L'EU per la prevenzione e il controllo delle zoonosi

- **Normative per rafforzare le attività di monitoraggio, sorveglianza e controllo**

- **Supporto finanziario alla ricerca**
  (EU 6th & 7th Framework Programs)

Strategie di controllo delle zoonosi nell'UE

Libro bianco sulla sicurezza alimentare

- **La sicurezza alimentare è una priorità strategica fondamentale**

- **Responsabilità definite per:**
  - Produttori (responsabilità primaria)
  - Autorità (controllo e sorveglianza)
  - Consumatori (conservazione e manipolazione)

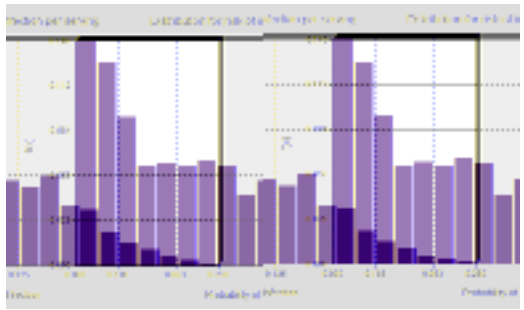
- **Istituzione dell'EFSA**

Strategie di controllo delle zoonosi nella UE

Raccolta di informazioni e loro analisi

- **Sistemi di monitoraggio e sorveglianza per l'identificazione precoce dei rischi potenziali (prevenzione delle emergenze)**

- **Sistemi di allarme per ritirare dal mercato prodotti pericolosi per il consumatore (gestione delle emergenze)**

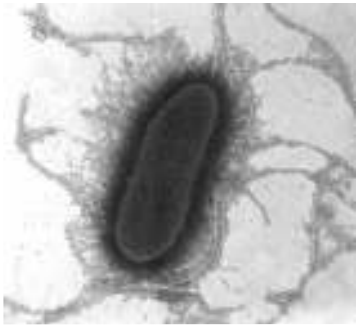


Controllo delle zoonosi: le nuove normative UE

La nuova "Direttiva Zoonosi"

- **Direttiva 2003/99/CE del 17 novembre 2003 sulle misure di sorveglianza delle zoonosi e degli agenti zoonotici (abroga la direttiva 92/117/CE)**

- **Regolamento CE n.2160/2003 del 17 novembre 2003 sul controllo della salmonella e di altri agenti zoonotici specifici presenti negli alimenti**



Direttiva zoonosi: obiettivi

Sorveglianza

- **Sorveglianza delle zoonosi e degli agenti zoonotici al livello primario**
- **Sorveglianza della resistenza agli antimicrobici ad essi correlata**
- **Indagine epidemiologica dei focolai di tossinfezione alimentare**

- **Scambio di informazioni (stati membri, EFSA, ECDC)**

Monitoraggio e sorveglianza delle zoonosi

- **Anagrafica e geo-referenziazione delle strutture produttive**
- **Monitoraggio degli agenti nelle popolazioni animali**
- **Sorveglianza di laboratorio delle infezioni nell'uomo**
- **Piani di campionamento alimenti**

Analisi del rischio

Direttiva zoonosi: priorità

Allegato I A - Prima fascia di priorità

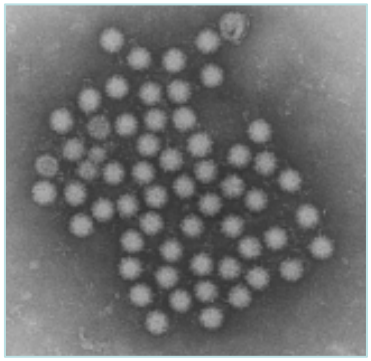
- **Salmonella**
- ***Escherichia coli* VTEC**
- **Campylobacter**
- **Brucella**
- ***Listeria monocytogenes***
- ***Mycobacterium bovis***
- **Echinococco**
- **Trichinella**

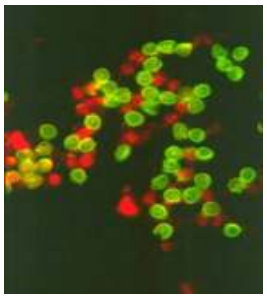
Direttiva Zoonosi 2003/99/EC

(Allegato I A Seconda fascia di priorità)

Agenti virali

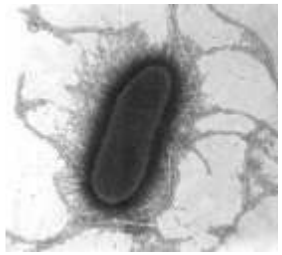
- **Calicivirus**
- Epatite A
- Influenza
- Rabbia
- Virus trasmessi da artropodi





Agenti parassitari

- Anisakiasi
- Criptosporidiosi
- Cisticercosi
- Toxoplasmosi



Agenti batterici

- Borreliosi
- Botulismo
- Leptospirosi
- Psittacosi
- Tubercolosi
- Vibriosi
- Yersiniosi

Gastroenterite acuta virale

	GE infantile endemica	GE epidemica
VIRUS	Rotavirus (gruppo A) Astrovirus Adenovirus enterici Rotavirus (gruppo C) Calicivirus (NLV & SLV) Coronavirus/torovirus Picobirnavirus Aichiivirus	Calicivirus (NLV & SLV) Rotavirus (gruppo B) Astrovirus
TRASMISSIONE	Contatto; fomites, droplets, aerosol; persona-persona	Contatto; alimenti, acque, droplets, aerosol
RESERVOIR	Uomo, animali?	Uomo, animali?
ANTICORPI	Alta prevalenza > 5 anni	Sieroconversione nelle epidemie
IMMUNITA'	Buona	A breve termine (calicivirus)
VARIABILITA' VIRALE	Limitato numero di sierotipi (eccetto calicivirus)	Limitato numero di sierotipi (eccetto calicivirus)
MISURE DI SANITA'	Vaccino per RV (gruppo A)	Controllo degli *outbreaks*; miglioramento della salubrità e manipolazione degli alimenti

DIARREE ACUTE IN ITALIA

- Mancanza di un sistema di sorveglianza delle diarree pediatriche a livello nazionale o regionale
- Mancanza di un sistema di sorveglianza degli episodi epidemici di diarrea (“classe IV”)
- Il sistema di allerta delle “tossinfezioni alimentari” è inefficiente
- Enorme sotto-notifica delle diarree

Prevalenza di patogeni enterici in pazienti con diarrea in Italia. Dati cumulati da 53 studi etiologici dal 1980 al 1996.

