

## Prevalence and Molecular Virology of Hepatitis Delta Virus in the Western Pacific Region

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## Introduction

HDV is endemic in Sub-Saharan Africa, the Amazon basin, Eastern and Mediterranean Europe, the Middle East and parts of Asia.

~15 million people infected world-wide

### Co-infection/super-infection with HDV

HDV co-infection is usually associated with more severe liver disease

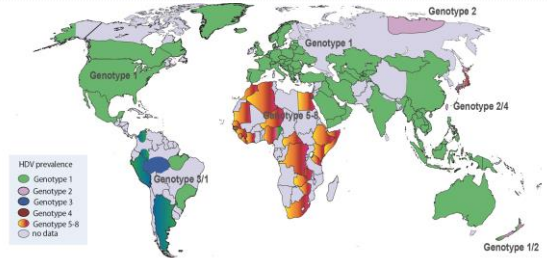
Fulminant hepatitis 10 times more common

Currently, prolonged treatment with PEG-IFN is the only therapy (HDV SVR in 25-30%)

## Hepatitis Delta Virus

- ss RNA virus, ~1700bp circular genome
- Viral RNA forms an unbranched rod-like secondary structure with more than 70% intra-molecular base pairing.
- The RNA encodes one ORF, delta antigen (HDAg)
- Replicates via a rolling circle mechanism, with subsequent self-cleavage by the HDV ribozyme.
- Requires HBsAg for viral envelope
- 8 genotypes have been described, with divergence of up to 16% within genotypes, and 20-40% between genotypes.

## Geographic Distribution of Hepatitis Delta Genotypes



Vaccine 18 (2000) 3059-3066



## The effectiveness of the infant hepatitis B immunisation program in Fiji, Kiribati, Tonga and Vanuatu

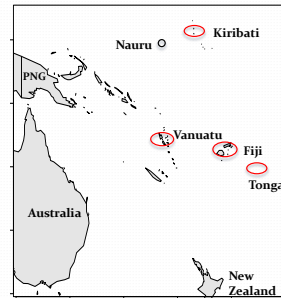
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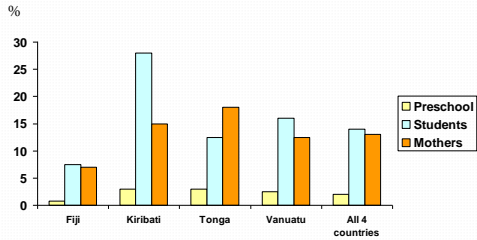
Received 3 September 1999; received in revised form 3 January 2000; accepted 14 February 2000



## Map of the Western Pacific Region



## Prevalence of HBsAg Positivity



Wilson, N et al 2000. Vaccine;8:3056-3066

## Aim

- ◆ To investigate the prevalence of HDV in the Western Pacific region.
- ◆ To determine the molecular epidemiology of HDV identified from the Western Pacific region.

## Methods

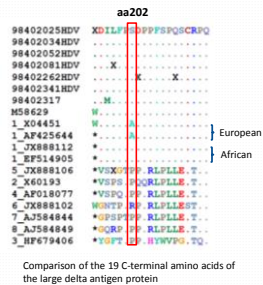
- Routine screening HDV PCR
- Quantitative HDV PCR
- Sequencing
- Phylogenetic Analysis

## Summary of HDV PCR positive sera

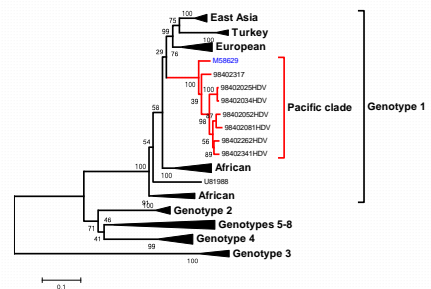
Pacific Island	Sample number	HDV RNA detected
Kiribati (Micronesia)	54	20(37%)
Tonga (Polynesia)	59	0
Fiji (Polynesia)	42	0
Vanuatu (Melanesia)	29	0
<b>Total</b>	<b>184</b>	<b>20</b>

## Origin of Kiribati HDV

- It has been suggested that a specific residue in the delta antigen may act as an "African motif" in HDV genotype 1 sequences (Le Gal et al. Arch Virol 2012).
- In Eurasian sequences, at residue 202 in the L-HDAg most samples have an alanine.
- In African sequences, at residue 202 all samples have a serine.
- Examination of initial sequence analysis of 12 samples from the Pacific clade of genotype 1 reveal a serine at position 202.



