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National Institute
for Public Health
and the Environment

Non-travel related Hepatitis E virus infections in the Netherlands

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HEV in The Netherlands

1993: Anti-HEV Seroprevalence in blood donors: 1.1%

(Zaaijer et al. 1993)

1999: HEV prevalence in NL pigfarms: 22%

(Van der Poel et al. 2001)

2003: First report of non-travel related HEV in 3 patients

(Widdowson et al. 2003)

2004: Fatal hepatitis E infection in a Dutch patient with a presumed hepatocellular carcinoma (Kraan et al., 2004 (Dutch)).

2004: new project: Endemic HEV in acute hepatitis patients

Aims

- Description of HEV gt3 patients.
- Generate hypothesis on endemic risk factors and transmission routes.

Specific

- Common factors?
- Direct molecular-epidemiological connection between patient and source?

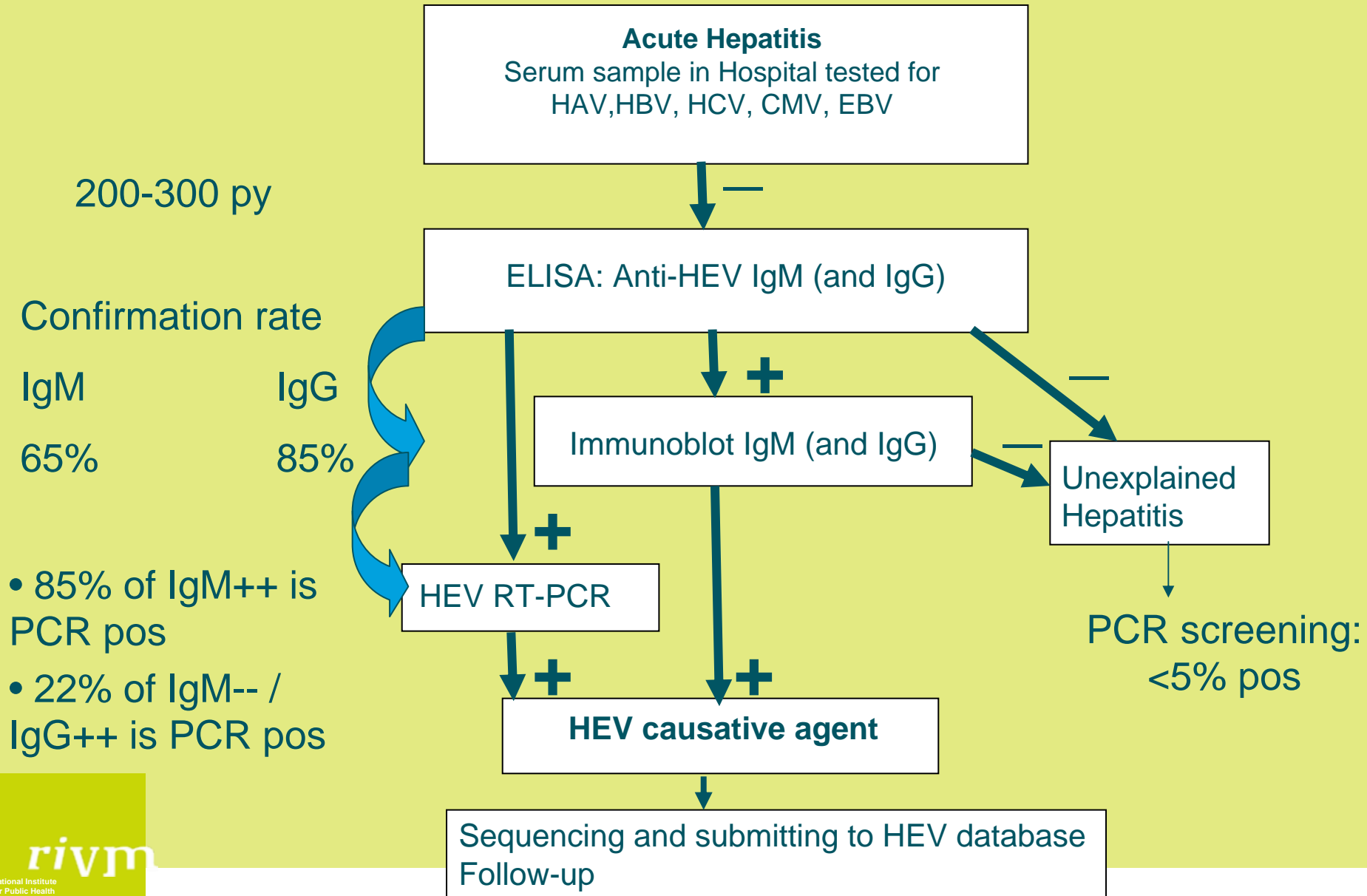
Approach

Case definition: Acute hepatitis in NL
IgM and/or PCR positive for HEV infection
no travel in 3 months prior to infection

Standardized questionnaire: Symptoms and medical history
Travel and contacts
Consumption of foods and water
Contact with surface water
Contact with animals

Sequencing and phylogeny: 148 nt in ORF2