Pathogen	No. of cases	No. of positives	Percentage
Rotavirus	**10677**	**2838**	**26.6**
Salmonella spp.	8942	1175	13.1
Campylobacter	9475	522	5.5
Adenovirus	**2109**	**105**	**5.0**
ETEC	1629	64	3.9
C. difficile toxin	618	23	3.7
Aeromonas	1179	35	3.0
Cryptosporidium	944	27	2.9
Astrovirus	**1405**	**32**	**2.3**
Giardia	3485	66	1.9
Shigella	5912	91	1.5
Yersinia	6472	97	1.5
EPEC	941	11	1.2
VTEC	618	5	0.8
C. perfringens toxin	618	5	0.8
EIEC	304	-	-

PREVALENZA DELLE GE VIRALI (UK)

- **Infantile viral gastroenteritis: on the way to closing the diagnostic gap.**

  Simpson R et al. *J Med Virol. 2003; 70:258-62.*

A total of 305 faecal specimens collected from children under the age of 5 who presented with symptoms of acute gastroenteritis either as inpatients at Addenbrooke's Hospital (N = 100) or to General Practitioners in East Anglia (N = 205) during 1999-2001 were tested for the presence of rotavirus, norovirus, sapovirus, enteric adenoviruses (Group F, serotypes 40 and 41), and astrovirus.

An aetiologic agent was found in 184 specimens (60.3%). The most commonly found single viral pathogen was **rotavirus (27.9%)**, followed by **norovirus (13.4%), enteric adenoviruses (7.9%), astrovirus (2.3%),** and **sapovirus (1%).** Mixed infections were observed in 27 specimens (8.9%), and no aetiologic agent was found in over a third of the specimens tested.

Journal of Medical Virology 78:1486–1492 (2006)

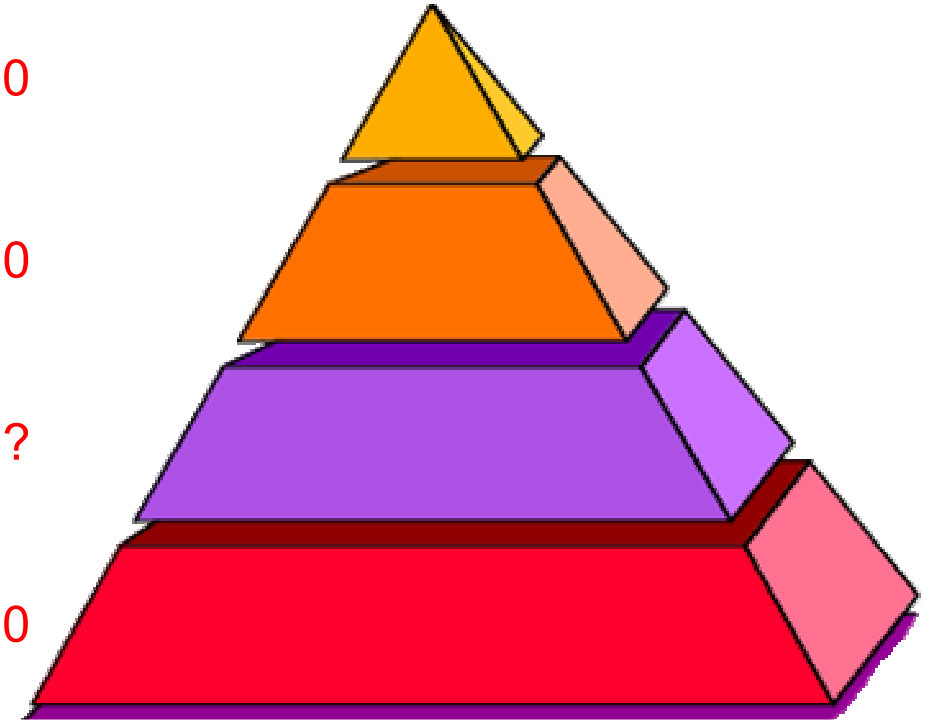
Molecular Epidemiology of Norovirus Infections in Sporadic Cases of Viral Gastroenteritis Among Children in Northern Italy

Maria Cristina Medici,[1]* Monica Martinelli,[1] Laura Anna Abelli,[1] Franco Maria Ruggeri,[2] Ilaria Di Bartolo,[2] Maria Cristina Arcangeletti,[1] Federica Pinardi,[1] Flora De Conto,[1] Giancarlo Izzi,[3] Sergio Bernasconi,[4] Carlo Chezzi,[1] and Giuseppe Dettori[1]

- Children hospitalized with acute diarrhea in 2002.
- Surveillance of norovirus infections in sporadic cases of pediatric gastroenteritis in one-year period in Italy showed that **noroviruses (41 cases, 10.4%)** were the second causative viral agent. The epidemic period of norovirus was September-December, peaking in September and November.
- Other viruses detected alone were rotaviruses (83 cases), enteric adenoviruses (7 cases), non-enteric adenoviruses (11 cases), enteroviruses (8 cases) and reovirus (1 case).

