HAV EPIDEMIOLOGY

in TURKEY

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November 30, 2007

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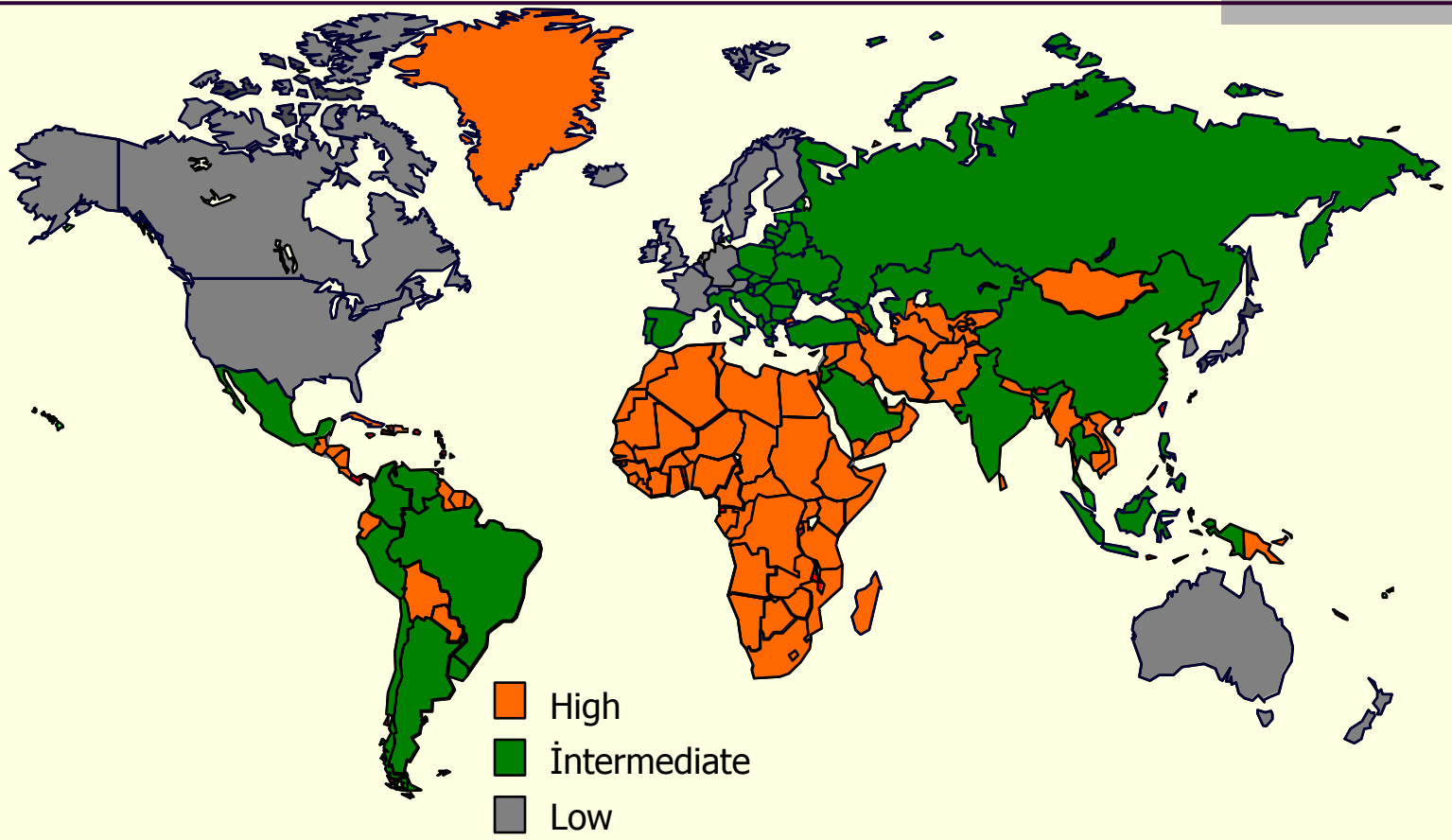
Introduction

- Hepatitis A (HAV) is a vaccine preventable disease with changing epidemiology
- Endemicity is related to hygene, infrastructure and socio-economic conditions
- However, even in the same country endemicity patterns may change over time.

"As world-wide standards of hygiene improve, the **morbidity and mortality from hepatitis A** infection may increase in certain target populations, **as a higher proportion of infections occur in later life,** with an associated increase in disease severity"

Dr. M. Kane

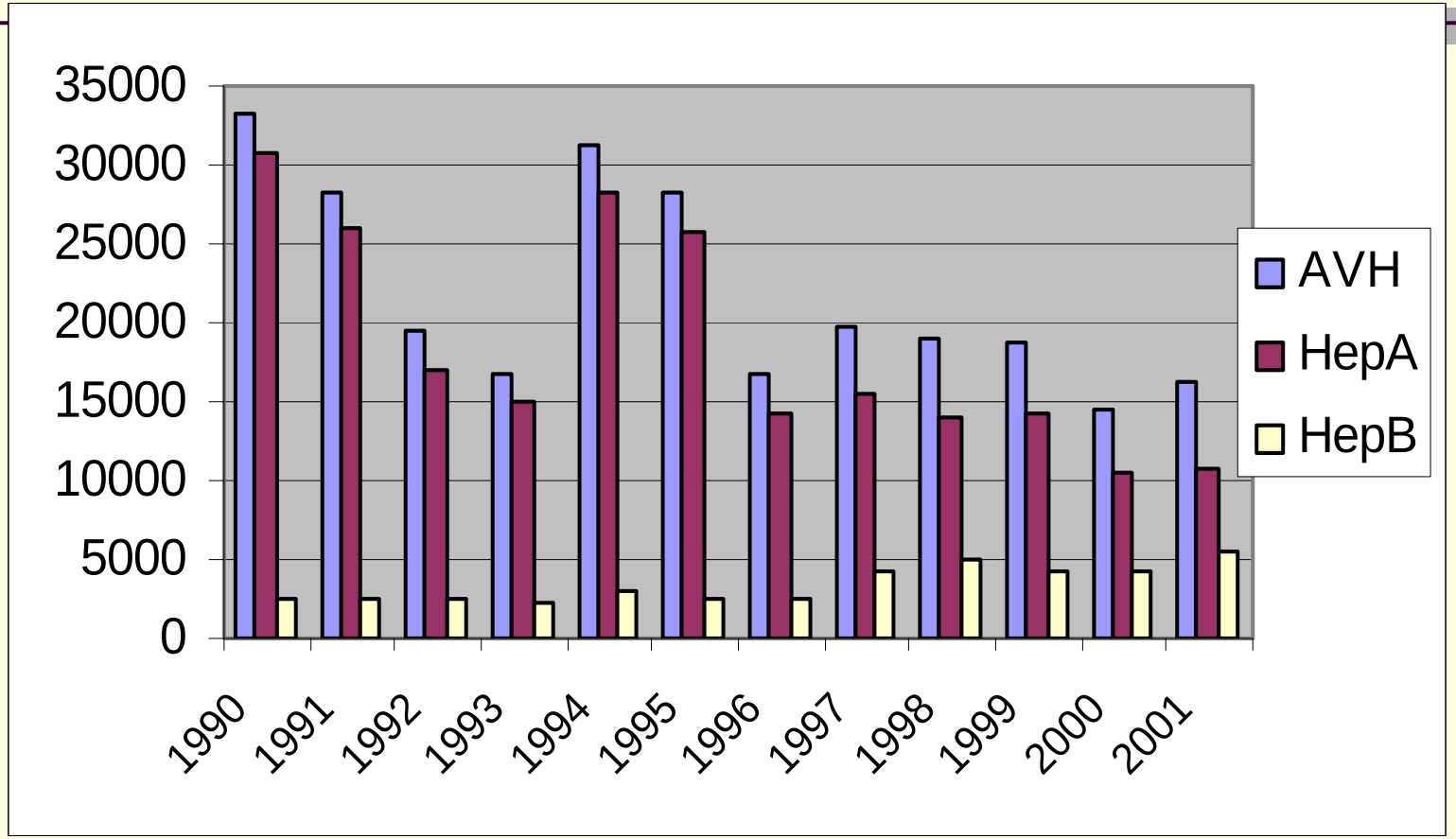
HAV Seroprevalance: Geographic Distribution



