

Hepatitis A in Australia in the 1990s: future directions in surveillance and control

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Abstract

The national notification data from 1952 to 1997 was examined in order to characterise hepatitis A virus (HAV) infection in Australia in the 1990s, and to determine whether currently available surveillance data are sufficient to inform disease control strategies and vaccination policies. Hepatitis A annual notification rates declined dramatically from a high of 123 notifications per 100,000 persons in 1961, to 3 per 100,000 in 1989. During 1991-97, the hepatitis A notification rate was 12 per 100,000 persons per year, although rates varied substantially between States and Territories. The Northern Territory had the highest notification rate of 52 per 100,000 persons per year. Seventy-six per cent of cases were adults, although in most regions notification rates were significantly higher in children than adults. Nationally, the male to female ratio was 1.7:1 ($p < 0.001$). The Northern Territory was the only area with no significant difference in notifications between the sexes. Large outbreaks were detectable through the notification system but risk factors for transmission could only be inferred from age and sex distribution of notifications, and from previous outbreak reports. National hepatitis A surveillance would be improved by collecting basic risk factor data, which identify cases as food-borne, sporadic, related to another case, or travel related. In addition, a population based serosurvey to measure age-specific hepatitis A susceptibility would assist vaccination policy development. Serosurveillance data are also needed, in conjunction with enhancements of the notification data, to provide baseline information against which the impact of changes in vaccination policy can be assessed. *Commun Dis Intell* 1999;23:113-120.

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Contents

Hepatitis A in Australia in the 1990s: future directions in surveillance and control	113
<i>Janaki Amin, Tim Heath and Stephen Morrell</i>	
The epidemiology of acute hepatitis A in North Queensland, 1996-1997	120
<i>Anthony Merritt, Dorothy Symons and Marlene Griffiths</i>	
Report of the Australian National Polio Reference Laboratory 1 January to 31 December 1998	124
<i>Margery Kennett, Kerri Anne Brussen, Vicki Stambos, Ann Turnbull, Aishah Ibrahim and Heath Kelly</i>	
Acute Flaccid Paralysis surveillance in Australia Progress Report 1995-1998	128
<i>Rennie D'Souza, Margery Kennett, Jayne Antony, Helen Longbottom, Elizabeth Elliott</i>	
Communicable Diseases Surveillance	132
Bulletin Board	140
Overseas briefs	141

Introduction

Hepatitis A is an infectious disease caused by an RNA virus.¹ Humans are considered the main reservoir for the hepatitis A virus (HAV),² and HAV is the predominant cause of infectious hepatitis transmitted by the faecal-oral route. HAV is primarily transmitted from person to person, and this type of transmission is most evident between household contacts and within institutions. Point source outbreaks also arise as a result of faecal contamination of water, transmission from infected food handlers, and contamination of raw or under-cooked foods.²

Age is the most important determinant of morbidity and mortality, with severity of the illness and its complications increasing with age.² In young children most infections are either asymptomatic or cause a mild non-specific anicteric illness. The duration of the illness varies, but most commonly cases are symptomatic for three weeks. Complications during the acute illness phase are unusual, with fulminant hepatitis and death being uncommon.²

During the past decade in Australia there have been several reports of wide scale hepatitis A activity including: a large food-borne outbreak related to consumption of oysters,³ outbreaks in men who have sex with men,^{4,5} high endemic rates in some parts of the country,⁶ and continued concern about transmission within institutions,⁷⁻⁹ particularly child care centres.¹⁰

This article aims to analyse the national notification data from 1952 to 1997, Australian Bureau of Statistics (ABS) mortality data, and liver transplant data and to interpret these data in view of reported hepatitis A outbreaks. Whether national data sources are sufficient for planning national hepatitis A control strategies and vaccination policies, will also be discussed. Currently the National Health and Medical Research Council (NHMRC) recommends HAV vaccination only for certain high risk groups¹¹ (see Box). Examination of national surveillance data is also necessary to establish a baseline prior to the possible introduction of a universal childhood hepatitis A vaccination program.