LE GE ACUTE NEGLI USA NEL 3° MILLENNIO

	Totale	Bambini
Morti	3000	300
Ospedalizzazioni	612,000	160,000
Visite medico	?	2,000,000
Episodi	267,000,000	19,400,000



Glass et al, 2001

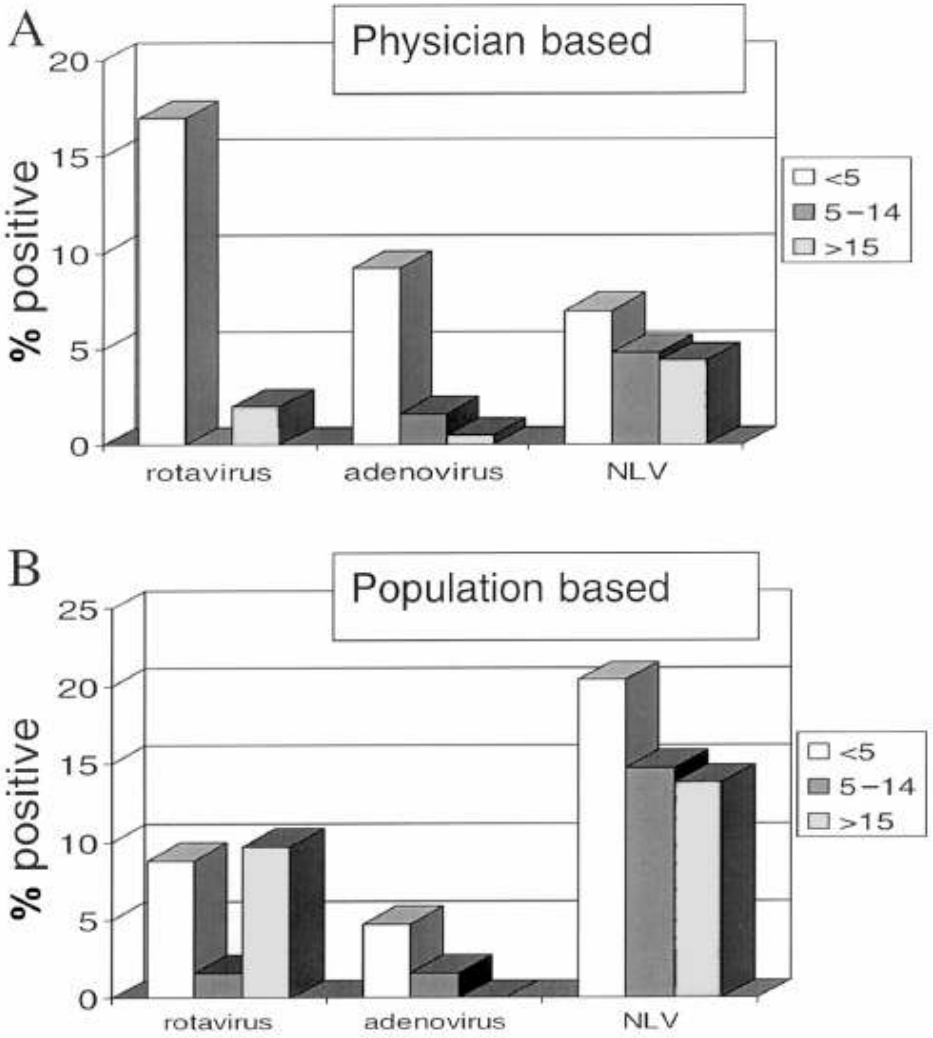
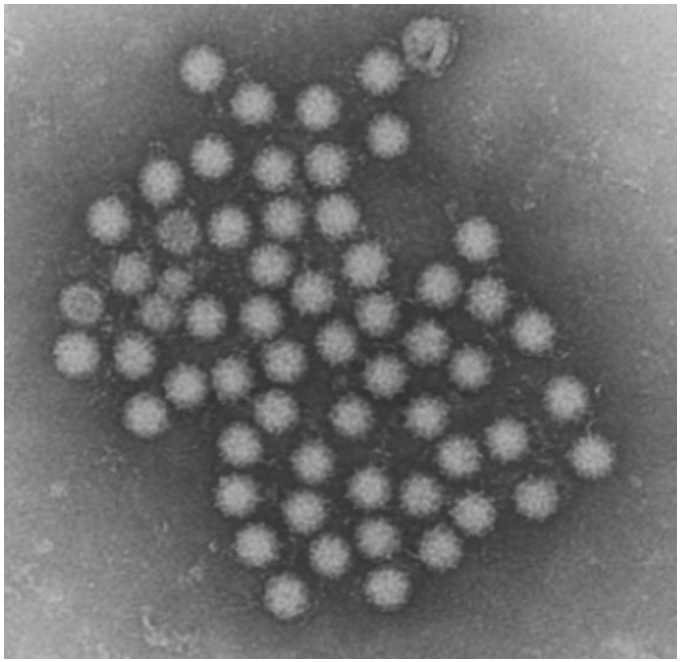


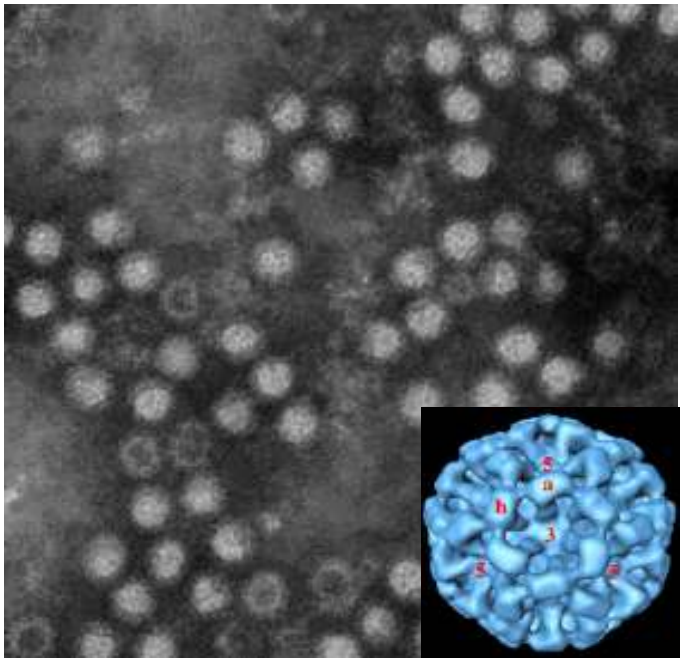
Figure 3. Age-stratified distribution of rotavirus and Norwalk-like virus (NLV) expressed as proportion of positive specimens per age (years) group. Data are from physician-based *(A)* and population-based *(B)* studies of gastroenteritis. (Note difference in scales used for *A* and *B.)*