DATA from MOH, TURKEY

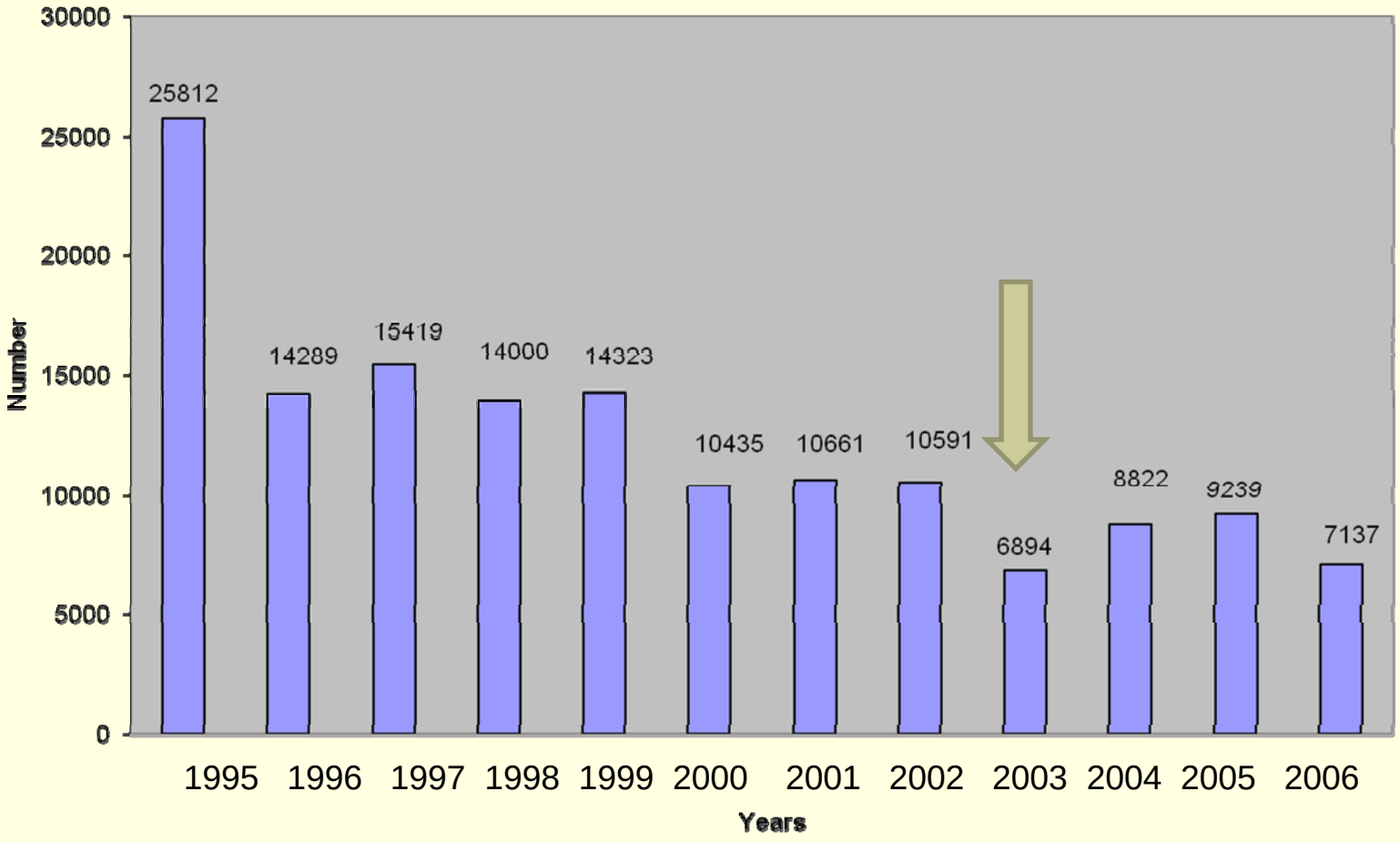
- Hepatitis A is one of the reportable diseases in Turkey.
- It is hard to assess disease burden,
  - since most cases are asymptomatic
  - significant under-reporting and
  - no reliable national data available on disease burden.

Viral Hepatitis Data from MOH, Turkey

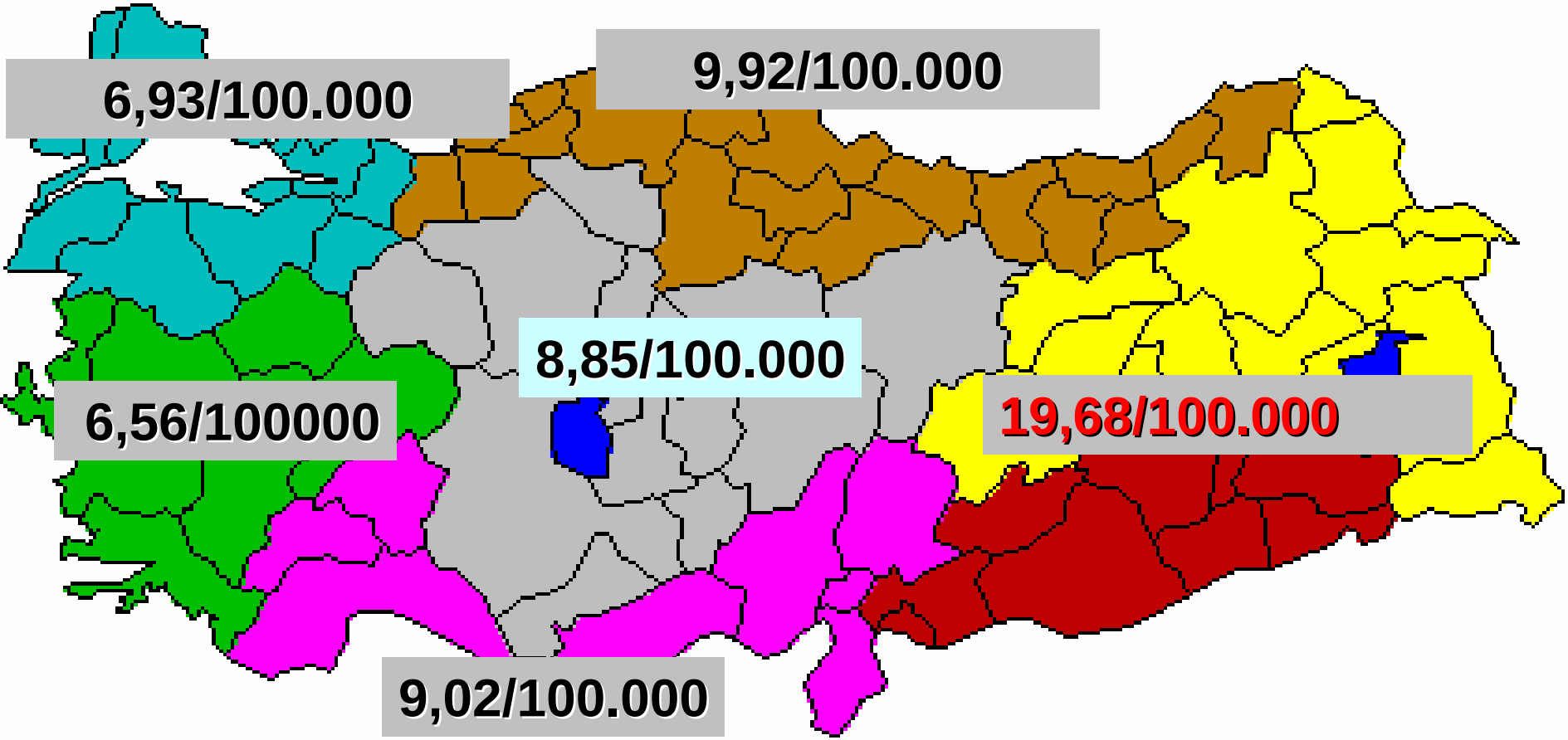


	1990	1991	1992	1993	1994	1995	1996	1997	1998	1999	2000	2001
AVH	33282	28351	19518	16671	31344	28235	16724	19762	19003	18685	14612	16239
HepA	30662	25896	16967	14895	28245	25812	14289	15419	14000	14323	10435	10661
HepB	2620	2455	2551	2276	3099	2423	2435	4343	5003	4362	4177	5578