Methods

Hepatitis A is notifiable by doctors and laboratories in all States and Territories of Australia. In 1991, the National Notifiable Diseases Surveillance System (NNDSS) was established, and since then notification data has been collated nationally in a de-identified format. The variables uniformly reported to NNDSS for hepatitis A are age, sex, postcode of residence, date of onset, and date the notification was received by the State or Territory.

The NHMRC definition for hepatitis A cases is:

- a) anti-HAV (antibody to hepatitis A virus) IgM positive, in the absence of recent vaccination;
- or
- b) demonstration of a clinical case of hepatitis (jaundice +/- elevated aminotransferase levels without a non-infectious cause) and epidemiologically linked to a serologically confirmed case.¹²

All States and Territories report cases on the basis of the NHMRC definition, except New South Wales (NSW) and Western Australia (WA) where positive anti-HAV IgM serology is required.

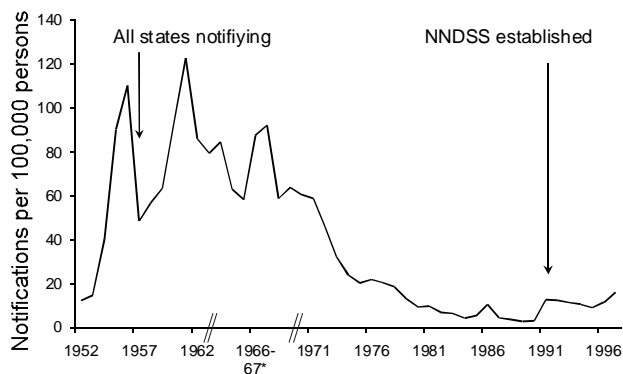
Notification data for 1952 through 1990 were obtained from the National Centre for Disease Control in summary format (Htoo Myint, data manager, personal communication, 1997). Until the 1970s, cases of hepatitis A included those classified as infectious/infective hepatitis. In March 1998 unit notification data with onset from 1 January 1991 to 31 December 1997 were extracted from the NNDSS database. Mortality figures for hepatitis A (ICD 9 codes 0700 and 0701) and mid-year population estimates were obtained from the Australian Bureau of Statistics (ABS). Notification rates were calculated using the average of the mid-year populations occurring within the period as the denominator, and were adjusted for age, sex and State as appropriate. All rates were reported per 100,000 population per year. For categorical analyses of age, persons aged less than 15 years were defined as children, and persons aged 15 years or older as adults. From 1991 to 1997 the Australian population increased from 17.3 million to 18.5 million, and persons aged less than 15 years accounted for 21-22% of the population during this period.

Box 1. Groups for whom hepatitis A vaccination is recommended^{11*}

- Travellers to areas of intermediate or high endemicity
- Occupations with significant risk of exposure:
 - carers for children in day care centres
 - teachers and close contacts of the intellectually disabled
 - staff and residents of residential facilities for the intellectually disabled
 - health workers and teachers in remote Aboriginal and Torres Strait Islander Communities
 - health care workers with paediatric, emergency and/or intensive care unit exposure
 - sewerage workers
- Men who have sex with men
- Individuals with chronic liver disease
- Recipients of blood products
- Food handlers

*Prevaccination screening is recommended for some groups

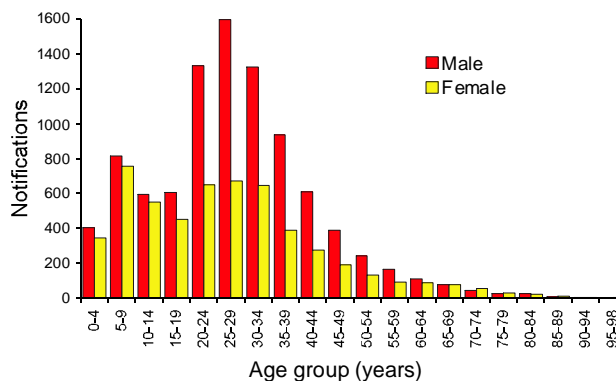
Figure 1. National hepatitis A notifications 1952 to 1995



* Only notifications tallied by financial year available from 1964 through 1969
 Year States/Territories began notifying- 1952: ACT, NT, Vic, WA; 1953 NSW; 1954 SA, Tas; 1957 Qld
 Reproduced with permission, NCDC