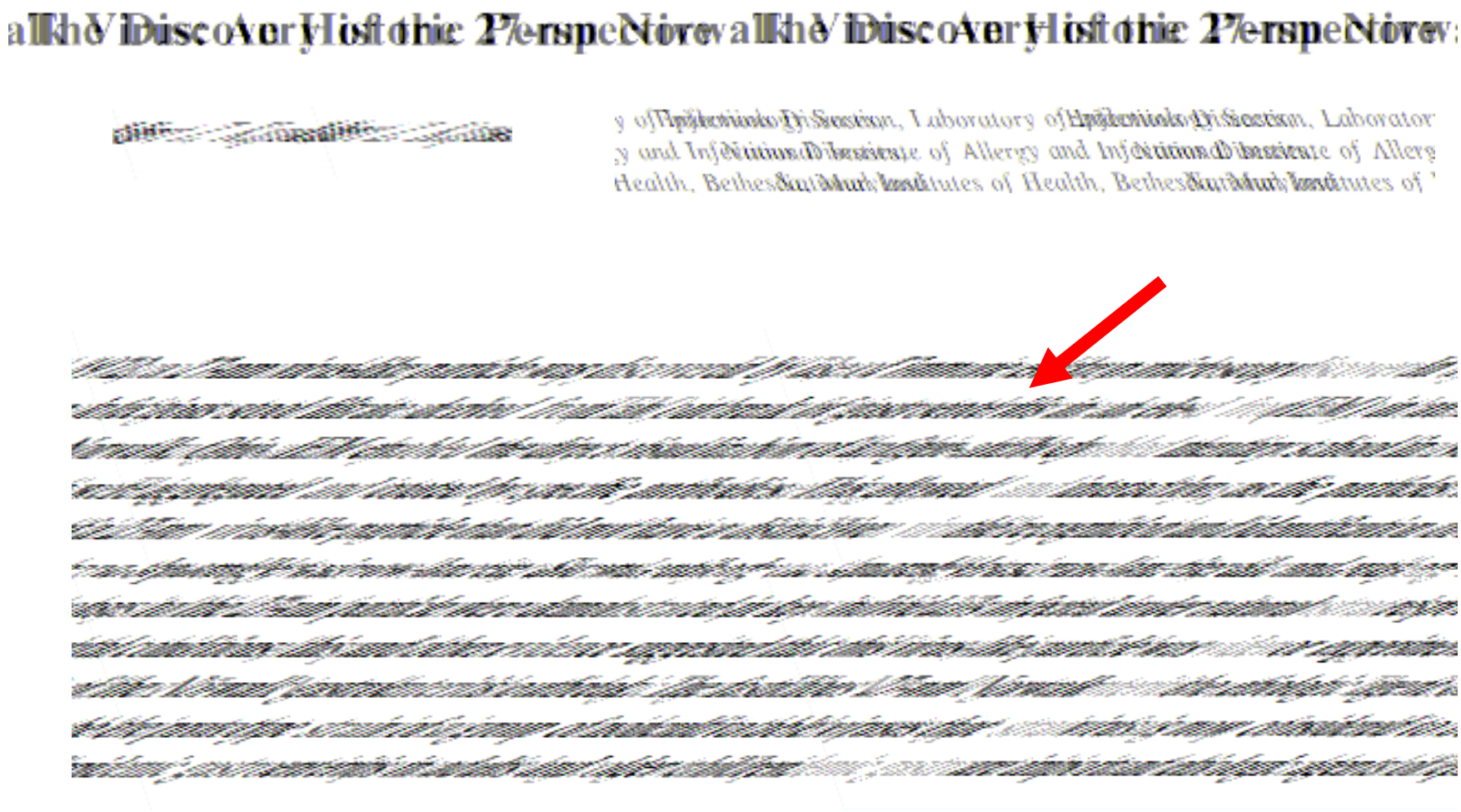
NOROVIRUS

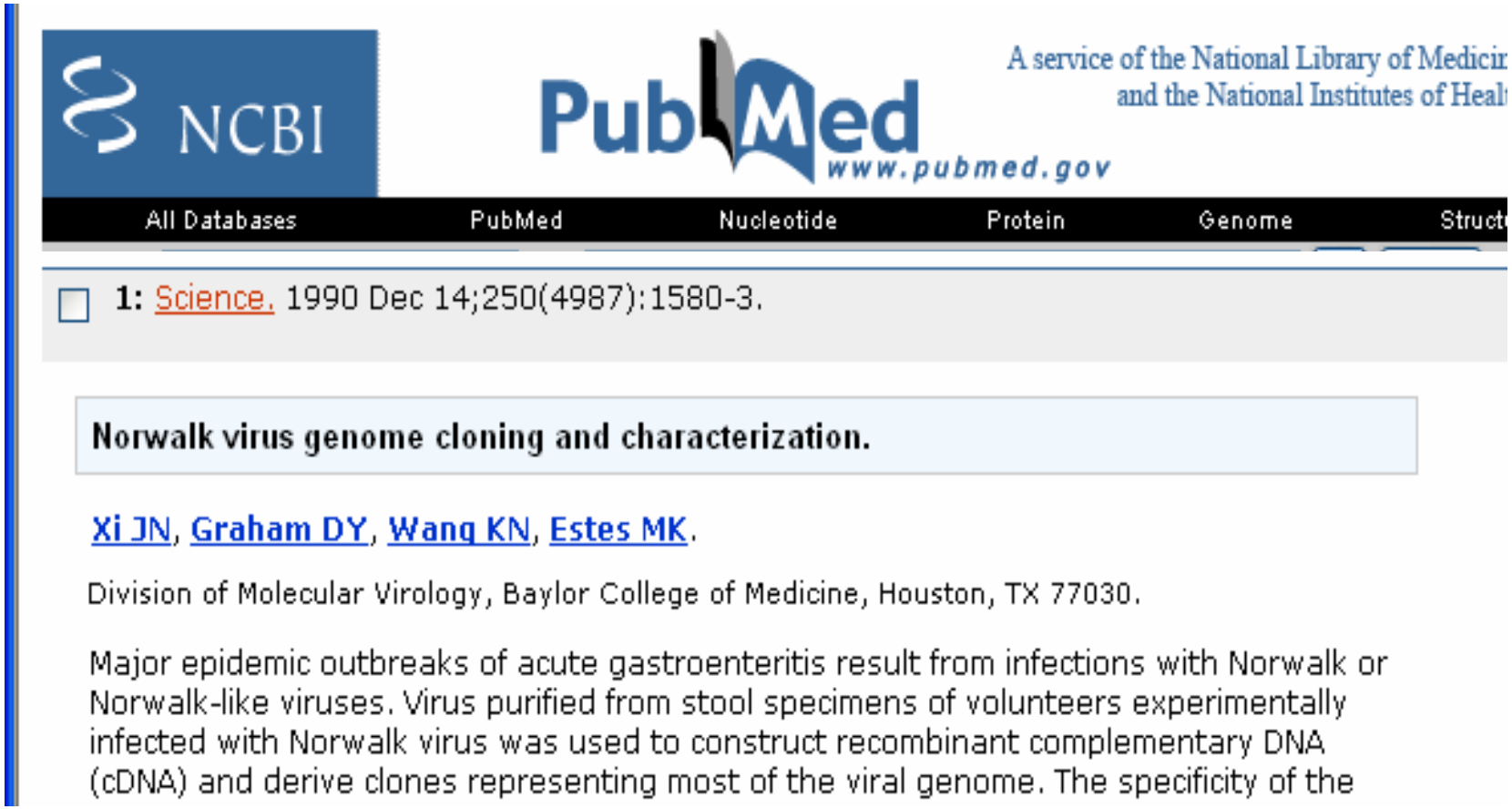
Virions by EM



Virus-Like Particles






NCBI
PubMed
www.pubmed.gov
A service of the National Library of Medicin
and the National Institutes of Healt
All Databases
PubMed
Nucleotide
Protein
Genome
Struct
1: Science. 1990 Dec 14;250(4987):1580-3.
Norwalk virus genome cloning and characterization.
Xi JN, Graham DY, Wang KN, Estes MK.
Division of Molecular Virology, Baylor College of Medicine, Houston, TX 77030.