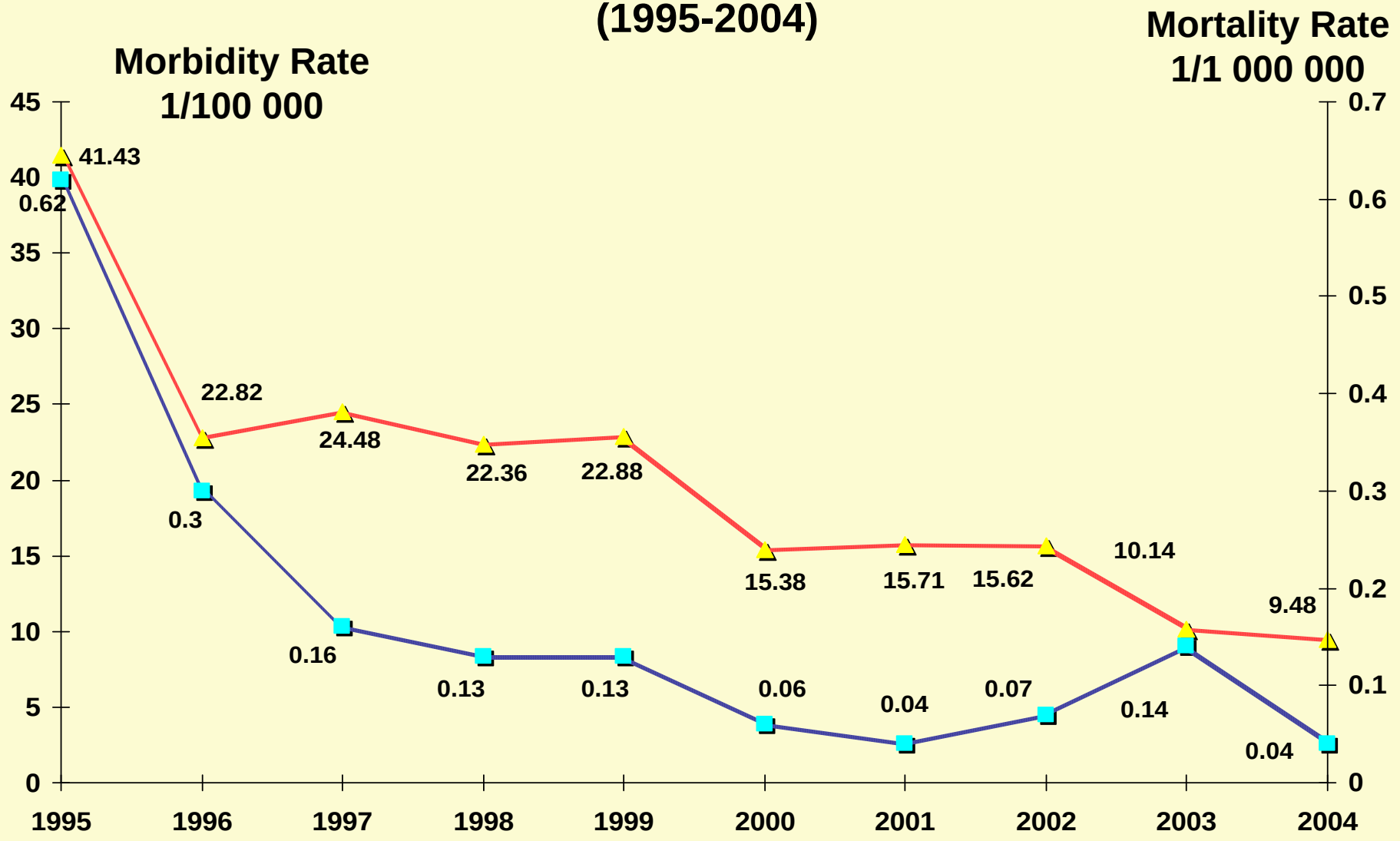
Distribution of Hepatitis A Cases by Years in Turkey, MOH (1995-2006)



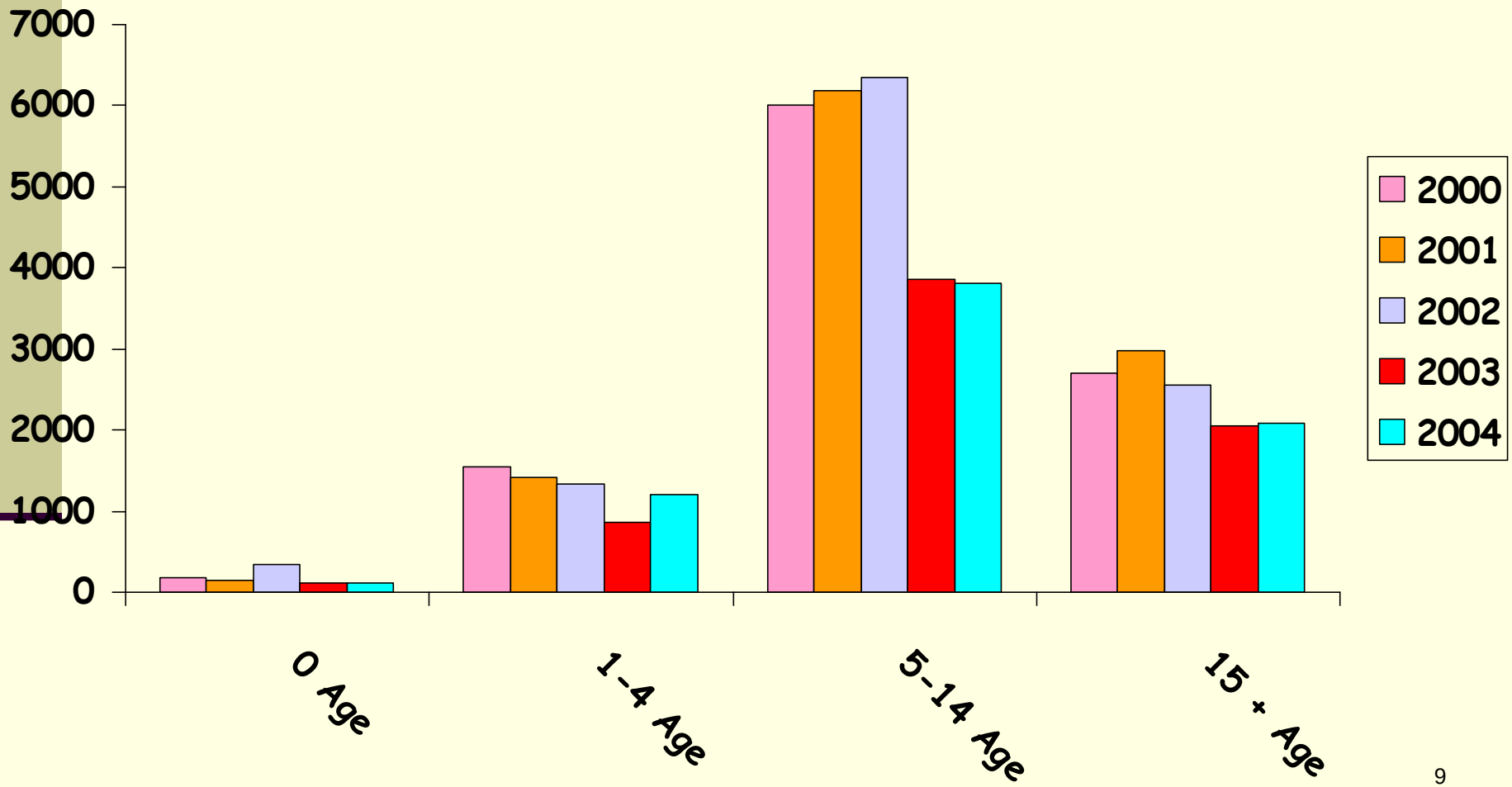
Hepatitis A Incidence by Province, MOH Turkey 2004



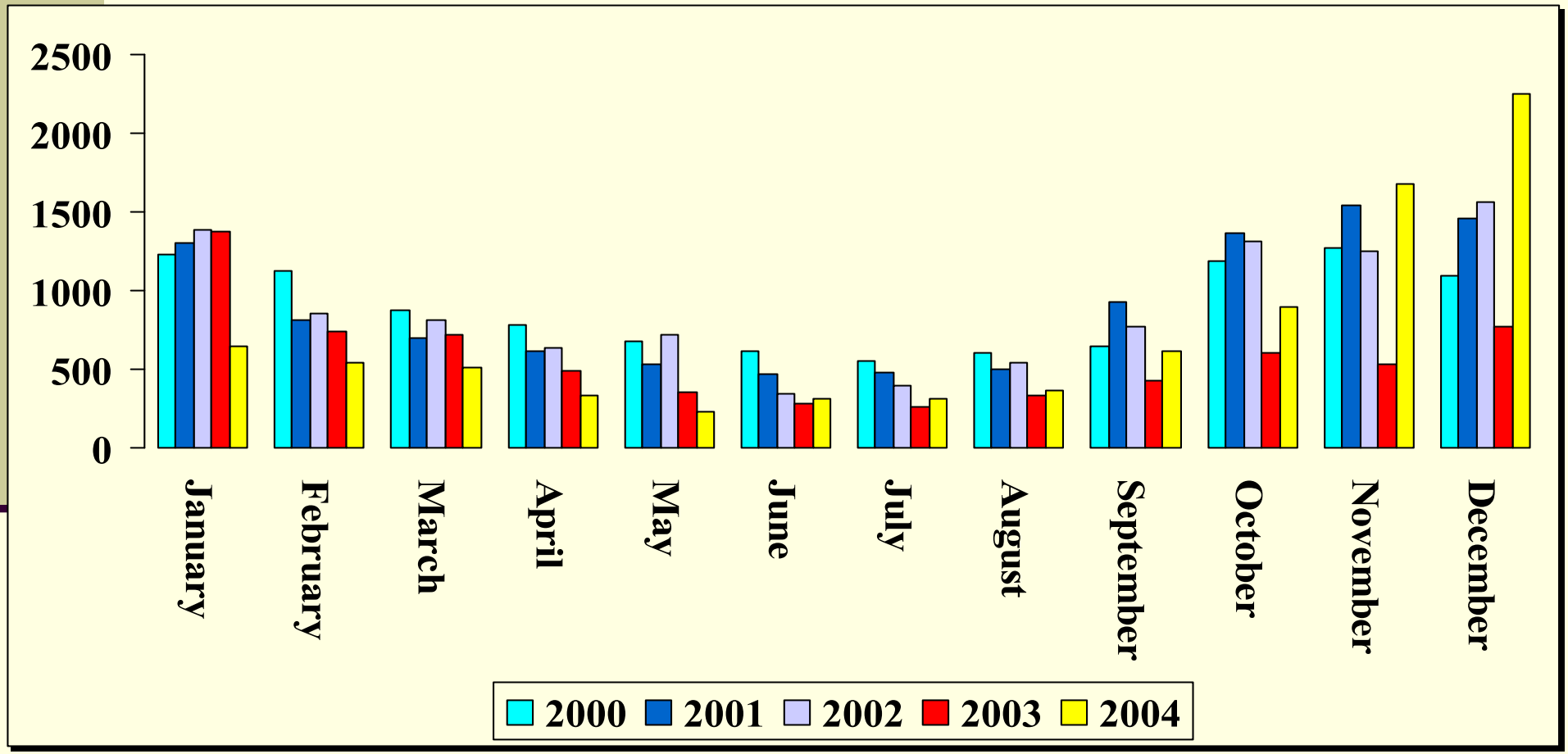
_Hepatitis A Morbidity and Mortality Rates by Years,Turkey (1995-2004)



