observed in groups III, V, and VIII. Intermediate levels of HB_sAg prevalence were found in groups I and VI.

Table XIV. Anti-HB_s Association with Admitting Diagnosis

Diagnosis[a] (class)	Anti-HB_s(+)	%	Chronic Carrier (HB_sAg)
I	5/43	11.6	0
II	0/6	0.0	0
III	1/49	2.1[b]	1
IV	16/106	15.1[c]	1
V	2/4	50.0[c]	0
VI	29/200	14.5[c]	2
VII	7/61	11.5	0
VIII	4/37	10.8	0
Unknown	3/18	16.7	0

[a] I=Mental retardation due to Infection
II=Mental retardation due to Intoxication
III=Mental retardation due to Trauma or Physical Agents
IV=Mental retardation due to Disorders in Metabolism, Growth, or Nutrition
V=Mental retardation due to New Growth
VI=Mental retardation due to Unknown Prenatal Influence
VII=Mental retardation due to Uncertain cause with Associated Structural Reaction
VIII=Mental retardation due to Uncertain cause with Associated Functional Reaction

[b,c] Percentages that differ in superscript are significantly different using the Odds-Ratio test (45, 46) $p \leq 0.05$.

Table XV. HB_sAg Association with Admitting Diagnosis

Diagnosis[a] (class)	$HB_sAg(+)$	%	Chronic Carrier (HB_sAg)
I	3/43	6.9	0
II	0/6	0.0	0
III	5/49	10.2	1
IV	2/106	1.9[b]	1
V	2/4	50.0[c]	0
VI	10/200	5.0[b]	2
VII	0/61	0.0[b]	0
VIII	2/37	9.1	0
Unknown	0/18	0.0	0

[a]I=Mental retardation due to Infection
II=Mental retardation due to Intoxication
III=Mental retardation due to Trauma or Physical Agents
IV=Mental retardation due to Disorders in Metabolism, Growth, or Nutrition
V=Mental retardation due to New Growth
VI=Mental retardation due to Unknown Prenatal Influences
VII=Mental retardation due to Uncertain causes with Associated Structural Reactions
VIII=Mental retardation due to Uncertain causes with Associated Functional Reactions

[b,c]Percentages that differ in superscript are significantly different using the Odds-Ratio test (45, 46) $p \leq 0.05$

Groups II, IV, VII and the undiagnosed patients were found to have relatively low levels of HB_sAg prevalence. A more thorough explanation of these Mental Retardation classifications appears in the appendix of this thesis.

DISCUSSION

The discovery of the hepatitis B surface antigen (HB_sAg) and the subsequent development of specific and sensitive tests (RIA) for its identification have provided the technology needed to further study this intractable disease (30-46).

The patient in an institution for the mentally and physically handicapped who harbors HB_sAg represents a complex public health problem. Evidence of the history of hepatitis B at Boulder River School and Hospital (BRSH) dates back to 1970 (47). Since 1970, there have been repeated outbreaks of hepatitis B, indicating there may be a population of patients who do harbor the hepatitis B virus. The detection of either anti-HB_s or HB_sAg in 16.8% of the 524 patient test population at BRSH indicates that hepatitis B is endemic there.

As each institution presents a unique epidemiological setting, epidemiological studies at BRSH are critical in spite of the numbers of related institutions studied to date. Data obtained from this study lends credence to the uniqueness of each institutional setting and presents new implications as to the risk of infection with hepatitis B.

The prolonged presence of HB_sAg seems to be related to age at the time of infection (34). Of the four HB_sAg chronic carriers identified in this study, three of these were found in the 20-24 years of age group. The fourth chronic carrier of the HB_sAg was found in the 25-29 years of age group. These data differ from other institutional studies

which imply that chronic carrier rates predominate in younger age distributions. The fact that the HB_sAg chronic carrier rate is only 0.7% at BRSH is remarkable considering previous studies at other institutions have reported chronic carrier rates as high as 25-30% (34). The present study at BRSH indicates that a high percentage of both the anti-HB_s positive patients and the HB_sAg positive patients are found in age ranges $\leq$20 years of age. These patients represent 74% of the anti-HB_s positives and 64% of the HB_sAg positives found in the entire study (Tables II, III). Based on statistical analysis, the elevated levels of anti-HB_s prevalence seen in the 20-24 and 25-29 year age groups is significant ($p \leq 0.05$) when compared with the 5-9 and 15-19 year age groups. There is then, in BRSH, a correlation with a limited degree of association between the prevalence of anti-HB_s and certain age groups. An interesting fact to note is that both the 20-24 and 25-29 year age groups were found to harbor all of the HB_sAg chronic carriers identified in this study.

