

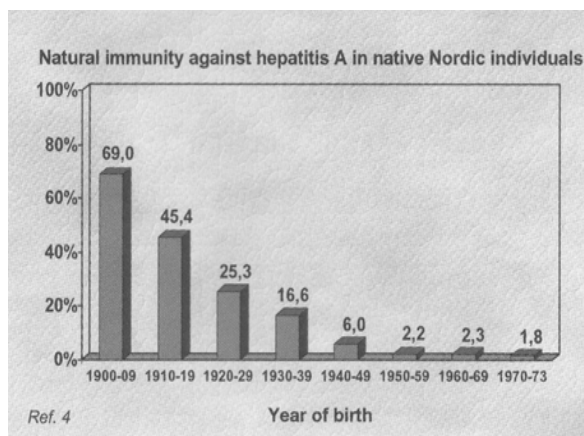
Hepatitis A in Sweden – same old story, or??
Lars Rombo VHPB sept 2003

Most of the material in this presentation originates from the department of epidemiology at the Swedish institute for infectious disease control – either by direct copies of excel files or indirect after calculation of the original data. This is gratefully acknowledged

Immunity

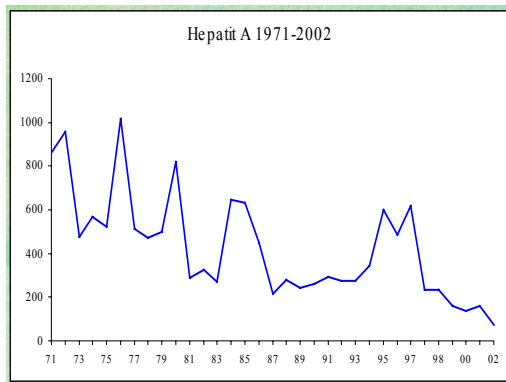
Forty years ago, Swedish recommendations for travellers to Mediterranean countries, including Spain, France, Italy and Greece were more or less unique. Even short term travellers to tourist areas were at the time recommended gammaglobulin for prophylaxis of hepatitis A and compliance was by and large satisfactory.

The rationale behind this recommendation, which was considered odd in some other countries, was the extremely low proportion of our population with acquired immunity. This is shown in the figure from a paper by Margareta Böttiger et al in 1997.



We were early to introduce sewage systems and the transmission of hepatitis A became very small as a consequence. Today, the rest of Europe are in the same situation and recommendations to give prophylaxis against hepatitis A for travellers to more endemic countries are standard.

Long term tendency of hepatitis A in Sweden.

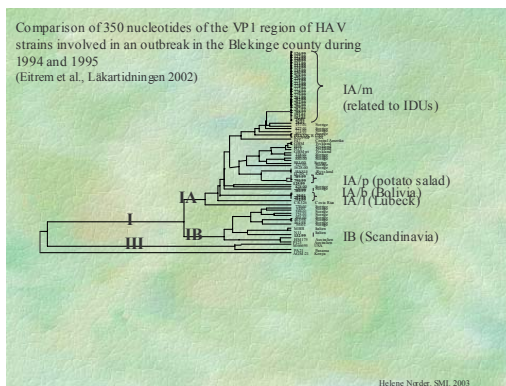


I find it interesting to compare with for example BCG introduction and the decline of TBC in Sweden 50-60 years ago. At that time, there was no change in the rate of decline due to BCG. In contrast, the shape of the incidence curve of hepatitis A was rather flat over a number of years from 1981 to 1995-98. After the widespread introduction of vaccine is started to decline further. Is there a causal relation?