Distribution of Hepatitis A Cases by Age Goups, MOH, Turkey
(2000 – 2004)



Distribution of Hepatitis A Cases by Months, MOH, Turkey
(2000-2004)



EPIDEMIOLOGICAL STUDIES

AETIOLOGICAL CLASSIFICATION OF HOSPITALIZED *ACUTE VIRAL HEPATITIS CASES* IN TURKEY (*ADULTS*)

CITY	STUDY GROUP	#	HBV (%)	HAV (%)	HCV (%)	HEV (%)
ANKARA	*Kurt, 1995*	1022	76.0	17.1	6.8	NA
BURSA	*Mıstık, 1998*	135	55.2	42.3	2.2	NA
DİYARB.	*Geyik, 1998*	148	61.1	22.9	2.0	14.8
İSTANBUL	*Özgüneş, 1998*	720	68	26	1.4	NA
İZMİR	*Okan, 2000*	518	61.3	28.1	2.0	NA
TOTAL		*4471*	*60.4*	*27.5*	5.5	0.5

AETIOLOGICAL CLASSIFICATION OF HOSPITALIZED ACUTE *VIRAL HEPATITIS CASES* IN TURKEY (*CHILDREN)*

CITY	STUDY GROUP	N	HAV (%)	HBV (%)	HCV (%)
ADANA	*Şahin, 1998*	338	38.6	35.8	0.5
ANKARA	*Uysal, 1998*	364	87.9	7.7	0.3
İSTANBUL	*Sıdal, 1990*	160	66.0	24.0	10.0
TOTAL		*912*	*63.1*	*22.4*	*2.1*

HAV Seroprevalence (%), Turkey

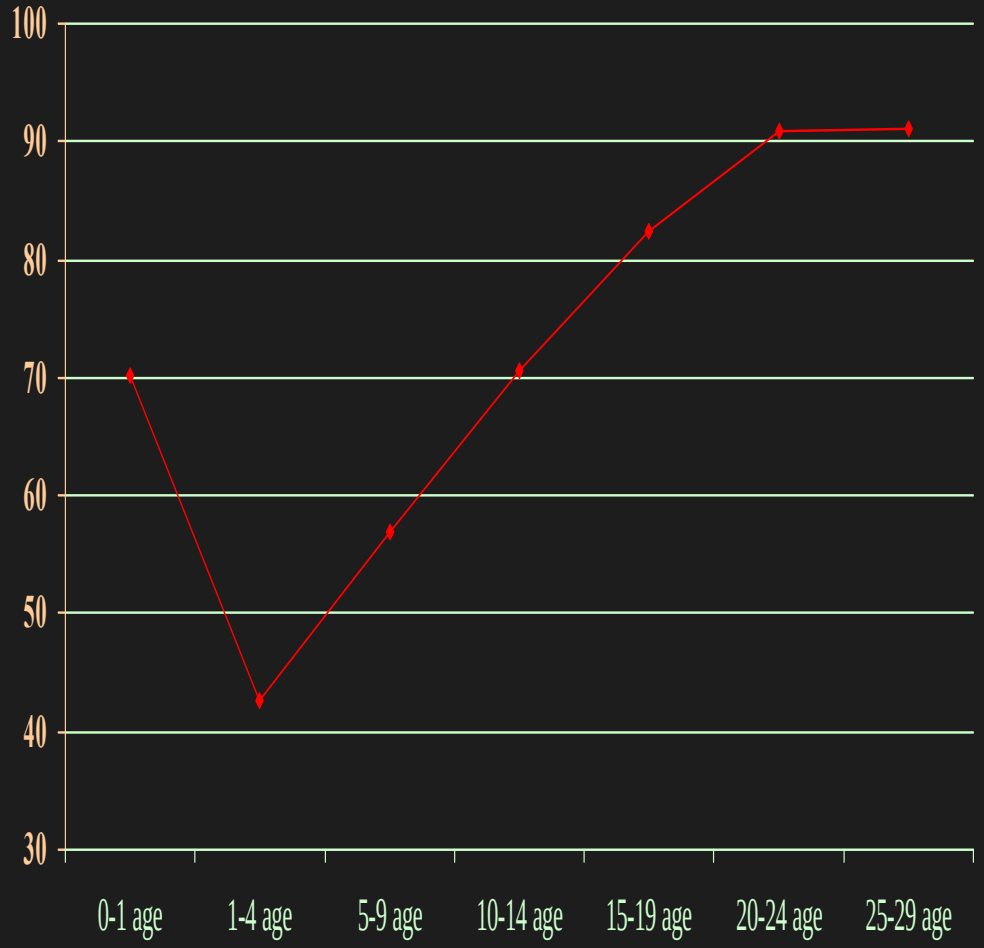
Study Gr.	City	Year	1-3 y	4-7 y	8-11 y	12-15y	16-30 y	>30 y
Şahin	*Adana*	1998	35,7	54,5	73,7	76,1		
Çolak	*Antalya*	1998	19,9	43,9				
Erdoğan	*Edirne*	2000	25,6		25	37,3	43,2	
Akbulut	*Elazığ*	1995	12,1	72,5		100		
Aslan	*İzmir*	2000	4,4	38,3	45,1			
Şahin	*Ist.*	1998	6,4	20	38,2	55,5		98,4
Sıdal	*Ist.*	2002	15,1			49,6		
Kanra	*TR*	2002	42,7	57	70,6	82,5	91,1	

Nationwide Study of Kanra et al. and "Turkish National Study Team"

- Total of *4462* samples studied in *9* provinces
- These provinces were representative of Turkey's geographic location, demographic, economic and social characteristics
- Cluster sampling size was determined based on the previous seroprevalence studies in each province.
  - İstanbul, Ankara, İzmir, Diyarbakır: 600 subjects for each
  - Samsun, Erzurum,Trabzon, Edirne: 450 subjects for each
- All subjects were under 30 years of age