Previous studies on the prolonged presence of HB_sAg in various institutions imply a male predisposition occurs in the chronic carrier rates (48). The HB_sAg chronic carriers identified in this study were male predominant (3:1). This male predominance pattern is also seen in the general prevalence levels of both anti-HB_s and HB_sAg seen throughout the institution (Tables IV, V). Statistical analysis

substantiates that, at BRSH, there is a significant male predisposition in the prevalence of both anti-HB_s and HB_sAg.

In view of the many variables that might affect the transmission of hepatitis B and its persistence within BRSH, the duration of each patients stay at BRSH was associated with the presence of either anti-HB_s or HB_sAg. The data (Tables VI, VII) indicate there were differences between the anti-HB_s and HB_sAg levels of prevalence of the duration groups. However, a statistical analysis of these data does not support a significant correlation. These data indicate that this disease may not be a "part" of the institution itself, but more a function of the patients housed at BRSH. It was not found that any single year had any significant levels of anti-HB_s or HB_sAg prevalence on a comparative basis with other lengths of institutional stay.

In order to obtain a better understanding of the transmission of hepatitis B and its subsequent persistence patterns at BRSH, the institutional location of each patient was associated with the prevalence of anti-HB_s and HB_sAg (Tables XIII, XIV). In an attempt to compensate for the male predisposition described earlier in this study, comparison of institutional location was carried out within each segregate group (Male, Female, and Co-ed). After compensating for this predisposition significant differences in anti-HB_s prevalence were observed in the male segregated cottages. Cottage 4 significantly differed from other male segregated cottages 6a, 10, and 104c. A

positive correlation between cottage 4 and anti-HB_s was therefore obtained. It is interesting to note that cottage 4 contains a chronic HB_sAg carrier. Although the HB_sAg prevalence data obtained for cottage 4 do not differ significantly from other male segregated cottages it does reflect a higher level of HB_sAg prevalence. Levels of anti-HB_s and HB_sAg prevalence in female segregated cottages did not differ significantly. Prevalence of anti-HB_s and HB_sAg in co-ed cottages was not found to differ significantly. It was interesting to note that in general the male cottage had the highest levels of anti-HB_s and HB_sAg prevalence, the co-ed cottages had intermediate levels of prevalence, and the female segregated cottages had the lowest levels of prevalence. The lack of accurate data on the frequency and location of patient relocation within the cottages hampers a more vigorous correlation between high anti-HB_s and HB_sAg prevalence in cottages and the presence of a HB_sAg chronic carrier. These data indicate there may be an environmental/ecological contact aspect of the transmission of hepatitis B within this institution. Because of this possibility it should prove interesting to initiate environmental surface testing for HB_sAg as well as studies on the frequency of sewer back-up, amount of supervision in the cottage, mobility of patients in the cottage, etc.

At an institution such as BRSH the modes of transmission of hepatitis B can be varied and numerous. Because of the poor sanitary habits of most of the patients an oral transmission of the disease is

quite possible. The lack of physical control in varying degrees by patients can also contribute to an aer-osol type of transmission, both respiratory and urinary. Also at BRSH there occur accidental parenteral forms of transmission such as bites, scratches, burns, and other accidental injuries all of which could serve to transmit hepatitis B. Because of the varied and numerous modes of transmission encountered in BRSH, a category was established in order to attempt preliminary correlations between anti-HB_s and HB_sAg prevalence and many of the habits and abilities common to the institutionalized mentally retarded (Tables XII, XIII).

Toilet Training analysis revealed that the group of patients classified as "completely" toilet trained was that group having the highest levels of anti-HB_s prevalence. The "partially" toilet trained group also had relatively high levels of anti-HB_s prevalence. The group having no toilet training skills were observed to have relatively low levels of anti-HB_s prevalence. HB_sAg prevalence remained relatively constant among the three toilet training groups. Statistical analysis of this data does not support a significant ($p \leq 0.05$) difference in anti-HB_s and HB_sAg prevalence levels among the toilet training groups. However, because the "completely" toilet trained individual is probably more mobile in the first place and also will receive the least supervision during toilet activities, the chances of this individual encountering fecal-oral contamination are greater than the individual with the

lowest level of toilet training. This line of reasoning may account for the high levels of prevalence seen in the more skilled patients. These data, when viewed in the institutional context, may support a nonparenteral mode of transmission of hepatitis B at BRSH.