Major epidemic outbreaks of acute gastroenteritis result from infections with Norwalk or Norwalk-like viruses. Virus purified from stool specimens of volunteers experimentally infected with Norwalk virus was used to construct recombinant complementary DNA (cDNA) and derive clones representing most of the viral genome. The specificity of the

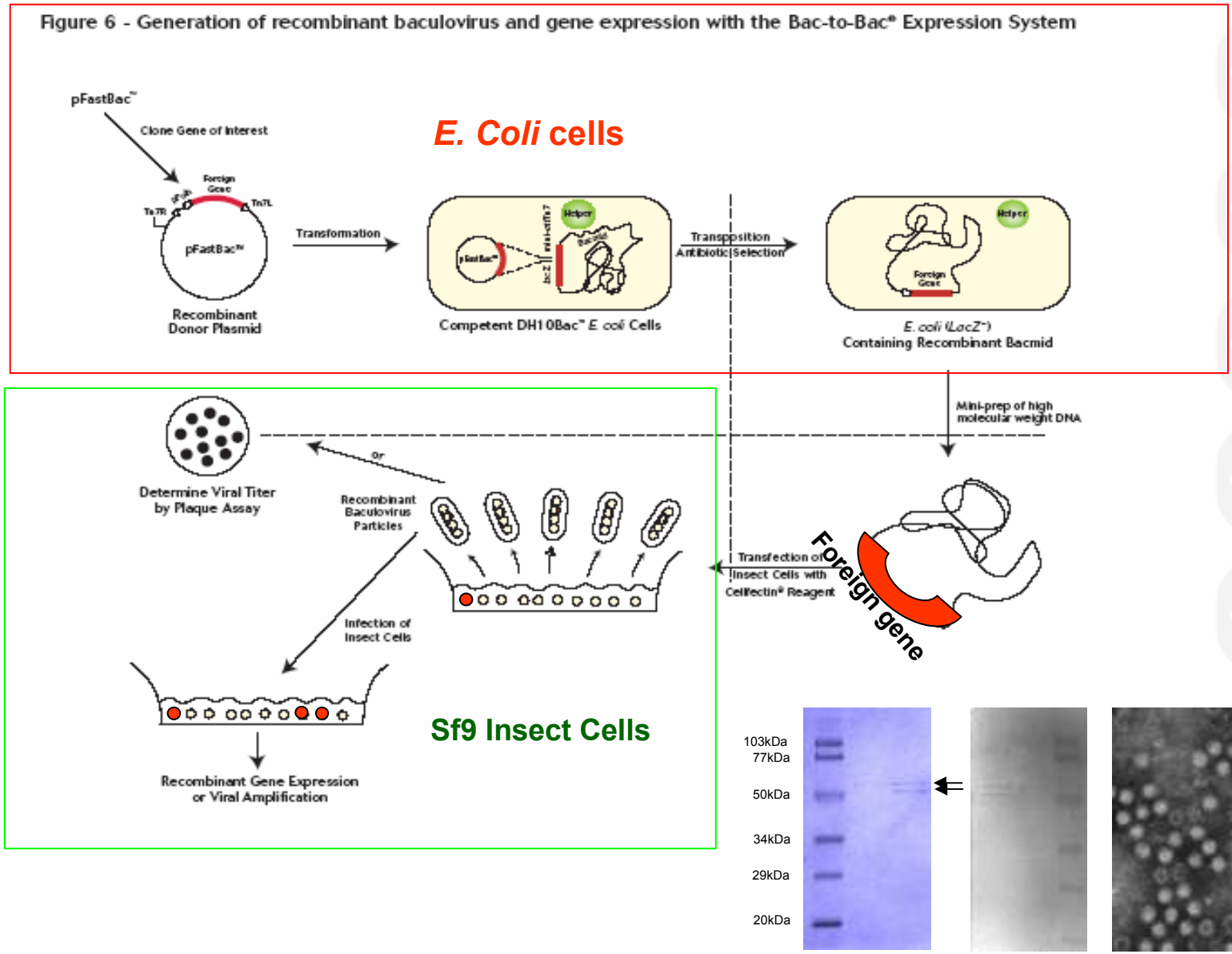
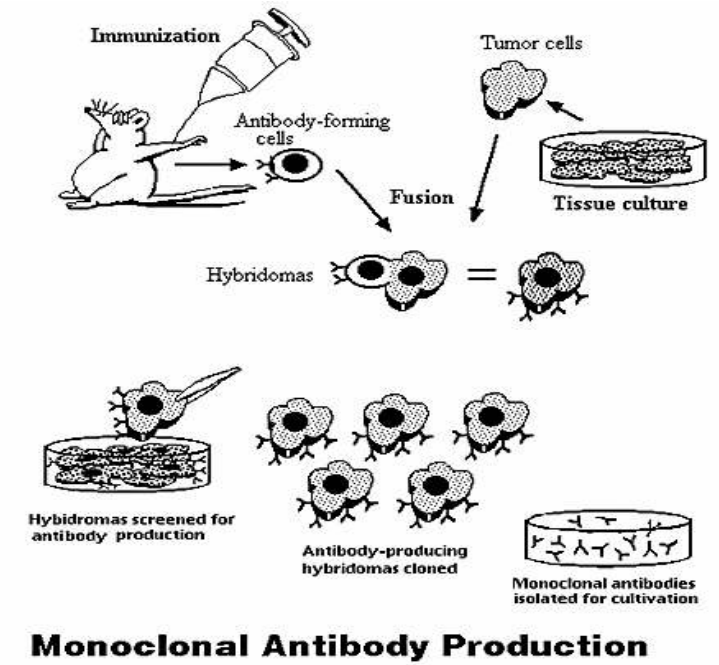
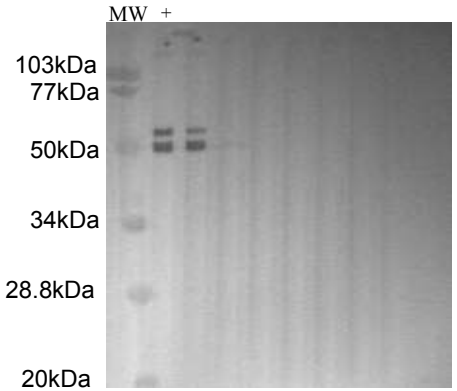