Testing algorithm HEV: low endemic countries



Results

		Cases	
		n	%
Total		19	100
Male		17	90
Age*	20-39	5	26
	40-59	9	47
	> 60	5	26
Preexisting disease	Any	11	58
	Cancer	3	16
	Cardiovascular	4	21
	Respiratory	2	11
Blood transfusions		2	11
Jaundice		16	84
Hospitalization**		11	58
HEV PCR positive		17	90

*Median 50 years (range 25-84)

**Median 8 days (range 2-23)

Direct contact with animals

	number	%	
Rats	0	0	
Other rodents	7	37	
pigs	1	5	
deer	2	11	
Wild boar	0	0	
Scheep	3	16	
goats	4	21	
cows	6	32	
Horses	7	37	
Poultry	2	11	
dogs	14	74	~20%
cats	6	32	~26%

Food consumption of endemic HEV infections: n=19

	≥ 1/week	<1/week	never
Food product	%	%	%
Pork	84	16	0
Beef	47	47	5
Chicken	68	32	0
Fish	47	47	5
Mutton	5	11	84
Turkey	5	47	47
Shellfish	5	32	63
Raw milk	5	11	84
Game/wild	0	26	74
Organs	0	37	63

Blood transfusion and liver transplants

- 2 patients in risk factor study had blood transfusion
- In NL <0.5% of blood donors HEV IgM positive

Chronic HEV infection in transplant patients (Haagsma et al., 2008)(immunosuppressed)

- Patient A:
 - PCR positive for years (serum and feces)
 - IgM and IgG negative (retrospectively)
- Patient B:
 - PCR positive for years (serum and feces)
 - IgM and IgG positive (retrospectively)
 - full recovery after retransplant