Kanra G, et al. Turk J Pediatr, 2002

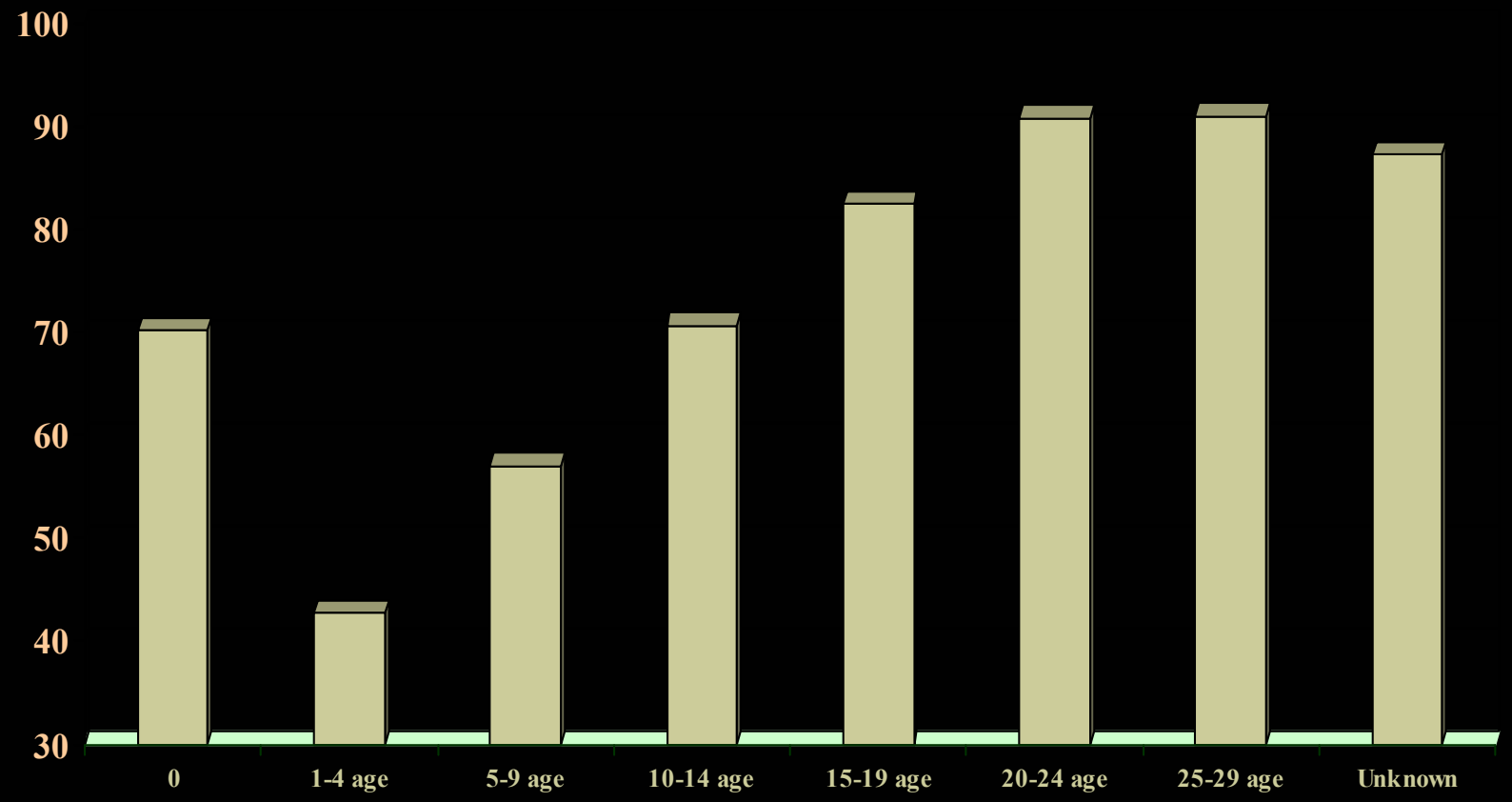
Hepatitis A Seroprevalence Study in Turkey



- In Turkey
  - High level of maternal antibodies start decreasing by the end of first year.
  - Level of anti-HAV IgG starts increasing with school age.
  - Peak is reached by late adolescence age

Kanra G, et al. Turk J Pediatr, 2002

HAV Seroprevalence in Different Age Groups in Turkey

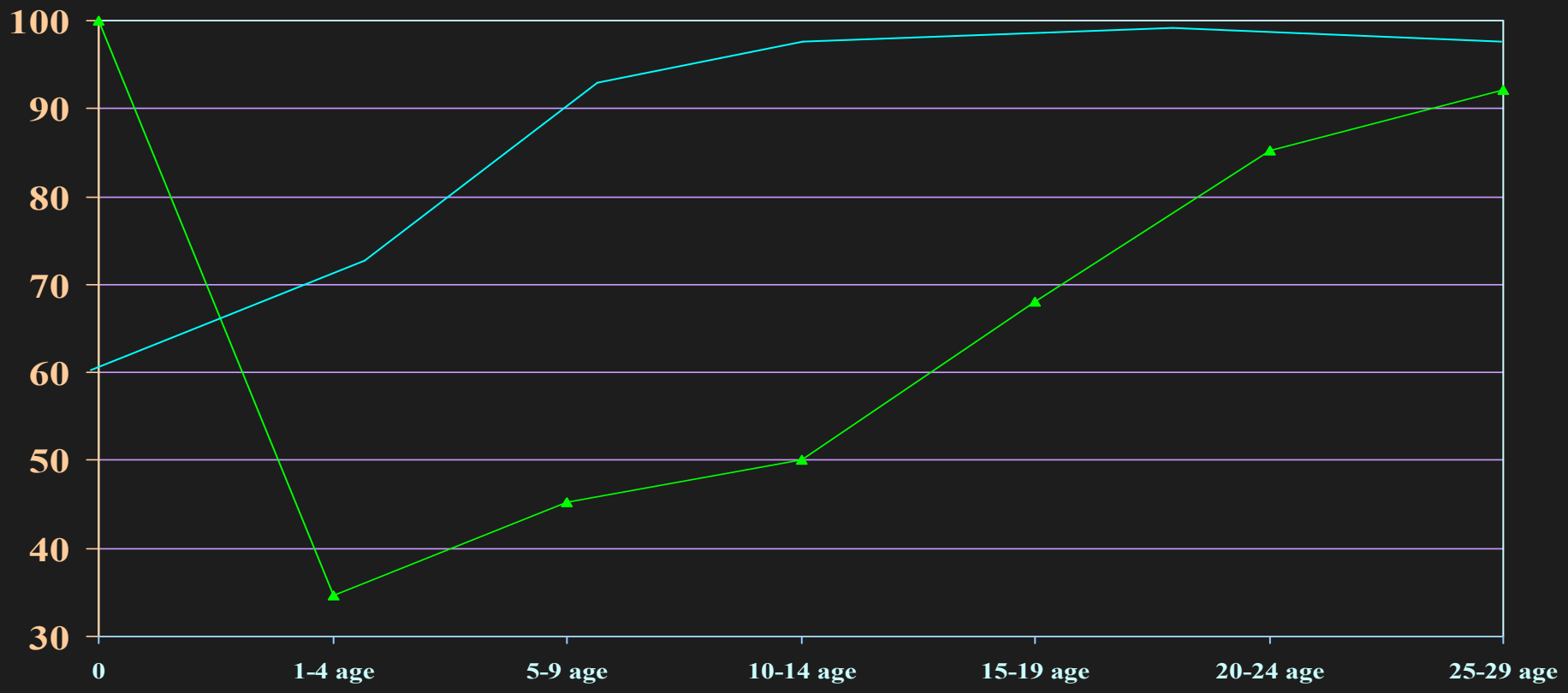


Kanra G, et al. Turk J Pediatr, 2002

Seroprevalance in Provinces of Relatively High and Poor Environmental Standarts

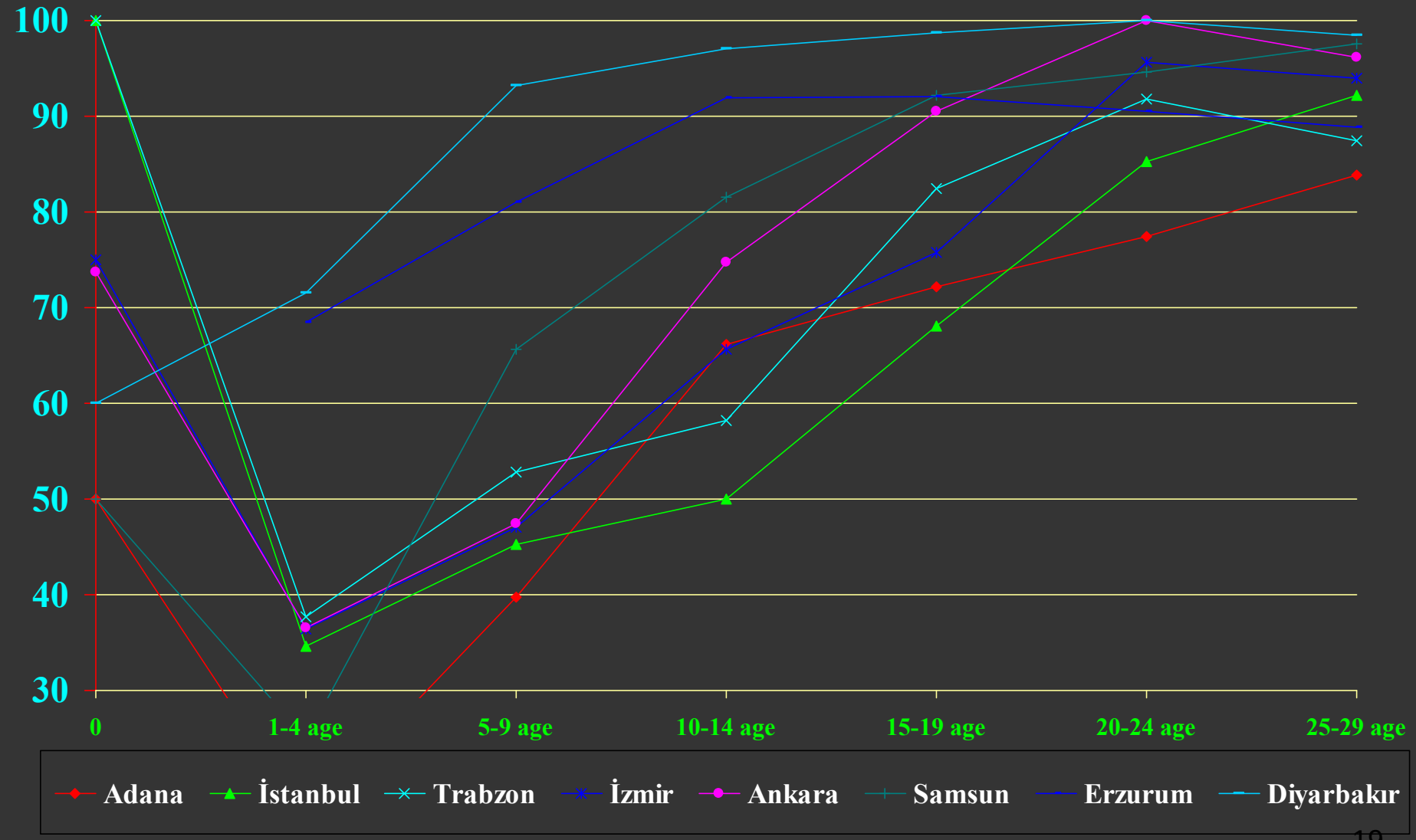
High: Ankara, İzmir, İstanbul,Trabzon, Samsun