Figure 6 - Generation of recombinant baculovirus and gene expression with the Bac-to-Bac® Expression System
pFastBac™
Clone Gene of Interest
Foreign Gene
Tn7R
Tn7L
pFastBac™
Recombinant Donor Plasmid
Transformation
E. Coli cells
Helper
Competent DH10Bac™ E. coli Cells
Transposition Antibiotic Selection
Helper
Foreign Gene
E. coli (LacZ-) Containing Recombinant Bacmid
Mini-prep of high molecular weight DNA
Transfection of Insect Cells with Cellfectin® Reagent
Foreign gene
Or
Determine Viral Titer by Plaque Assay
Recombinant Baculovirus Particles
Infection of Insect Cells
Sf9 Insect Cells
Recombinant Gene Expression or Viral Amplification
103kDa
77kDa
50kDa
34kDa
29kDa
20kDa

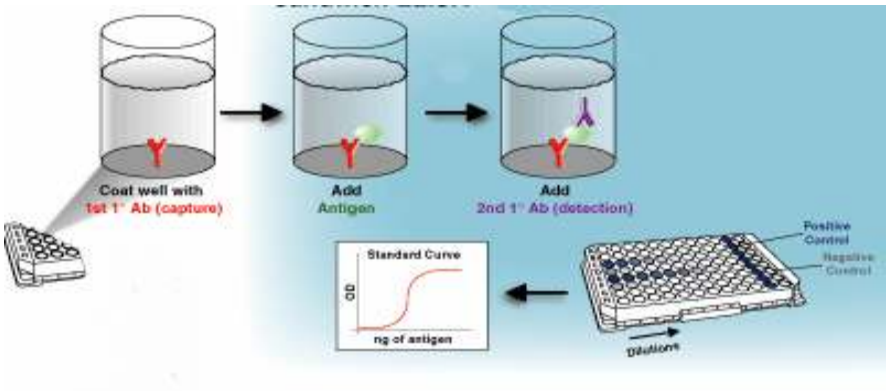


Monoclonal Antibody Production

