


**Prevalence of Hepatitis B,C infection  
among Mongolian population and  
genotype characterization**

**DR J.Oyunbileg, Kh.Tsatsral, L.Altantuya, P.Nyamdawaa**  
Dr.Sc, prof  
Public Health Institute,  
Mongolian Academy of Medical Sciences

**German-Mongolian Symposium on Hospital Hygiene, Infection Prevention and Control**  
14-15 September, 2016



Department of Biotechnology and Molecular Biology,  
Public Health Institute

№	Stages of Development	Activities
1	1974 years	Set up the control Virology Laboratory and Biopreparation Control Laboratory at The State Institute of Hygiene, Epidemiology and Microbiology
2	1985 years	Research Center for Virology at SIHEM
3	1987 years	Was elaborated Complex Program for Controlling Viral hepatitis

**German-Mongolian Symposium on Hospital Hygiene, Infection Prevention and Control**  
14-15 September, 2016



Were done 18 research project  
including Basic, Applied and  
Technological Projects.

German-Mongolian Symposium on Hospital Hygiene, Infection Prevention and Control

14-15 September, 2016



## Results

- Was detected Mongolian Marmot Hepadnavirus in Mongolian Marmot Population (*Marmota Sibirica*, Radde, 1862)
- Was done complete sequence of this virus (3323 pairs of nucleotides)
- First determined the prevalence of Hepatitis B and C viruses among Mongolian population and genotype specificities.
- First determined HTLV-I,II prevalence- 1.62%
- Were elaborated 13 technology instructions, models of products.

German-Mongolian Symposium on Hospital Hygiene, Infection Prevention and Control

14-15 September, 2016



## Known orthohepadnaviruses and their hosts

orthohepadnavirus	Host	Literature
Hepatitis B virus (HBV)	Man (Homo sapiens sapiens)	Dane et al. (1970)
Chimpanzee hepatitis B virus (GhHBV)	Chimpanzee (Pan troglodytes)	Vaudin et al. (1988)
Gibbon hepatitis B virus (GiHBV)	White-handed gibbon (Hylobates lar)	Norder et al. (1996)
Orangutan hepatitis B virus (OuHBV)	Orangutan (Pongo pygmaeus pygmaeus)	Warren et al. (1999)
Gorilla hepatitis B virus (GoHBV)	Gorilla ( <i>Gorilla gorilla</i> )	Grethe et al. (2000)
Woolly monkey hepatitis B virus (WMHBV)	Woolly monkey (Lagotricha)	Lanford et al. (2000)
WHV	Woodchuck (Marmota monax)	Summers et al. (1978)
Ground squirrel hepatitis virus (GSHV)	Ground squirrel (Spermophilus beecheyi)	Marion et al. (1980)
Arctic squirrel hepatitis virus (ASHV)	Arctic squirrel (Spermophilus parryi kennicotti)	Testut et al. (1996)

German-Mongolian Symposium on Hospital Hygiene, Infection Prevention and Control

14-15 September, 2016




## Seroprevalence of hepadnavirus infection in the population of Mongolian marmots

Aimags	total	Positives					
		anti-WHc+		WHsAg+		anti-WHs+ %	
		numbers	%	numbers	%	numbers	%
Khentii	14	9	64.3	0	0	3	21.4
Dornogobi	4	0	0	0	0	0	6.7
Gobi-Altai	60	11	18.3	0	0	4	8.9
total	79	20	25.3	0	0	7	8.9