Significance values were calculated using Pearson's Chi-square. The case fatality rate (CFR) was calculated by dividing the number of hepatitis A deaths from 1979 to 1996 by the number of hepatitis A notifications for the same time period. Liver transplant data were obtained from the Australian National Liver Transplant Unit, Clinical Experience Report, 1986 to 1997.¹³ Outbreaks (peak periods of notifications) for the seven year period 1991 to 1997 were determined using a probability distribution methodology developed by the authors. The method used involves calculating the threshold number of notifications above which an outbreak is defined to occur. The outbreak level (O) is defined as the number of notifications occurring in a month for which the probability of that number occurring is less than 0.05, based on the expected number

Figure 2. Hepatitis A notifications by age group and sex, 1991 to 1997



of notifications per month being the average number of notifications per month. Expected and outbreak numbers of notifications were calculated for adult males, adult females and children. For analysis of the national data all expected monthly counts were greater than 45, therefore the outbreak level was determined on the basis of a chi-square distribution. For each State/Territory where the expected monthly count was less than 45, a Poisson error distribution was used as the basis for determining the outbreak level.

SAS version 6.12, Excel 5.0 and Epi Info 6 were used for analysis and presentation of data.

Results

Notification data

Secular trends

The summary data from 1952 to 1997 (Figure 1) showed peaks in crude notification rates in 1956, 1961 and 1968 with a gradual drop in notification rates occurring from

Table 1. Distribution of hepatitis A notifications by State/Territory and age, 1991 to 1997

State/Territory	Number of notifications (Notification rates per 100,000 population per year)				Total	
	0-14 years		≥15 years or over			
ACT	56	(11.8)	147	(9.0)	205	(9.7)
NSW	1,352	(14.9)	4,767	(14.2)	6,138	(14.4)
NT	230	(68.5)	386	(43.4*)	633	(51.7)
Qld	1,084	(21.8)	3,093	(17.8*)	4,207	(18.9)
SA	146	(7.0)	405	(5.0*)	551	(5.4)
Tas	7	(0.9)	55	(2.2*)	62	(1.9)
Vic	320	(4.8)	1,833	(7.4*)	2,214	(7.0)
WA	313	(11.6)	681	(7.4*)	1,002	(8.4)
Australia	3,508	(13.0)	11,367	(11.6*)	5,012	(12.0#)

*Significant difference between children and adults, p<0.001.

All State/Territory total rates were significantly different to that for Australia as a whole, p<0.001

1971 to 1985. There were three small peaks in notification rates in 1986, 1991 and 1997. There was no apparent national seasonal pattern to notifications.

Age and sex

For the time period 1991 through 1997 the age distribution was bimodal, markedly so in males, with peaks in the 5 to 9 and 20 to 39 year age groups (Figure 2). Because of the bimodal age distribution of notifications, further analysis of the impact of age was made by comparison of those aged 0-14 years (children) to those aged 15 years or older (adults). Seventy-six per cent of notifications were for adults. The national notification rate in children, 13.0 per 100,000 persons per year, was significantly but not substantially higher than for adults, 11.6 per 100,000 per year ($p < 0.001$) (Table 1).

Significantly more notifications occurred for males than females, resulting in a male to female ratio of 1.7:1 ($p < 0.001$). This ratio differed significantly by age group, with the ratio for adults (2.0:1) being significantly greater than that for children (1.1:1) ($p < 0.001$). More males than females were notified in all age groups up to 64 years. The median age for males and females was 27 and 24 years respectively.

Regional differences

The mean annual crude notification rate for States and Territories during 1991-97 ranged from 1.9 to 51.7 per 100,000 per year (Table 1). New South Wales had the

Table 2. Male to female ratio by State/Territory, 1991 to 1997

State/Territory	Male : Female
ACT	1.6:1*
NSW	1.9:1*
NT	1.1:1
Qld	1.4:1*
SA	1.5:1*
Tas	2.4:1*
Vic	2.4:1*
WA	1.4:1*
Australia	1.7:1*

*Significant difference between males and females, $p < 0.001$.

highest number of cases and the NT had the highest notification rate. The NT, Queensland and NSW all had significantly higher notification rates than Australia overall. In all States/Territories adults accounted for the majority of notifications (State/Territory range 61-89%, Australia 76%). However, the notification rate in children was greater than that in adults in all States and Territories except Tasmania and Victoria.