Poor: Erzurum, Diyarbakır



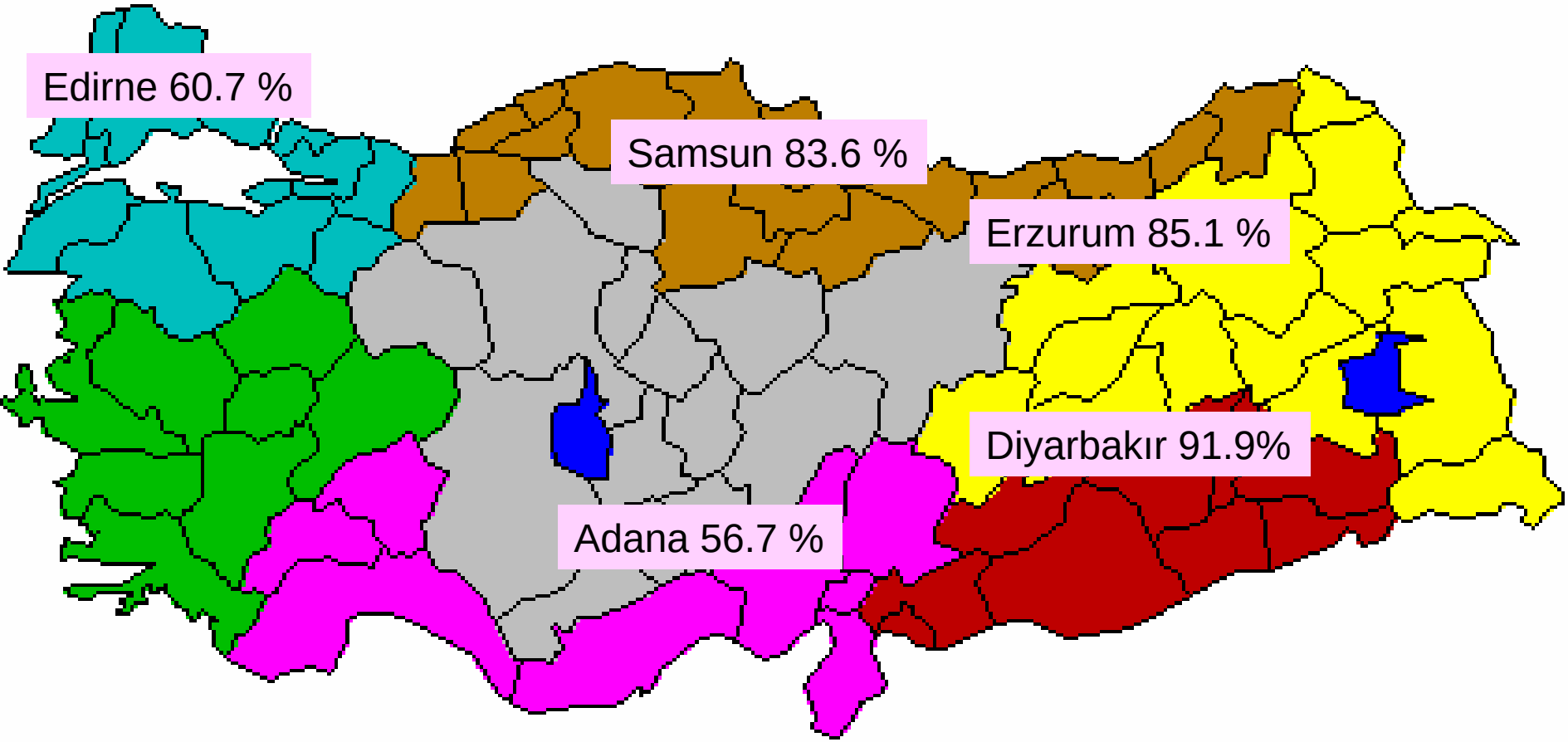
Kanra G, et al. Turk J Pediatr 2002

Seroprevalence Differs from Province to Province in Turkey



Kanra G, et al. Turk J Pediatr 2002

Hepatitis A Seroprevalence by Province



Kanra G, et al. Turk J Pediatr 2002

Summary of the Results

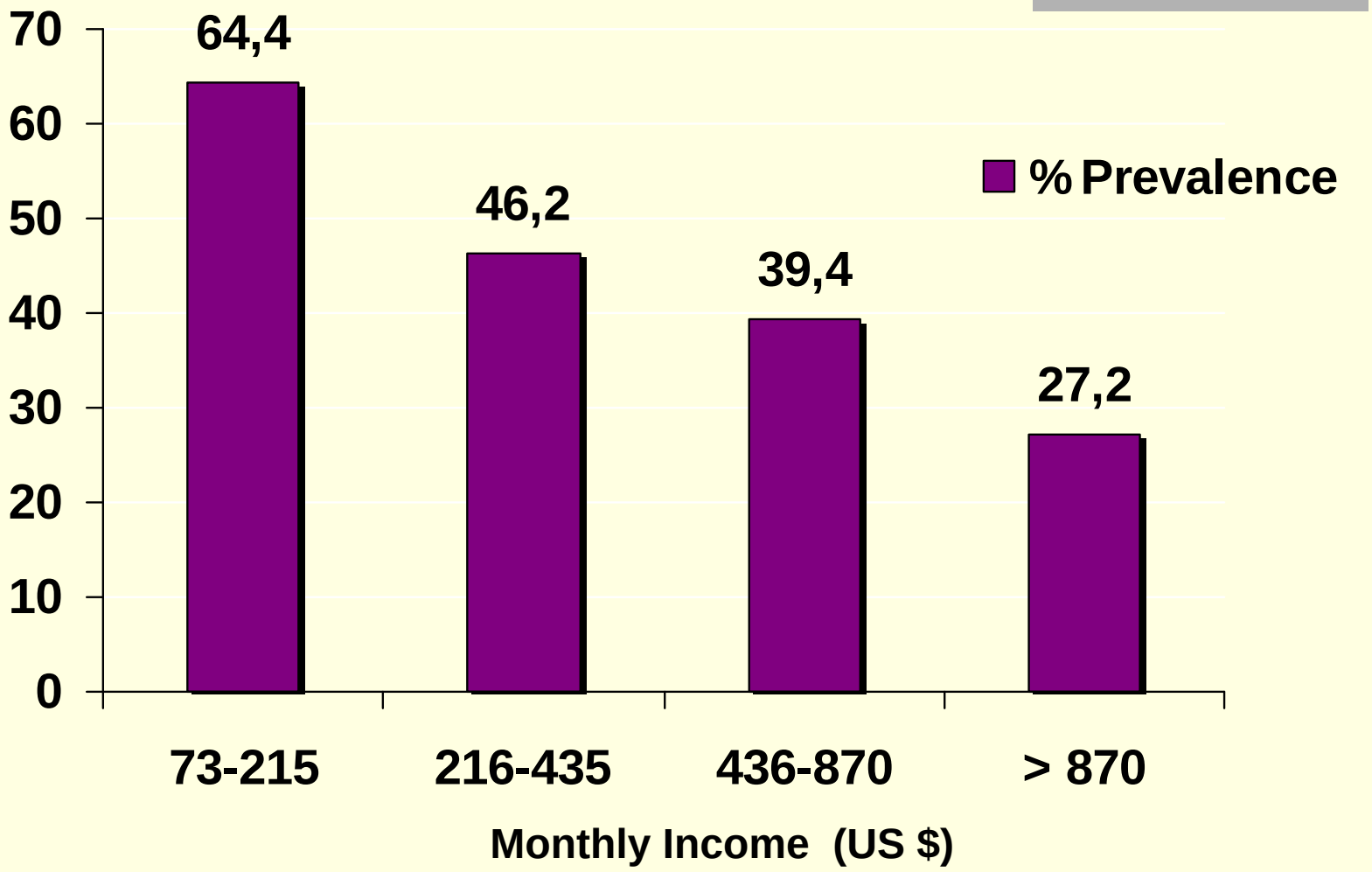
- Throughout the country 50% of the children are seropositive by age 10
- Lowest seropositivity: *Adana Province* (% 56,7)
  Highest seropositivity: *Diyarbakır Province* (% 91,9)
- Seropositivity decreases in western provinces
- Gender has no effect
- Socio-economic status determines
- Family size has effect in low income families

Seropositivity changes from province to province.