German-Mongolian Symposium on Hospital Hygiene, Infection Prevention and Control

14-15 September, 2016



## Hepatitis B virus

**Biotype** → **Virus**

↓

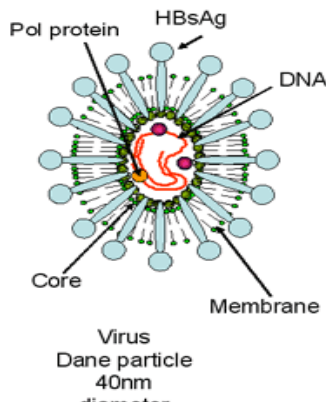
**Serotype** → **1**

↓

**Subtype** → **αw2**

↓


**Genotype** → **D**



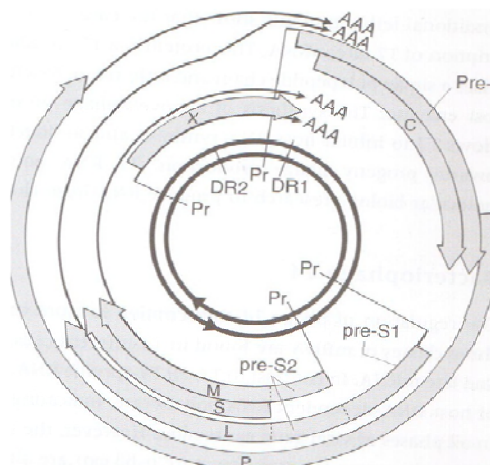
**Virus**  
Dane particle  
40nm  
diameter

**German-Mongolian Symposium on Hospital Hygiene, Infection Prevention and Control**

14-15 September, 2016




Hepatitis B virus genome map. The closed circular DNA is transcribed from four promoters (Pr): arrowheads indicate 3' ends. For details of protein expression, see text. Pre-S1, pre-S2 are the designations given to the upstream portions of the S reading frame which, when added to the N terminus of S, give rise to the longer I. and M surface proteins. DR1, DR2 are repeated sequences shown to orientate the map.



**German-Mongolian Symposium on Hospital Hygiene, Infection Prevention and Control**

14-15 September, 2016



### Comparison of nucleotide and amino acid sequences of MMHV and WHV

Gene regions	Number of nucleotide and amino acid		Differences in nucleotides		Differences in amino acids	
	WHV	MMHV	numbers	%	numbers	%
Gene "S" (Pre-sI+Pre-sII+s)	1296/432	1296/432	0	0	0	0
Gene "X"	426/142	402/134	5	1.24	4	2.98
Gene "C"	678/226	678/226	1	0.14	0	0
Gene "P"	2655/885	2655/885	11	0.41	7	0.79

**German-Mongolian Symposium on Hospital Hygiene, Infection Prevention and Control**


14-15 September, 2016





**German-Mongolian Symposium on Hospital Hygiene, Infection Prevention and Control**

14-15 September, 2016




## Etiology of HCC in Mongolia

Patients numbers	From them HBsAg + (%)	Anti - HDV (+)	HBsAg, anti HDV (+) (%)	Anti HCV (+) (%)	HBsAg, Anti HDV, Anti-HCV (-) (%)	Anti - HCV, HBsAg, Anti - HDV (-) (%)	Anti-HCV (+) HBsAg, Anti - HDV (-) (%)	HBsAg, Anti HDV, Anti-HCV (+) (%)
29	14/29 (48.2)	16/29 (55.20)	21/29 (72.4)	18/29 (62.1)	2/29 (6.9)	6/8 (75)	12/21 (57.1)	27/29 (93.1)

**German-Mongolian Symposium on Hospital Hygiene, Infection Prevention and Control**

14-15 September, 2016



## Visitors of Dental Clinic

Hepatitis Viruses Markers	Numbers investigated	From them				Positive		From them	
		Men		Women		num bers	%	Men	Woman
		num bers	%	num bers	%				
HBsAg	449	159	35.4	290	64.6	33	7.3	159/12 7.5%	290/21 7.2%
Anti-HCV	442	156	35.3	286	64.7	78	17.6	156/23 14.7%	286/55 19.2%

**German-Mongolian Symposium on Hospital Hygiene, Infection Prevention and Control**

14-15 September, 2016



## Hepatitis Markers

	Number	From them HBsAg (+) (%)	Anti HCV (+) (%)	Negative on 2 markers (%)	Anti HCV (+) HBsAg (-)	Anti HCV (-) HBsAg (+)	Positive on 2 markers
Patients with HCC	29	14 (48.3)	18 (62.1)	4 (13.3)	11/15 (73.3)	7/14 (50)	7 (24.1)
Patients with chronic Hepatitis	28	17 (60.7)	13 (46.4)	14(3.6)	10/11 (90.1)	3/17 (17.6)	3 (10.7)
Healthy People	190	13 (6.8)	31 (16.3)	146 (76.8)	29/17 (16.3)	2/17 (15.4)	2 (1.0)