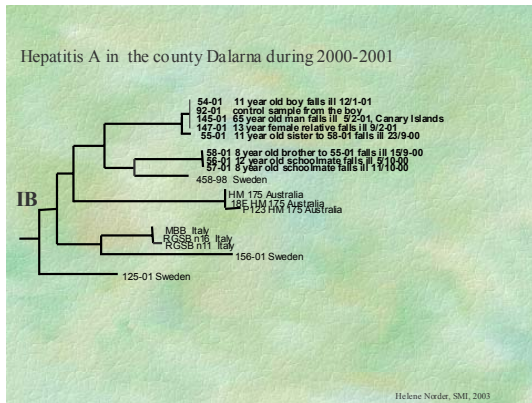
Diagnostic possibilities

Detection of IgM anti-HAV antibodies is mandatory for diagnoses.

During the last ten years, fingerprinting has been carried out in a number of Swedish small epidemics. These studies have been performed by Lars Magnius and Helen Norder at the Swedish institute for infectious disease control in Sweden.



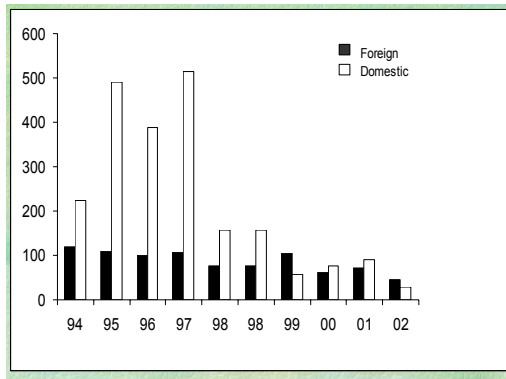
In the first figure, you see an example of an epidemic among drug addicts in a county in southern Sweden. At the same time and in the same county, 3 persons fell ill with hepatitis A due to potato salad and three other persons fell ill with different strains after travelling. Without fingerprinting, all cases would probably have been included in the epidemic among drug addicts.



In the next figure, from another county, a micro-epidemic originating from two siblings is shown. The strain of the boy spread in the local school while the strain from the sister only revealed itself 4 months later in a family with no known contact with the siblings. In the latter family, grandparents had travelled to the Canaries which then was initially considered to be the source of infection.

Epidemiology over the last six years.

Hepatitis A must be notified in Sweden and we believe that the majority of icteric patients are reported (good compliance also in this respect)



As you can see, 1995-1997 gave a rewarding harvest of cases. This was due to an epidemic of hepatitis A among drug addicts. These years are therefore not representative. Also in 1998, a number of drug addicts contributed with a small number.

Year	1997	1998	1999	2000	2001	2002
Abroad/total	112/693	73/261	105/184	57/152	69/169	44/75

Total number of patients with hepatitis A during the the last six years

	1997	1998	1999	2000	2001	2002
Infected in Sweden	27%	57%	31%	51%	54%	36%
Infected abroad	16%	28%	57%	38%	41%	59%
No information	57%	15%	12%	11%	5%	5%

This table shows the proportion of cases acquired abroad and in Sweden. There was a majority of cases acquired within Sweden during 4 of the last 6 years. Even if we disregard the years 1997 and to some extent 1998 (with the epidemic in drug addicts), there is still quite a lot of indigenous cases of hepatitis A. The explanation is most certainly not endemic foci in Sweden but micro-epidemics in families, nurseries etc. where a single patient with hepatitis acquired abroad transmits hepatitis A to persons in the immediate surrounding. They will then be registered as domestic cases.

All the same, the origin of domestic infection remains unknown in a substantial proportion of patients.

I sometimes use this disturbing fact as an argument to travellers who cannot make up their minds whether to take hepatitis A vaccine or not, and especially, whether to come back for a second dose already after 6-12 months even if they do not plan to travel at that time.

Where from?