> Overall seropositivity was: 71.3%

Kanra G, et al. Turk J Pediatr 2002

Seroprevalance in Different Socio-economic Groups in *Adana*, Turkey



Ages 2 -16.5

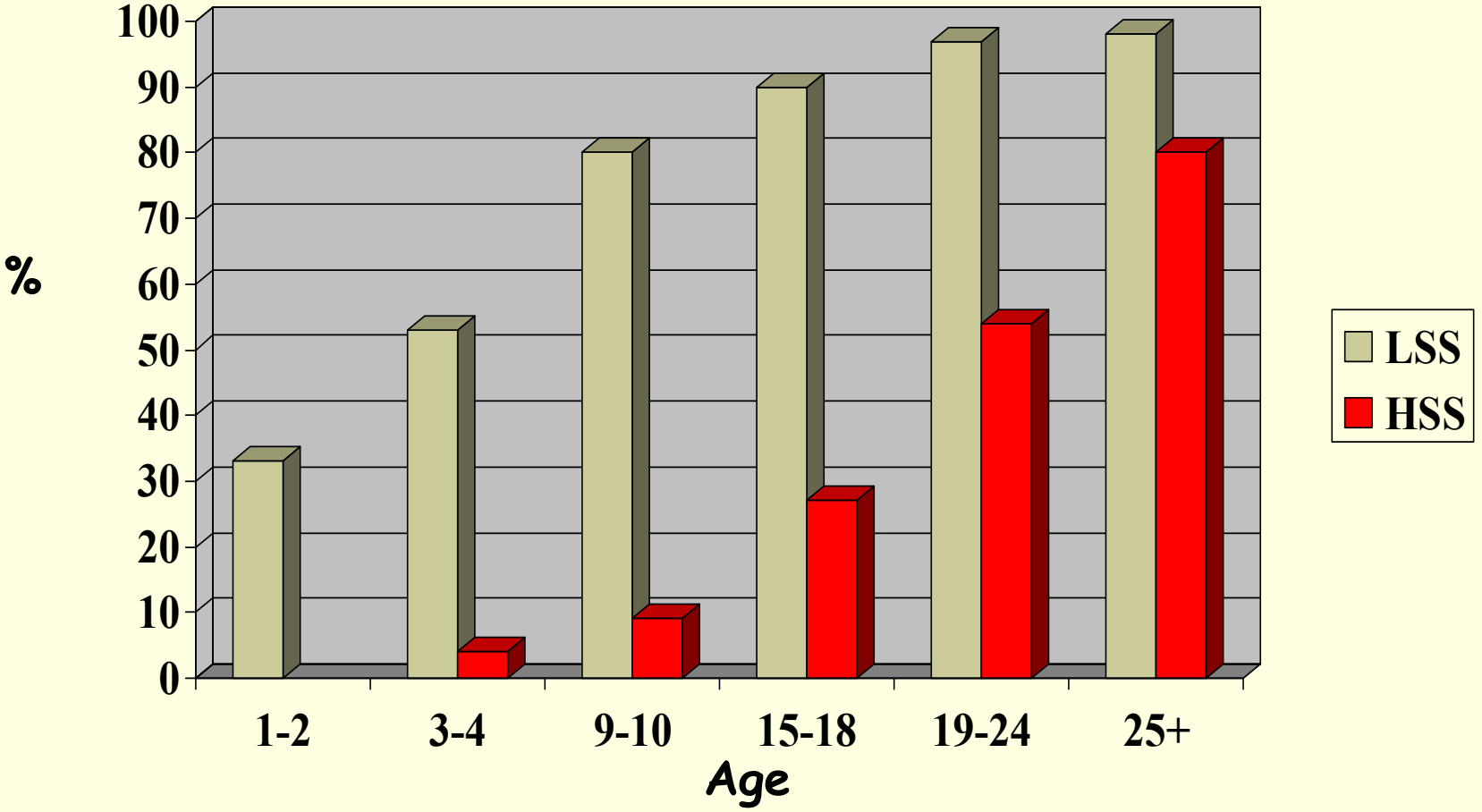
(Yapicioglu et al., Indian J. Pediatrics, 2002)

Seroprevalance in Different Age Groups in *Adana*, Turkey

Age	Anti-HAV %
2-4	10.6
4-6	28.8
6-12	49.8
12-16.5	68
Overall	44.4

(Yapicioglu et al., Indian J. Pediatrics, 2002)

Seroprevalance in Different Socio-economic Groups in *İzmir*, Turkey



Özkınay F, Kurugöl Z 2002 et al

Seroprevalence of HAV and HEV in Healty Individuals in Marmara Region, Turkey

Age Group	Anti-HAV(+), %	Anti-HEV(+), %
0 - 9	25,9	2,4
10 - 19	68,8	1,1
20 - 29	93,8	3,9
30 - 39	97,1	4,9
40 - 49	96,4	10,7
50 - 59	97,4	5,3
> 60	98,2	13,8

Yenen OŞ, Badur S, 1996

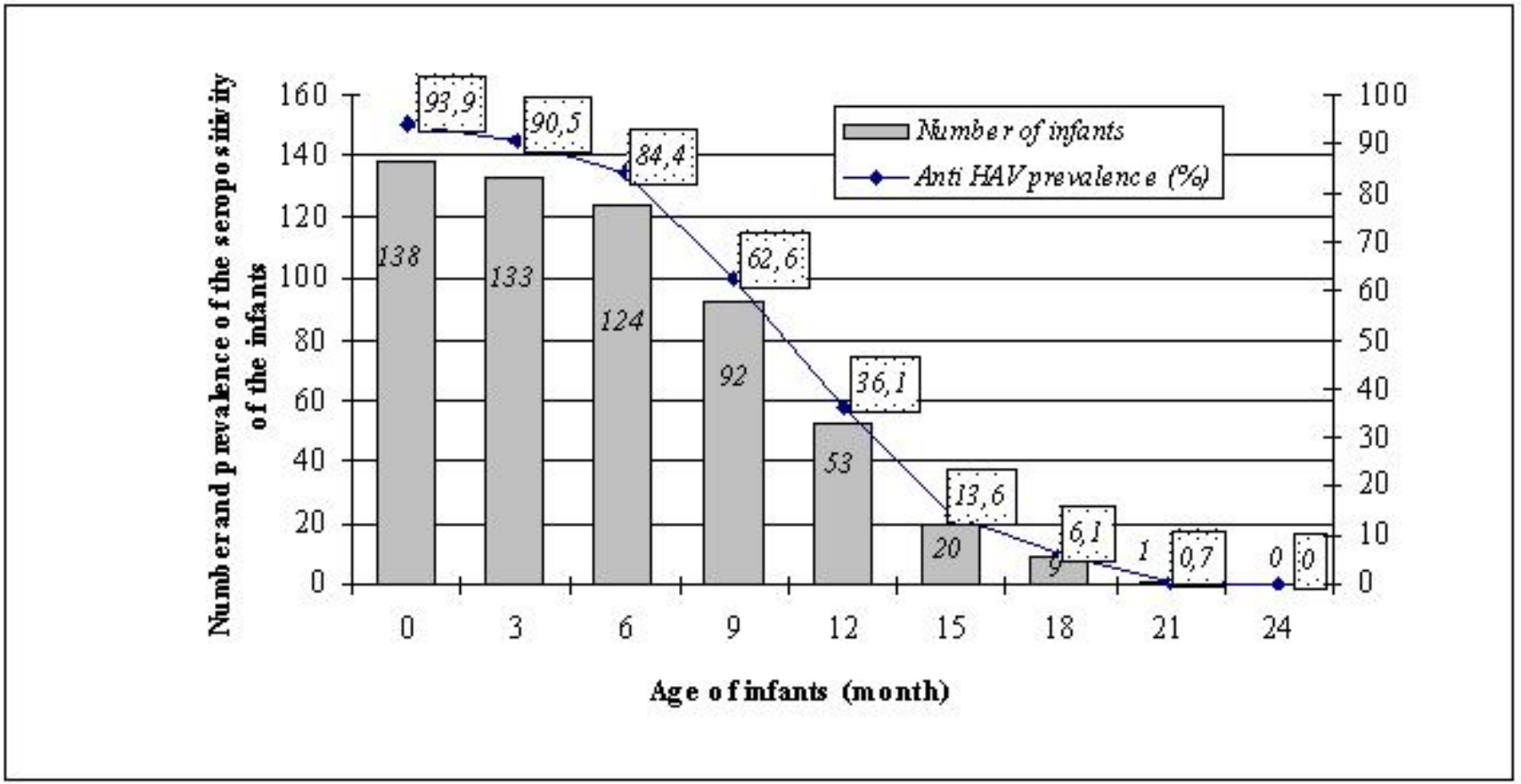
Results Indicate that Turkey is Presented with Three Endemic Regions

- High regions
- Intermediate regions
- Low regions

Vaccination

- HAV vaccine available
- Not included in NIP

Decline of Maternal Antibodies



Alabaz D, Aksaray N, Alhan E, Yaman A. Am J Trop Med Hyg,2005

Vaccination When?