The male to female ratio also varied by State and Territory. The NT was the only area with no significant difference between the number of male and female notifications

(Table 2). Tasmania, Victoria, and NSW had male to female ratios greater than Australia as a whole.

Table 3. Outbreak threshold number of notifications* for States/Territories by age and sex

State/Territory	Adult males (notifications per month)	Adult females (notifications per month)	Children (notifications per month)
ACT	4	3	3
NSW	48	24	23
NT	6	6	7
Qld	30	21	19
SA	7	5	5
Tas	3	2	2
Vic	23	11	8
WA	9	8	8
Australia	120	65	60

* See methods for details of calculation.

Secular trends, 1991 to 1997, by age, sex and region

Nationally, there were 15,012 notifications of hepatitis A from 1991 through 1997, equivalent to a crude annual notification rate of 12 per 100,000 persons.

Adults

Analysis of monthly outbreak data from 1991 through 1997 for Australia shows the extent of temporal variability in hepatitis A notifications (Figure 3). The expected number of notifications per month and the outbreak number of notifications for males were estimated to be 100 and 120 notifications respectively, and 50 and 65 notifications respectively for females (Table 3).

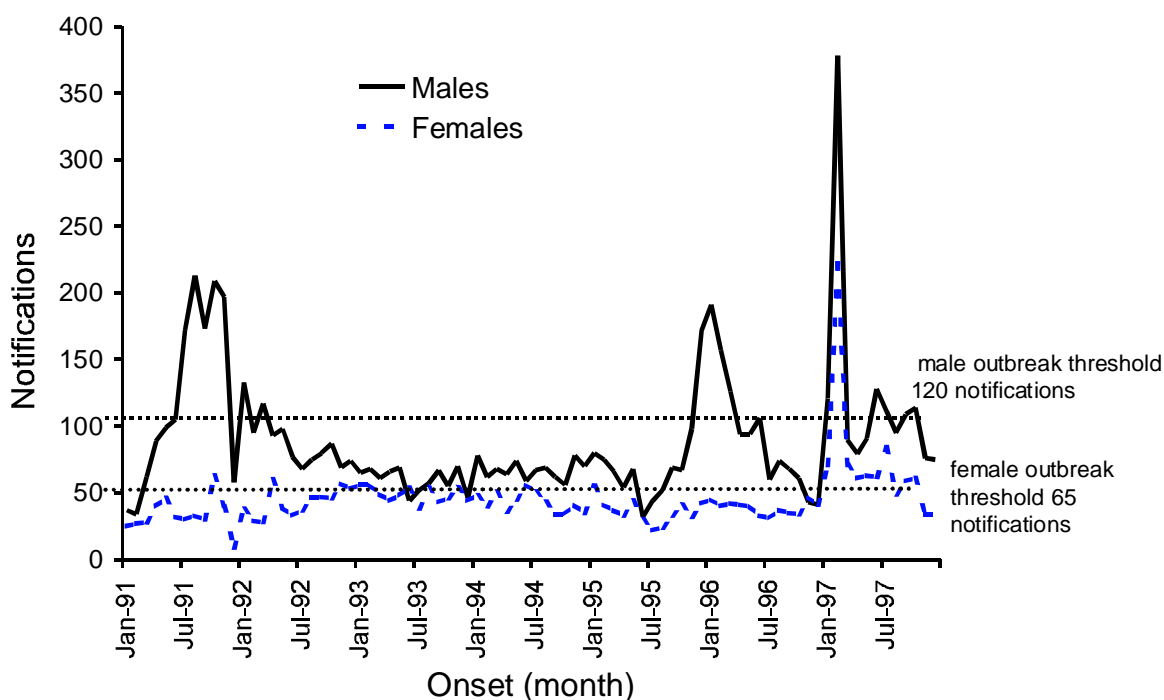
a) Peaks 1 and 2

Two sustained peaks occurred when the number of notifications for males exceeded the outbreak level of 120 notifications per month (Figure 3). Peak 1 occurred from July 1991 to January 1992, and peak 2 from December 1995 to March 1996. The male to female ratio for notifications was 4.8:1 in peak 1 and 3.8:1 in peak 2. States and Territories reporting higher numbers of male notifications than their respective outbreak levels (Table 3) during the peak periods were: the Australian Capital Territory (ACT), NSW and Victoria for both peaks; South Australia (SA) for peak 1 only; and Western Australia (WA) for peak 2 only.