1997	1998	1999	2000	2001	2002
Turkey 12	Turkey 15	Turkey 20	Former Yugoslavia 9	Spain 9	Chile 7
Spain 10	India 5	Former Yugoslavia 18	Turkey 4	Syria 6	Turkey 6
Ethiopia 6	Morocco 3	Syria 10	Spain 3	Tunisia 5	Former Yugoslavia 5
Eritrea 5	Libanon 3	Libanon 7	Morocco 3	Brazil 5	Iraq 3
USA 5	Syria 3	Macedonia 5	Syria 3	Pakistan 4	Greece 3
Libanon 4	Russia 3	Morocco 4	Tunisia 2	Dom. rep. 4	Somalia 2
Russia 4	UK 3	Pakistan 4	India 2	Russia 4	Brazil 2
UK 4	Spain 2	Norway 3	Bulgaria 2	Turkey 4	Tunisia 1

Which countries are missing?

The fact that countries from tropical Africa are entirely absent from the top list is surprising. (When looking at the total and most updated list of countries, which I did not find space for in the table, I admit that there is a single case of hepatitis A from Gambia in 2003. (The total list of countries over the period 1997-2003 also includes isolated cases both from Germany (5) France (6) and UK (9).

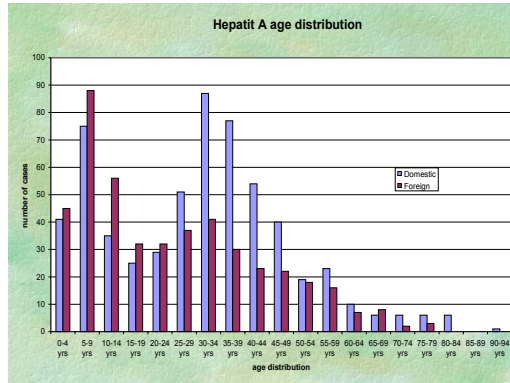
I believe that the explanation for the non-existence of tropical African countries is once again good Swedish compliance to national recommendations. The long tradition of prevention against hepatitis A has a profound influence on travellers, at least to developing countries, towards protection against hepatitis A and we therefore see no cases from “developing countries”

Which nationality?

It would be interesting to know the background of patients who fell ill with hepatitis A acquired in Turkey as well as in the other commonly listed countries. Were they visiting

friends or relatives (VFR) or Swedish tourists? I have tried to estimate this by asking for information on how many of these cases that had “non Swedish” names but this unscientific approach did not give me access to data.

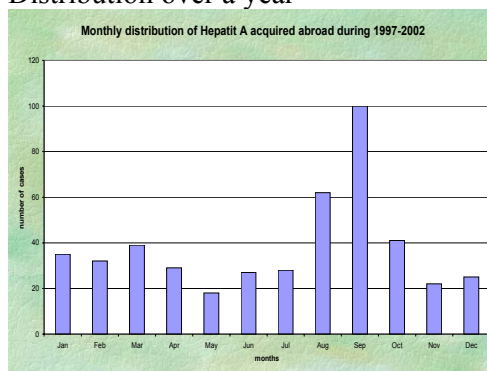
Age distribution



In this figure you can see 2 age peaks both for domestic and foreign transmission. It is tempting to assume that non-immune children are infected when they go with their immune parents as VFRs. Thus, in this age group, foreign transmission exceeds domestic. In adults, the reverse is true.

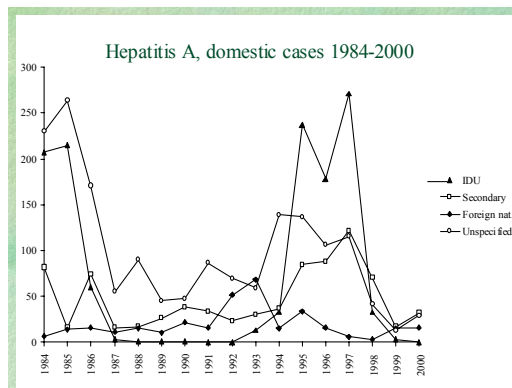
There are several possible explanations for this difference – one of them is the input of drug addicts which has been classified as domestic transmission. A second is the immunity of parents to immigrant children visiting VFRs. They will not fall ill and therefore not add to the number of cases in the age group above 20. A third and similar explanation is the transmission of hepatitis A from non-immune non-icteric children in nurseries etc to their non-immune Swedish parents who will then be icteric and diagnosed.