## HDV Phylogeny



### HDV full genome nucleotide divergence within genotype groups

HDV Groups (n)		Distance (%)		SE (%)	
Pacific clade (8)		4.5		0.33	
Genotype 1 (34)	African(14)	16.4	16.1	0.64	0.68
	Non-African(20)		13.3		0.60
Genotype 2 (7)		4.1		0.35	
Genotype 3 (6)		8.5		0.58	
Genotype 4 (9)		8.1		0.49	
Genotype 5 (4)		10.1		0.63	
Genotype 6 (2)		11.7		0.87	

### Full genome average nucleotide divergence between HDV from the Pacific clade vs other genotypes (%)

	Genotype 1 African	Genotype 1 European/Asian	Genotype 2	Genotype 4	Genotype 5	Genotype 6	Genotype 7	Genotype 8	Genotype 3
Pacific clade	17.1	17.3	33.0	33.0	39.4	35.3	37.5	35.7	52.1
Genotype 1 African		18.6	33.5	35.9	40.2	36.6	39.2	37.7	53.9
Genotype 1 European/Asian			33.6	36.1	42.0	37.3	39.7	38.9	55.4
Genotype 2				28.1	31.2	31.2	35.8	31.5	52.1
Genotype 4					33.4	31.8	32.5	31.5	50.4
Genotype 5						32.5	33.3	32.8	54.2
Genotype 6							36.0	32.2	50.0
Genotype 7								28.1	53.3
Genotype 8									56.4

## HDV Viral Load

- HDV viral load was obtained from 17 samples.
- Range: 4.33 to 9.45 log<sub>10</sub> copies/mL
- Median: 7.25 log<sub>10</sub> copies/mL
- Similar in students and mothers

## HBV viral load (log<sub>10</sub> IU/ml)

	Total (n)	Mothers (n)	Students (n)
Total	8.78 (27)	5.15 (8)	8.93 (19)
HDV negative	8.74 (13)	3.93 (3)	8.85 (10)
HDV positive	8.82 (14)	5.35 (5)	9.01 (9)

## Quantitative HBs (log<sub>10</sub> IU/ml)

	Total (n)	Mothers (n)	Students (n)
Total	4.89 (34)	4.16 (12)	5.03 (22)
HDV negative	4.83 (18)	4.32 (5)	4.86 (13)
HDV positive	4.96 (16)	3.99 (7)	5.19 (9)

(All samples tested were HBV Genotype D4, serotype ayw2)

## Conclusions

- HDV is endemic in Kiribati (Micronesia), however was not detected in the other islands (Fiji, Tonga, Vanuatu).
- The prevalence of HDV viraemia in Kiribati was 37%.
- HDV RNA viraemia was very high (7.25 log<sub>10</sub> copies/ml).
- Full genome sequence analysis identified a Pacific clade of Genotype 1.

## Future Work

- Full genome sequencing HBV
- Relationship between HDV and HBV
- Re-visit Kiribati



## Acknowledgements

Disclosure statement: The authors declare no conflicts of interest.

- Funding for the initial epidemiological study was provided by UNICEF.
- The mothers and their children and students from the 4 countries who consented to participate.
- Jennie Leydon (VIDRL) – for long term sera storage and identification.
- Dr. Meifang Han (Wuhan, China).
- Staff at VIDRL in the Molecular R&D and Molecular Microbiology laboratories.