b) Peak 3

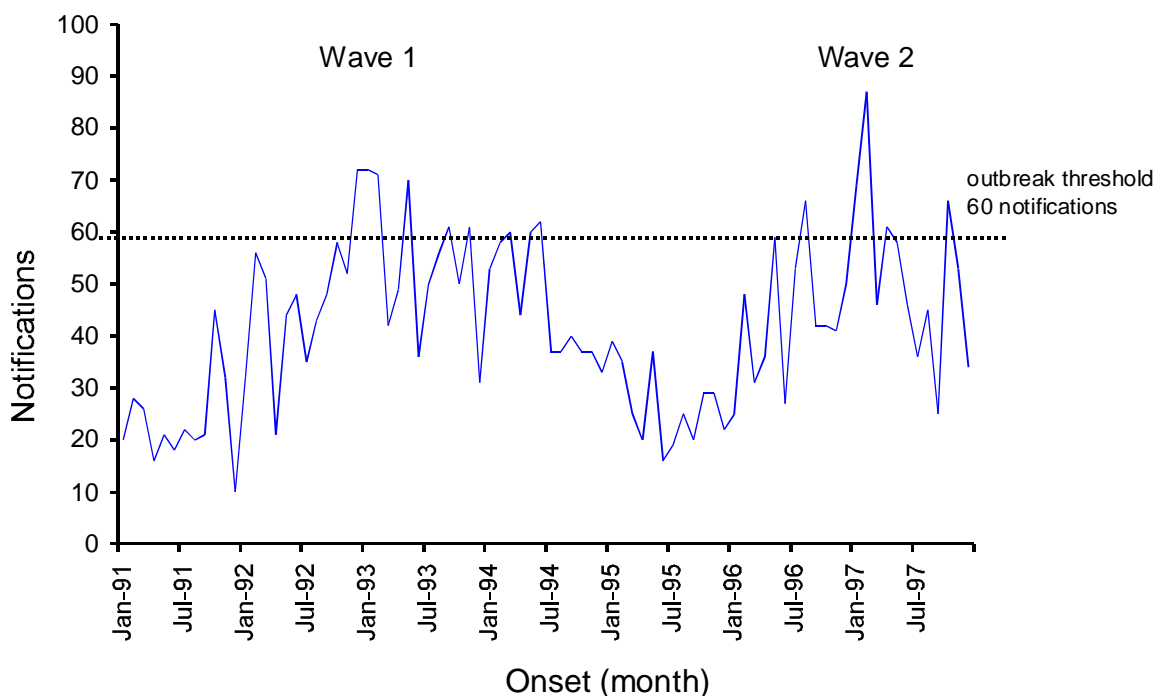
There was a sharp peak in the notifications in early 1997 (peak 3) (Figure 3). Notifications were higher than the outbreak level for men from January 1997 to February 1997 and for females from January 1997 to March 1997. The States reporting a higher number of notifications than their respective outbreak levels for males and females (Table 3) during this peak were: the ACT, NSW,

Figure 3. Adult hepatitis A notifications by sex and month of onset, 1991 to 1997, Australia



* Peak periods are where plot is above the outbreak threshold, see methods for detail

Figure 4. Childhood hepatitis A notifications by month of onset, 1991 to 1997



Queensland and Victoria. SA reported outbreak numbers for females only in this period.

Children

For children the expected number of notifications nationally per month was 47 and the outbreak number of notifications was estimated to be 60 notifications (Table 3).

The national notification pattern for children showed two waves of increased notifications, during 1993-94 and 1996-97. However, the number of notifications exceeded the outbreak level of 60 for only relatively short periods (Figure 4). During the first wave, all State/Territories except Tasmania reported notification counts above their respective threshold levels (Table 3). During the second wave, the ACT, NSW, NT, Queensland and SA reported

notification counts above their respective outbreak threshold levels (Table 3).