- Recommended by pediatricians at university hospitals and private clinics.
  - At IU Faculty of Medicine, Pediatric Clinic first dose at 18 months, repeated after 6 months.
  - 6 year olds checked for IgG first.

Recommendations for Vaccination Strategies 1

- Kanra G et al.,
  - Since there are differences in seroprevalance between provinces a vaccination program similar to program in US can be recommended in Turkey.
- Yapıcıoglu et al.,
  - Children living and attending school in higher socioeconomic districts should be vaccinated before they start school (before 6 years of age)

Recommendations for Vaccination Strategies 2

- Alabaz D et al.,

  Children should be immunized because:

1-They play a major role in transmission

2-To reduce the disease incidence and to avoid creating a pool of susceptible adults (especially for those children coming from high SES conditions)

- Öncül O et al., IV. National Sypmosium on Infections Transmitted through Fecal-Oral Route (May 2005, Mersin, TR
- For the past ten years incidence of HAV infections is decreasing with the occurence age shifting towards adults. This brings out the need for a vaccination policy.

Antigenic Characteristics of HAV in Turkey 1

- 7 genotypes with 15-25% difference in their sequence.
- Type I and III have A and B subtypes (IA, IB, IIIA, IIIB)
- Most common genotype throughout the world is type I followed by type III.
- Type IA in America And Russia
- Type IB in Europe and Mediterannian Countries

Is there is difference between genotypes regarding patogenicity?

Normann A et al.,

Genetic Analysis of HAV from 50 Samples

IB

```
                1
No4             GAATCAATGA TGAGCAGAAT TGCAGCTGGA GACTTGGAGT CATCAGTAGA TGATCCTAGA
AG6084          .......... .......... .......... ..T.....A. .......G.. ..........
H-152           .......... .......... .......... .......... .......G.. ..........
IS23            .......... .......... .......... .......... .......G.. ......C...
IS27            .......... .......... .......... .......... .......G.. ......C...
IS28            .......... ....T..... .......... .......... .......G.. ..........
IS29            .......... .......... .......... .......... .......G.. ..........
IS35            .......... .......... .......... .......... .......G.. ...C......
Jor88           .......... .......... .......... ..T....... .......G.. ..........
H-153           .......... .......... .......... .......... .......G.. ..........
HM175           .......... .......... .......... .......... .......G.. ..........

                61
No4             TCAGAGGAGG ATAAAAGATT TGAGAGTCAC ATAGAATGCA GGAAACCCTA TAAAGAATTG
AG6084          ........A. .C........ .........T .....G.... ....G..A.. .......C..
H-152           ........A. .......... .........T .......... ....G..A.. .......C..
IS23            .......... .C.G...... .......... .......... ....G..A.. ..........
IS27            .......... .C.G...... .......... .......... ....G..A.. ..........
IS28            .......... .......... .......... .......... ....G..A.. ..........
IS29            .......... .C........ .......... .......... ....G..A.. ..........
IS35            .......... .......... .......... .......... ....G..A.. ..........

                121                                                          168
No4             AGATTGGAAG TTGGGAAACA AAGACTCAGG TATGCTCAGG AAGAATTG
AG6084          .....A.... .......... .........A .......... .........
H-152           .....A.... .......... .........A .......... NNNNNNNN
IS23            .....A.... .......... .........A .......... .........
IS27            .....A.... .......... .........A .......... .........
IS28            .....A.... .......... ......T.A. .......... ....33...
IS29            .....A.... .......... .........A .......... .........
IS35            .....A.... .......... ......T.A. .......... .........
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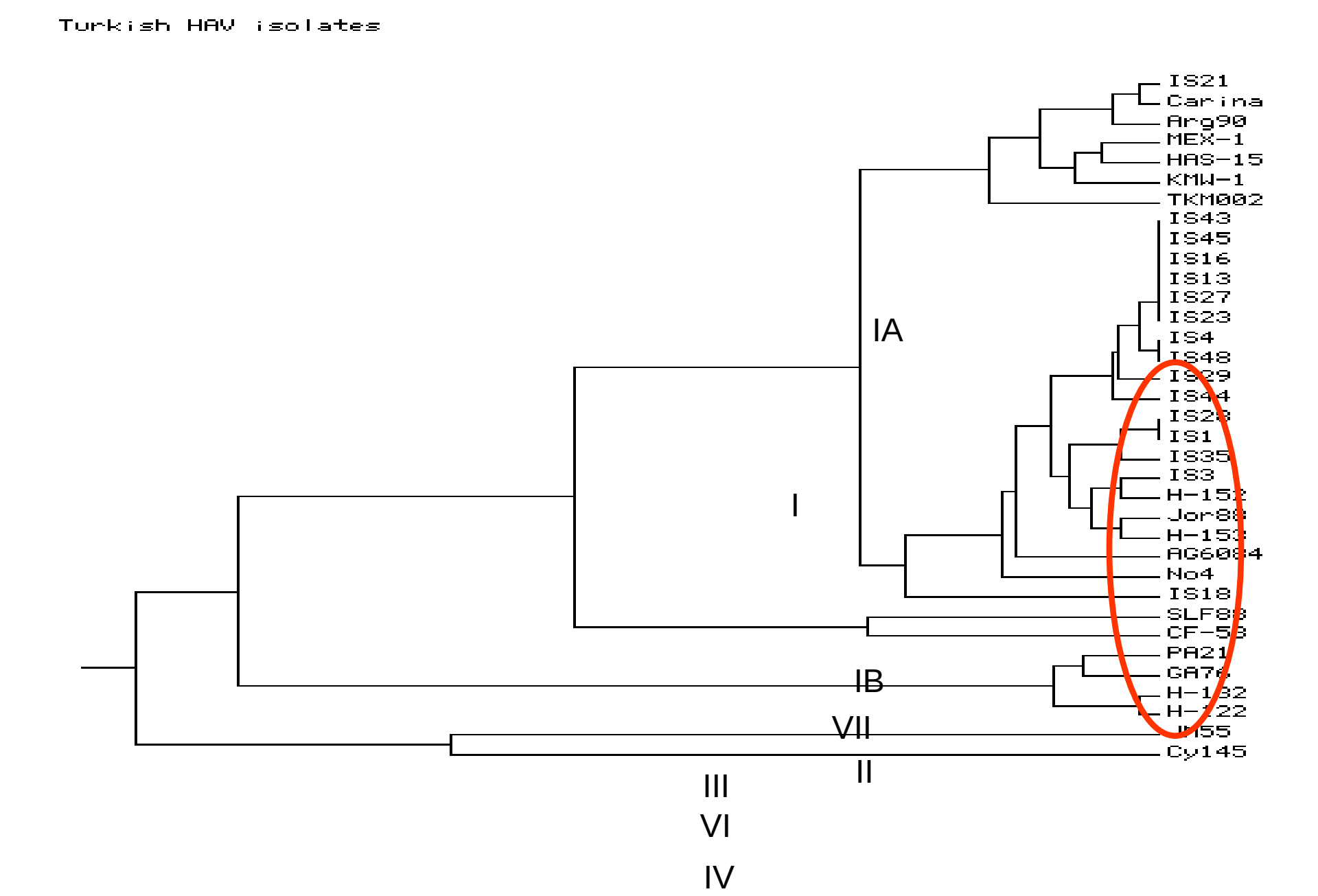
Normann A et al.,



Normann A et al.,

TABLE I. Comparison of Patients' Genotypes to Viral Load and Duration of Viremia

Patients	Genotype	Maximal viral load genome equivalents/ml	Duration of viremia days
B.J.	IA	6.1×10^3	77
B.U.	IA	2.0×10^3	51
S.Ax.	IA	1.9×10^4	113
S.An.	IB	2.7×10^4	82
S.M.	IA	2.6×10^4	69
E.K.-H.	IA	3.1×10^5	186
W.P.	IB	1.9×10^5	41
W.G.	IA	1.0×10^5	490
R.H.	IA	3.0×10^4	149
K.S.	IA	3.0×10^4	408
K.H.	IA	2.4×10^3	122

(Normann A et al; J Med Virol 2004; 72:10)

Conclusion

- Reporting of HAV cases should be enforced to collect more relaible data
- Surveillance system needs to be updated
- Burden of the disease should be studied effectively to estimate the cost-effectiveness and public health benefit of the vaccination to recommend vaccine for inclusion in NIP

Thank You for Your Patients