Distribution over a year



As shown in this figure, an increased number of cases are reported in August and September which is well in line both with the fact that Swedish tourists usually have their leave during summer time and that immigrants visiting their relatives and friends mostly go away during summer time.

Risk factors



This figure illustrates the distribution of domestic cases in Sweden over a period of years. The marked epidemics of drug addicts dominate but unspecified cases are close behind. Cases with foreign nationalities are few- probably due to immunity.

Clinical presentations

When I looked into the medical records of a very small number of patients with hepatitis A who were admitted at hospitals in the county where I work, I noticed a striking difference in the way that the diagnoses were established. All patients with names indicating a foreign ancestry were diagnosed with serology obtained at the first visit or, at least, before other interventions.

The diagnostic procedures in patients with common Swedish names were not so straight forward. All such patients without history of drug addiction or other known risk factors were first admitted to surgical departments and examined with ultrasonography of liver and gall bladder in order to look for cholecystitis or choledocolithiasis. The median time between the first contact with medical services and blood samples for serology was 3 days.

I will shortly give an example of another drawback with delayed diagnosis:

A 40 year old male came back from a holiday in southern Europe with his mate. He was admitted to department of medicine with fever and nausea as well as prominent headache. Lumbar puncture and CT-scan negative. Returned home after improvement. Three days later he became icteric and was readmitted. Transaminases were high and hepatitis B suspected due to known risk factors. The patient continued to serve himself from the buffet and to share toilet facilities with the other patients. When the serology for Hep B turned out to be negative, hepatitis A was suspected and confirmed 9 days after admission. We now have to look for at least 40 other patients who were admitted during the same time and took food from the same buffet in order to give them post exposition prophylaxis.

Discussion

Can the decreasing number of cases be explained by less travel?

Maybe in 2001 and 2002 but not otherwise. Swedish travel statistics show the opposite.

Can the decreasing number of cases be explained by increasing proportion of travellers protected against hepatitis A?

Interesting hypothesis. The percentage of protected travellers from Sweden outside Europe is in the approximate range of 50% but a very high percentage of travellers to highly endemic areas must be protected today as we see very few cases originating from such countries.

Can the decrease be explained by introduction of the vaccine?

I believe that hepatitis A vaccines have contributed to a further reduction of number of cases. They are certainly both more effective and long lasting compared to gammaglobulin. All the same, it is difficult to estimate the extent of this additional protection.

Can the decreasing number of cases be explained by changes in travel preferences?

The contrary would be closer to the truth. Swedes do travel more to distant countries and spend more time in the country-side of those countries

Can the decreasing number of cases be explained by less risk in visited areas?

The global risk of hepatitis A is decreasing. A number of studies of epidemiology in areas which are considered highly endemic illustrates this. During a meeting of travel medicine in Shanghai last year a Chinese abstract presented data from an area where attenuated live hepatitis A vaccine was used with a calculated risk of only 8/100.000 for hepatitis A each year. (Chen Yinzhong, poster 131 4 APTHC Shanghai 2002). Similarly, less than 50% of university students in Bangkok are immune.

Conclusions

1. The number of cases of hepatitis A has decreased in Sweden. The disease is now so rare that hepatitis is primarily not even suspected in icteric Swedish patients.
2. There are extremely few cases acquired from tropical Africa which indicates that Swedish travellers to such countries are well protected.
3. Cases acquired abroad are sometimes considered to originate from countries which are not highly endemic. Finger printing might show different origin of infection.
4. Domestic cases are more common than cases acquired abroad. Thus, micro-epidemics occur also in Sweden which is an argument for a second dose of vaccine even in absence of further travel.