Each patient's ambulatory abilities were also considered. There was found to be a significant ($p \leq .05$) difference in the levels of anti-HB_s and HB_sAg prevalence between the ambulatory and non-ambulatory patients. This again, lends credence to the key concept that the mobility of a patient is heavily associated with the prevalence of the disease.

Because of the possibility of oral transmission of hepatitis B (49), arbitrary levels of feeding skills were considered in this study. Groups classified as possessing "complete" and "partial" were found to have higher levels of anti-HB_s prevalence than the group of patients classified as having no feeding skills. Statistical analysis substantiates this difference as being significant ($p \leq 0.05$). Although not statistically significant, the same pattern can be observed in the levels of HB_sAg prevalence. This may support the theory that the more adept a patient is at using his utensils, the less supervision he is likely to receive during meals. Those patients who have no feeding skills are hand fed by patient care technicians. The unsupervised patient may therefore drop his utensils, eat off the floor, eat off of other patients' plates and generally encounter more of a risk of

oral contamination during eating activities. These data may support a possible nonparenteral transmission of hepatitis B at BRSH.

In addition to the various abilities observed earlier, an arbitrary set of habits were observed for their association with the prevalence of anti-HB_s and HB_sAg. These habits were some of the classic examples of behavior exhibited by the mentally retarded at institutions (Tables XII, XIII). Of these habits the only habit that presented sound statistical significance upon comparison with the other groups was that group of patients that drink from the faucets, sinks, and tubs of the institution. Viewed within the institutional context, these data may support nonparenteral forms of transmission of hepatitis at BRSH.

Blumberg et al. (34) emphasize the association between mongolism and the persistence of HB_sAg. Krugman et al. (35) were not able to support this observation with their work. Because of this apparent discrepancy, an attempt to associate admitting diagnosis with the prevalence of anti-HB_s and HB_sAg was made (Tables XIV, IV, Appendix). Data from BRSH do indicate that there are high levels of anti-HB_s in groups IV, V, and VI. However, a statistical analysis reveals that these groups differ significantly with only one other group (III) thereby limiting the degree of association of this positive correlation. HB_sAg prevalence, although providing a significant difference between

group B and groups IV, VI, and VII, also is limited in its degree of association due to the small sample size of group V.

The results of this study, although interesting, would have no meaning without application. Possible solutions to the problem of hepatitis B at BRSH should be included in current institutional policies. One possible solution might be to employ the technique of "cohorting." This involves the placement of all HB_sAg positive patients in the same residence area. No other patients would be placed in this area unless they demonstrated a detectable titer of anti-HB_s. Personnel should be alerted to the possible danger these patients present to other patients as well as to the staff.

Cottages that have been shown to have an abnormally high prevalence of either anti-HB_s or HB_sAg should be studied in detail in order to eliminate any environmental aspect of the transmission of hepatitis B. Environmental surface testing for HB_sAg in trouble areas could be used to eliminate this type of transmission (50).

Another policy of importance is the routine screening of incoming patients and staff for both anti-HB_s and HB_sAg. An annual screen of the entire institution could be useful in the control of the disease at this institution.

Since the course of hepatitis B has been shown to be dependent upon the immune status of the infected individual (62) a study of the immune competence of patients at BRSH could prove valuable in

pinpointing high risk patients likely to develop fatal forms of this disease such as chronic aggressive hepatitis. A study of this type could prove to be helpful in the control of other disease processes as well.

It is probable that hepatitis B will never be completely eliminated from BRSH. However, one of the purposes of this study was to more accurately determine the risk a patient encounters at BRSH. Other goals were to elucidate problem areas within the institution and to make suggestions as to possible solutions to lower the prevalence of the disease.