German-Mongolian Symposium on Hospital Hygiene, Infection Prevention and Control

14-15 September, 2016




## Comparison of viroids other infectious RNAs

Characteristic	Viroids	Hepatitis Delta Virus	Satellite RNA	Virusoids	Satellite Viruses
Replication	Autonomous	Helper	Helper	Helper	Helper
Protein encoded	No	Yes	Yes	No	Yes
Capsid source	No capsid	Capsid-self Envelope-helper	Helper	Helper	Self
Circular RNA	Yes	Yes	No	Yes	No
Size (in bases)	250-400 Yes	1700	475-1375	325-390	1240
Rolling circle replication	Yes	Yes	No	Yes	No
Host	Plant	Animal	Plant	Plant	Plant
Complementarity to 7S host RNA	Yes	Yes	-	-	-

German-Mongolian Symposium on Hospital Hygiene, Infection Prevention and Control

14-15 September, 2016



**Rolling circle replication of viroids**

(1) Rolling circle replication: A circular genome (+) is replicated to form a negative-strand concatemer (-).


(2) Synthesis of new genomic concatemer: The negative-strand concatemer serves as a template to synthesize a new positive-strand genomic concatemer (+).

(3) Cleavage of genomic concatemer: The long positive-strand genomic concatemer is cleaved into individual genomic molecules (+).

(4) Circularization: The individual genomic molecules (+) are circularized to form new circular genomes (+).

A model for viroid replication. Rolling circle replication of viroids appears to involve formation of a negative-strand concatemer from the positive-strand viroid molecule (step1). The negative-strand concatemer, a linear molecule, then serves as the template for the synthesis of new genomic molecules (step 2). The mechanism of cleavage of the positive-strand concatemer (step 3) and ligation to form circular genomic molecules (step 4) is unclear.

**German-Mongolian Symposium on Hospital Hygiene, Infection Prevention and Control**  
14-15 September, 2016



**Subviral entities, viral evolution, and viral emergence**

Two forms of hepatitis delta antigen are produced by RNA editing. Delta antigen S is translated from an mRNA made directly from the viral genome. Delta antigen L is produced when an antigenomic RNA is edited to convert an adenosine in the stop codon site into an inosine (shown as a larger letter). This change produces a tryptophan codon rather than a stop codon in the resulting mRNA, so the protein translated from it is 19 amino acids longer.


**Genomic RNA**

Pathway 1: Genomic RNA → mRNA (UAG Stop) → Delta antigen S (199 amino acids)

Pathway 2: Genomic RNA → Antigenomic RNA (UAG) → RNA editing (UIG) → "Antigenomic" RNA → "Genomic" RNA (ACc) → "mRNA" (UIGG Trp) → Delta antigen L (213 amino acids)

**German-Mongolian Symposium on Hospital Hygiene, Infection Prevention and Control**  
14-15 September, 2016






<b>Genotypes of the Hepatitis Viruses in Mongolia</b>			
Hepatitis viruses	Authors	No of investigated samples and method	Results
<u>HBV</u>	J.Oyunbileg, 2001`s	54- Phylogenetic analysis	D genotype-100%
	Ts.Oyunsuren, 2005`s	248- RFLP	D genotype-99.6%
	M.Takahashi, 2005`s	22- Phylogenetic analysis	21-D genotype 1-F genotype
<u>HCV</u>	Ts.Oyunsuren, 2005`s	634- Genotype specific PCR	99.7%-1.6 genotype
	M.Takahashi, 2005`s	36-Genotype specific PCR	97%-1 b genotype
	D.Baatarkhuu, 2006`s	54-Genotype specific PCR	98.2%-1b genotype
<u>HDV</u>	M.Takahashi, 2005`s	20	I genotype 100%

**German-Mongolian Symposium on Hospital Hygiene, Infection Prevention and Control**

**14-15 September, 2016**




## Conclusion

1. Hepatitis B prevalence is dropping since universal vaccination (1991 years), Hepatitis C prevalence is still higher
2. The genotype of dominating Strain of HBV is D, (ayw2 subtype) of HCV is 1b both are extremely infectious and difficult to treat
3. Mongolian marmots and MMHV can be alternative model for researching on Hepadnavirus immunopathogenesis, satellite delta virus and liver cancer mechanisms.
4. All activities focused on prevention and treatment of Viral Hepatitis should be based on evidence and innovation driven approach.

**German-Mongolian Symposium on Hospital Hygiene, Infection Prevention and Control**

**14-15 September, 2016**



**Thank you**

German-Mongolian Symposium on Hospital Hygiene, Infection Prevention and Control

14-15 September, 2016