Western blotting with MabS

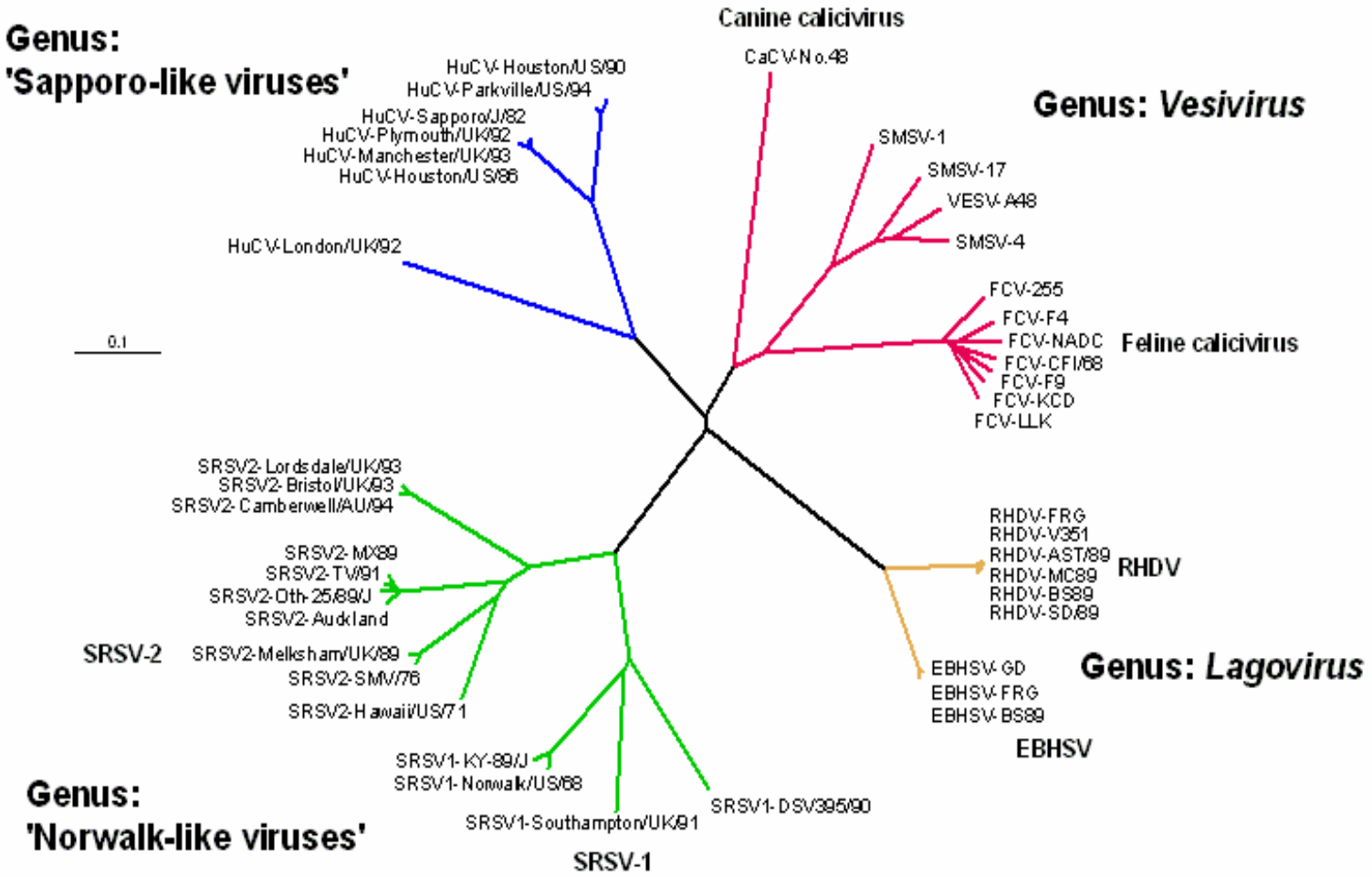


Double antibody sandwich ELISA (DAS-ELISA)

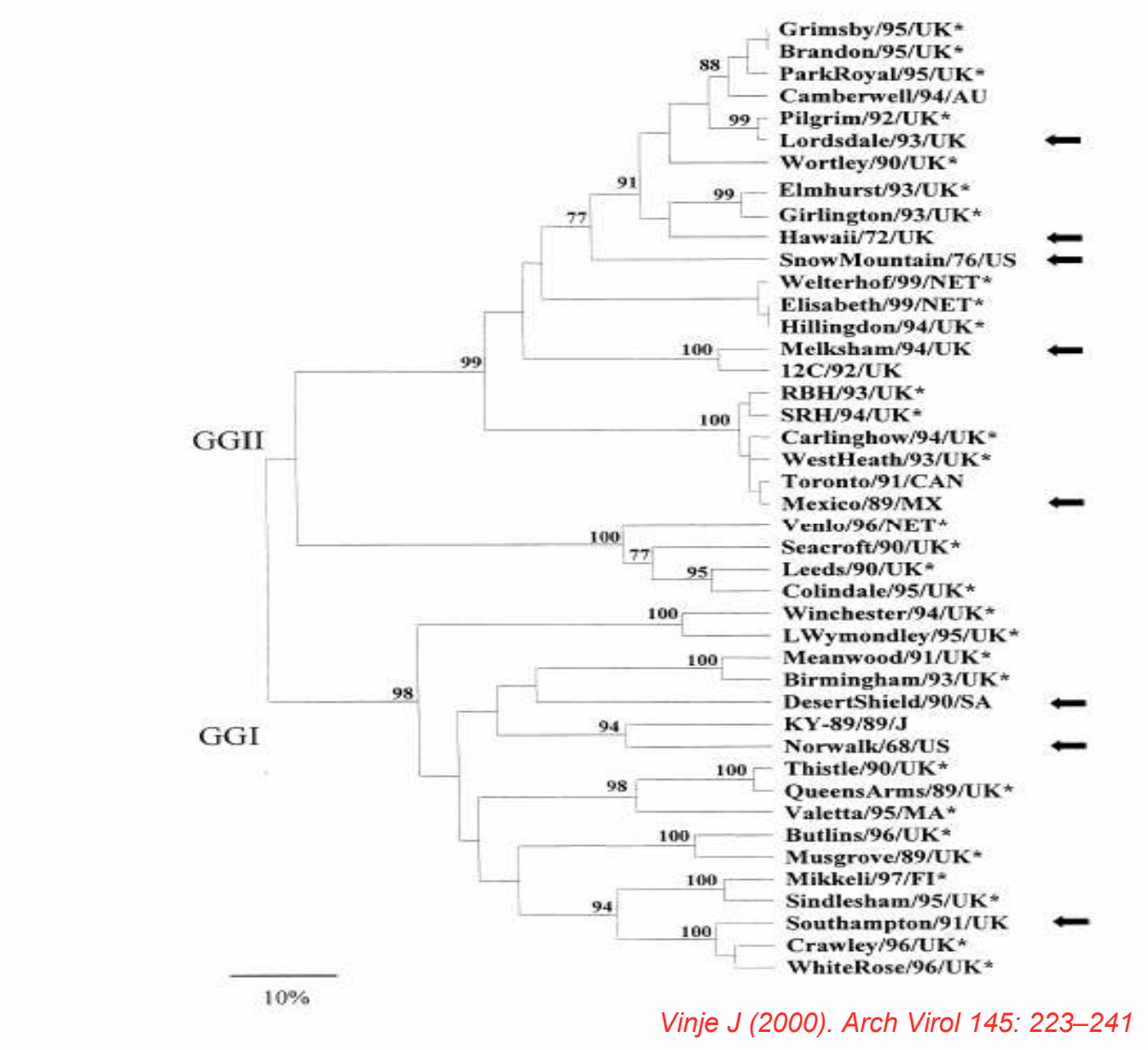


The relationship between caliciviruses capsid proteins

N.J. Knowles, 24 May 1998



Neighbor-joining tree produced using Clustal-X



Vinje J (2000). Arch Virol 145: 223–241

Epidemie di gastroenterite da norovirus

- ✓ Sintomi: diarrea, vomito, crampi addominali, febbricola e nausea
- ✓ Periodo di incubazione: 12-48 ore
- ✓ La patologia ha un decorso acuto e auto-limitante (24-60 ore)
- ✓ I sintomi scompaiono subito dopo la fase acuta, senza ricorso ad ospedalizzazione
- ✓ Alto potenziale epidemico per la ridotta carica infettante ($<10^2$), l'alta resistenza nell'ambiente e l'assenza di immunità persistente