CONCLUSION

The Boulder River School and Hospital Hepatitis B Study consisted of screening 524 patients of that institution for the presence of the hepatitis B surface antigen (HB_sAg) and the antibody to this antigen (anti-HB_s), using a radioimminoassay technique. 16.8% of the test population (16 to 32 times the normal incidence in the USA) were found to be positive for either of these markers of hepatitis B infection. Correlations were attempted between these markers and the patients age, sex, length of stay in the institution, institutional location, habits and abilities, and admitting diagnosis. Statistically significant correlations were found in these categories. By elucidating specific areas of high risk, more accurate determinations are obtained as to the risk of acquiring hepatitis B at BRSH. Suggestions concerning the control of this disease at BRSH were included.

APPENDICES

APPENDIX I

Simplified Medical Classification of Mental Retardation

code	
	I
	MENTAL RETARDATION ASSOCIATED WITH DISEASES AND CONDITIONS DUE TO INFECTION
11	Encephalopathy, congenital, associated with prenatal infection
12	Encephalopathy due to postnatal cerebral infection
	II
	MENTAL RETARDATION ASSOCIATED WITH DISEASES AND CONDITIONS DUE TO INTOXICATION
21	Encephalopathy, congenital, associated with toxemia of pregnancy
22	Encephalopathy, congenital, associated with other maternal intoxications
23	Bilirubin encephalopathy (Kernicterus)
24	Post-immunization encephalopathy
29	Encephalopathy, other, due to intoxication
	III
	MENTAL RETARDATION ASSOCIATED WITH DISEASES AND CONDITIONS DUE TO TRAUMA OR PHYSICAL AGENT
31	Encephalopathy due to prenatal injury
32	Encephalopathy due to mechanical injury at birth
33	Encephalopathy due to anoxemia at birth
34	Encephalopathy due to postnatal injury

Appendix I (continued)

IV

MENTAL RETARDATION ASSOCIATED WITH DISEASES AND CONDITIONS DUE TO DISORDER OF METABOLISM, GROWTH OR NUTRITION

40 Cerebral lipoidosis, infantile (Tay-Sach's disease)

41 Encephalopathy associated with other disorders of lipid metabolism

42 Phenylketonuria

43 Encephalopathy associated with other disorders of protein metabolism

44 Galactosemia

45 Encephalopathy associated with other disorders of carbohydrate metabolism

46 Arachnodactly

47 Hypothyroidism

48 Gargoylism (Lipochondrodystrophy)

49 Encephalopathy, other, due to metabolic, growth, or nutritional disorder

V

MENTAL RETARDATION ASSOCIATED WITH DISEASES AND CONDITIONS DUE TO NEW GROWTHS

51 Neurofibromatosis (Von Recklinghausen's disease)

52 Trigeminal cerebral angiomatosis (Sturge-Weber-Dimitri's disease)

53 Tuberous sclerosis

59 Intracranial neoplasm, other

Appendix I (continued)

VI

MENTAL RETARDATION ASSOCIATED WITH DISEASES AND CONDITIONS DUE TO (UNKNOWN) PRENATAL INFLUENCE

61 Cerebral defect, congenital

62 Cerebral defect, congenital, associated with primary cranial anomaly

63 Laurence-Moon-Biedl syndrome

64 Mongolism

69 Other, due to unknown prenatal influence

VII

MENTAL RETARDATION ASSOCIATED WITH DISEASES AND CONDITIONS DUE TO UNKNOWN OR UNCERTAIN CAUSE WITH STRUCTURAL REACTIONS MANIFEST

71 Encephalopathy associated with diffuse sclerosis of the brain

72 Encephalopathy associated with cerebellar degeneration

78 Encephalopathy associated prematurity

79 Encephalopathy, other, due to unknown or uncertain causes with structural reactions manifest

VIII

MENTAL RETARDATION DUE TO UNKNOWN (OR PRESUMED PSYCHOLOGIC) CAUSE WITH FUNCTIONAL REACTION MANIFEST

81 Cultural-familial mental retardation

82 Psychogenic mental retardation associated with environmental deprivation

83 Psychogenic mental retardation associated with emotional disturbance

Appendix I (continued)

84 Mental retardation associated with psychotic (or other major personality) disorder

89 Mental retardation, other, due to uncertain cause with the functional reaction alone manifest

Simplified Supplementary Term Listing

1 With Genetic Component

2 With Secondary Cranial Anomaly

3 With Impairment of Special Senses

4 With Convulsive Disorder

5 With psychiatric Impairment

6 With Motor Dysfunction