Transplants

From 1986 through 1997 three patients with hepatitis A were assessed for transplantation.¹³ One person, with acute fulminant hepatic failure, received a transplant and survived 5 years post transplantation.

Mortality

Mortality data for hepatitis A specifically have been collected by the ABS since 1979. From 1979 to 1996, 57 deaths (median 3, range 0 to 6 per year) were attributed to hepatitis A, resulting in an average mortality rate of 0.02 per 100,000 population per year, and a case fatality rate (CFR) of 0.2%. Three deaths occurred in children under 10 years of age, 20 in adults 20 to 59 years and 34 in those aged 60 years or over. CFRs for age groups could not be calculated as age groups for notifications prior to 1991 were not available. The male to female ratio of deaths was 1.4:1, compared to 1.7:1 for notifications. The number of deaths by region was: NSW 22; Queensland 11; and all other States/Territories less than 10.

Discussion

The epidemiology of hepatitis A in Australia has changed dramatically in the last four decades. In the 1950s and 60s notification rates were high, peaking at 123 per 100,000 persons in 1961. These rates fell steadily to low levels through the 1970s and early 1980s. These data need to be interpreted with caution as the fall in notifications may be partly attributable to increased specificity of hepatitis A diagnosis following the introduction of a serological test for the HAV antibody in the 1970s. The 1990s were characterised by low baseline notification rates, with epidemic peaks related to the re-emergence of hepatitis A amongst particular risk groups and a large foodborne outbreak. The peaks may also have been more obvious because of improvements in the surveillance system from the 1980's onward. While the majority of notifications during the 1990s were for adult males, notification rates in children were higher than for adults overall. The NT was the only area with no significant sex difference. The overall epidemiology of hepatitis A in Australia in terms of notification rates and sex differences is similar to that reported in other western countries.^{14,15} Rates of hepatitis A mortality and transplantation were very low, in keeping with the known course of illness for hepatitis A. The impact of hepatitis A differed between States and Territories, most notably during peak periods.

In order to assess i) how well the peaks in notification data reflect hepatitis A epidemiology at a State/Territory level; and ii) how the notification data can be used to interpret trends at a national level, the data presented here need to be compared to local reports of hepatitis A outbreaks.

Recent outbreaks

Men who have sex with men

The finding that the adult notifications for males exceed those for females is likely to be a result of a real increase in transmission of HAV between men who have sex with men. Since 1990 there have been two reported major hepatitis A outbreaks in men who have sex with men. The first occurred in 1991 in Victoria, NSW and SA;^{4,5,16,17} the

second in 1995-96 in south-eastern Sydney.¹⁸ Both these outbreaks were discernible in our analysis of the national notification data (Figure 3). The 1991 peak in notifications (peak1) may be partly attributable to improved reporting of hepatitis A following the introduction of NNDSS. However, the striking adult sex difference in notifications during this time suggests a real increase in adult male HAV infections. The States'/Territories' reports of notification numbers exceeding their respective outbreak threshold levels for adult males during the peak periods also suggests that both outbreaks may have been more widespread than previously reported.

Food-borne

A large scale outbreak associated with contamination of oysters occurred in NSW in 1997.³ Peak 3 in the national notification data (Figure 3) corresponds with this outbreak, and the dramatic peak (short duration) in above-threshold notifications, moreover across both sexes, is indicative of a common source outbreak. Analysis of the national data found that adults and children were affected by the outbreak and that the outbreak affected residents of a number of States and Territories.

Children

While only 24% of notifications were for children, the notification rate in children was significantly higher than for adults. The true rate of HAV infection in children is likely to be even higher than reported, since infection of children is often asymptomatic or anicteric. A more accurate indication of the role of children in HAV transmission can be ascertained by active case finding. The notification data show that from 1991 to 1997 there were two waves of hepatitis A notifications for children under 15 years of age which occurred in 1991-94 and 1996-97. Considering the extended time for which these elevated rates were reported, the waves are unlikely to be a result of single point source outbreaks. The wave pattern of notification has been previously described¹⁹ and is probably a result of successive cohorts of susceptible children becoming infected. Outbreaks in child care centres and schools, and spread of infection from these places to older siblings and household members have been reported.^{14,20-23} These modes of transmission probably account for most childhood infections. The wave pattern may also have occurred as result of distinct outbreaks in separate states overlapping in time resulting in large numbers of cases nationally.