Anti-HEV-IgG

in general population ~2%

in liver transplant recip.~4%

Person to person spread: contacts

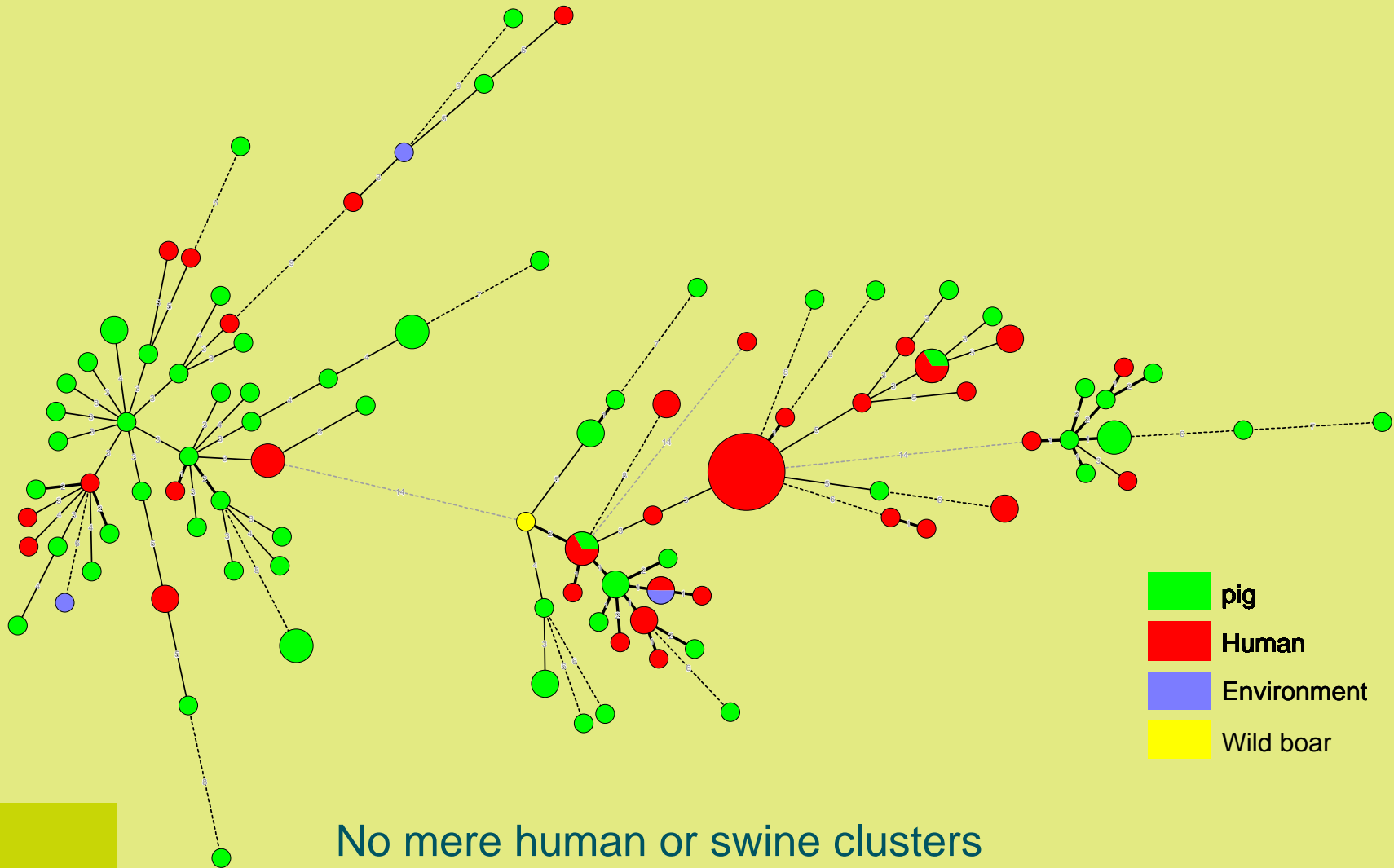
- IgM and IgG of 18 contacts of 13 patients: NEGATIVE
- IgM and IgG of husband and child of patient A: NEGATIVE

Fatal case in NL: female, farmer

Husband	IgM negative, IgG positive
Sister of husband	IgM and IgG negative
Son	IgM and IgG negative
Daughter in law	IgM and IgG positive

Risk factors?: Farm with horses and cows, consumption of pork organs

Minimum spanning, 148 nt ORF2, Netherlands



No mere human or swine clusters

Some strains of swine and human 100% identical

HEV in The Netherlands: part 2

2005: HEV seroprevalence of 6% in non-A, B, C hepatitis patients (Waar et al. 2005)

2007: Optimisation and validation of HEV diagnostics for low-endemic regions. (Herremans et al., 2007, 3x)

2007: HEV prevalence in NL pigfarms: 55% (Rutjes et al., 2007)

2007: Chronic HEV infections detected (Haagsma et al., 2008)

2007: Hepatitis E virus RNA in 4/62 (6.5%) commercial porcine livers in The Netherlands. (Bouwknegt et al., 2007)

2008: Reproduction ratio (R_0) in pigs by contact exposure: 8.8 !
(Bouwknegt et al., 2008)

2008: HEV in 4% of wild boar feces, and 17% of surface water
(Rutjes et al., 2009)

Conclusions

- Sporadic endemic HEV gt3 infections do occur
- Contact with pigs does NOT seem to be a risk factor for Hepatitis E.
- Person-to-person spreading does NOT seem to be an efficient transmission route for HEV.

- Risk factors: Male, >50 yrs, underlying disease
- For further study:
 - blood transfusion
 - pork, organs
 - horses, cows, dogs?

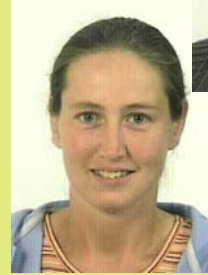
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