These comparisons show that large outbreaks are discernible through a probability analysis of NNDSS data and that patterns of infection in terms of region, sex and age are reflected in those described at a national level. Analysis of the notification data did indicate that outbreaks might have been more widespread than have been previously reported; however this is difficult to determine without additional risk factor information. Other outbreaks of hepatitis A related to food,²⁴ institutions,⁷ injecting drug use²⁵ and person to person spread²⁶ have been reported in Australia. While these small outbreaks were not detected in the present analysis of national-level data, they can in principle be determined by probability analysis at the State and Territory level.

Seroepidemiology

The usefulness of notification data for determining the incidence of HAV infection and anti-HAV seroprevalence is limited by under reporting generally and as a result of asymptomatic and anicteric HAV infection specifically. It has been postulated that the true incidence of clinical hepatitis A in developed countries is at least five times greater than reported, with the prevalence of infection many times higher.¹⁹ As such, seroprevalence studies are a useful adjunct for estimating age-specific incidence and prevalence.

To date there have been no Australia wide HAV serosurveys. Comparison of Australian hospital-based serosurveys conducted in the 1950s to those in the 1970s²⁷ indicate, as reflected in the notification data, a fall in the transmission of HAV over this time period as seroprevalence in the 1950s was higher than in the 1970s. These surveys also show an age cohort effect to have occurred, as during the 1950s seroprevalence was close to 100% from the age of 41, but 20 years later seroprevalence only reached 100% at age 60 years or older. A hyperendemic pocket has been identified in a rural aboriginal community in the NT.⁶ This study found seroprevalence rates of 90% in all age groups. There may also be other areas of the NT in which hepatitis A is highly endemic or hyperendemic. If so, this would account for the high notification rate and lack of sex difference in this territory.

The National Centre for Immunisation Research and Surveillance of Vaccine Preventable Diseases plans to carry out a national HAV serosurvey. Information from such a survey conducted periodically, in conjunction with analysis of notification and other morbidity data, will be important for estimating incidence, determining seroprevalence and targeting and evaluating prevention strategies, such as vaccination.

Future directions

While analysis of the NNDSS data did allow large outbreaks to be detected, the impact of point source versus person-to-person outbreaks of hepatitis A was not discernible due to the lack of risk factor information at a national level. However, a number of characteristics of the NNDSS data can be used to signify possible point-source outbreaks, including their characteristic short outbreak periods, and the spread of infection across the sexes and age groups. Additionally, as postcode information is on the NNDSS dataset, it is possible to do more detailed regional or small-area analyses to investigate possible outbreaks. The probability methodology described in this paper would be well suited to predictive outbreak detection and for setting an alert level to indicate unusually high counts for closer monitoring, and action levels at which point active surveillance or intervention would commence.

A number of risk factors have been documented to be associated with hepatitis A.^{14,28} It would be most useful and efficient to collect all risk factor information at a State/Territory level. Cases could then be classified as: food-borne, sporadic, related to another case, travel related, and/or occurring in an aboriginal person. These classifications, along with routinely collected case information, could be relayed to the NCDC to enable outbreaks with a common source or risk factor to be identified across borders and allow national interventions

to be instigated if warranted. Collation of this information would also help in developing and evaluating control strategies.

Interventions to control hepatitis A historically have involved improving sanitation and hygiene and control of outbreaks through the use of human immunoglobulin.²⁹ Recently there has been discussion regarding the use of hepatitis A vaccines for the control of outbreaks, including mass vaccination of defined communities and incorporation into routine childhood vaccination schedules.^{30,31} Current surveillance data provides little information regarding groups for whom HAV vaccination should be recommended. The differences between States/Territories in terms of notification rate, sex and age of those notified, suggests that vaccination policies may need to be tailored to regional epidemiology. In conjunction with the surveillance data presented here, risk factor data, timely serosurveillance, and HAV hospitalisation data, are essential for informed HAV vaccination and control policies as we enter the next century.

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