In crociera con il Norovirus

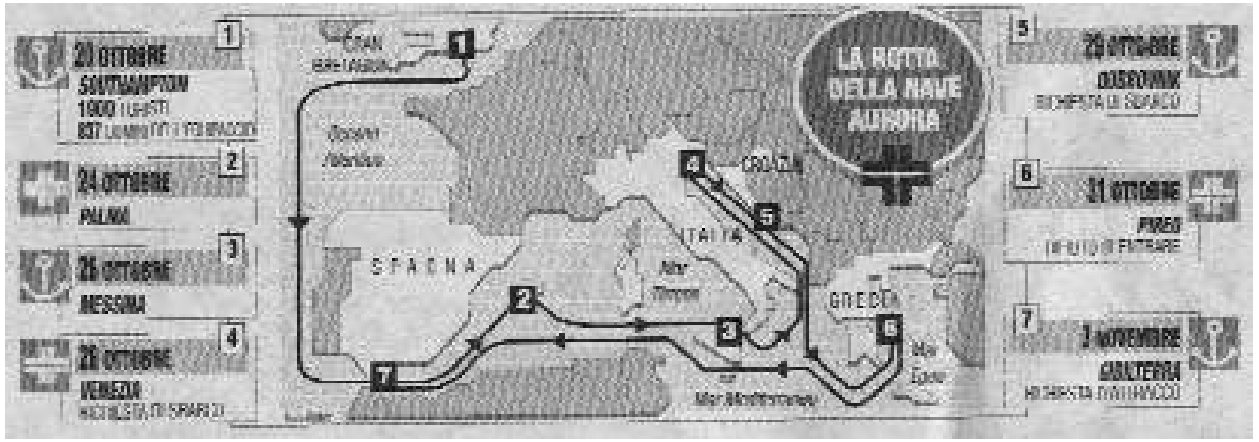
La crociera degli appestati

Una nave con 450 turisti ammalati respinta da tre porti

DAL NOSTRO CORRISPONDENTE
ENRICO FRANCESCHINI

LONDRA — Lo slogan era un classico: «Farete una vacanza indimenticabile». Nessuno potrà dire, tra i passeggeri dell'Aurora, che fosse esagerato: non scorderanno per un pezzo la crociera partita il 20 ottobre da Southampton, nel sud dell'Inghilterra, per due settimane di *grand tour* del Mediterraneo. E non la scorderà neppure la P&O,

mancò il tradizionale battesimo, facendo finire in mare la bottiglia di champagne. Al primo viaggio, la nave ebbe un'avaria e dovette essere rimorchiata in porto. L'anno scorso ha sofferto un altro virus, di minori dimensioni. La crociera "indimenticabile" di questi giorni costava 4mila sterline (quasi 6mila euro) a testa: ora centinaia di sposini in luna di miele, famiglie, coppie di pensionati, annunciano che faranno causa al-



Chicago Tribune

700 ill on cruise ship in suspected virus outbreak

(Published November 17, 2006)

FT. LAUDERDALE -- More than 700 people aboard a trans-Atlantic cruise have fallen ill with flulike symptoms, cruise line officials said.

The outbreak, thought to be a **norovirus**, struck people aboard the Carnival Cruise Lines' Liberty, according to a statement issued by the Miami company.

The ship left Rome on Nov. 3 with about 2,800 paying passengers and more than 1,150 crew members. The boat is due in Ft. Lauderdale on Sunday.

"Within 24 hours of sailing, they had a lot of people sick. It has tapered off considerably over the past couple days," said David Forney of the Centers for Disease Control and Prevention in Atlanta.

cbs4.com – Norovirus Outbreak Hits Queen Elizabeth 2

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Jan 19, 2007 12:07 pm US/Eastern

Norovirus Outbreak Hits Queen Elizabeth 2

(CBS4) FT. LAUDERDALE The Queen Elizabeth 2 has become the first cruise ship in 2007 to suffer a serious outbreak of norovirus illness, with about 16 percent of passengers sickened since the ship left Southampton, England, on Jan. 2.

Members of the U.S. Centers for Disease Control and Prevention will board the ship Friday in Acapulco, Mexico. So far 263 passengers and 27 crewmembers have shown signs of norovirus, a common ailment that causes vomiting and diarrhea for 48 to 72 hours.

The Cunard Line ship is on a 106-night world cruise that included a stop in Fort Lauderdale last week. After a dockside meeting with Queen Mary 2, the two ships left Port Everglades on Jan. 10 on separate itineraries.

Plane quarantined in Britain after passengers taken sick

AFP Photo: An airplane comes in for a landing. A plane from the Dominican Republic to Britain...

Thu Aug 9, 3:12 PM

LONDON (AFP) - A plane from the Dominican Republic to Britain was temporarily quarantined on arrival at Glasgow airport Thursday, after passengers fell sick with a stomach bug, a spokesman said.

Some 27 passengers fell ill on the MyTravel flight, which landed at the Scottish airport Thursday morning.

"The aircraft was quarantined on arrival," said Donald Morrison, a spokesman for the British Airports Authority (BAA) in Scotland, adding that a team of four doctors was organized to check the passengers over.

"They were diagnosed with the novovirus, more commonly known as winter vomiting bug," he added.

The passengers had all stayed at the same hotel in the Dominican Republic, one of the world's poorest countries. All affected passengers received treatment and none required hospital attention before being allowed home.

IN THE NEWS

Failed Tests
Drug use keeps 250 Cdn troops at home

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Bin Laden calls for 'caravan' of martyrs

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Tuesday, 22 January, 2002, 20:38 GMT

Virus leads to second hospital closure

The Victoria Infirmary remains closed

Intestinal germ leaves trail of misery

The Boston Globe

City's ERs see more than 3,700 sufferers

By Stephen Smith, Globe Staff | January 17, 2007

More than 3,700 patients stricken with nausea, vomiting, and diarrhea have visited Boston's emergency rooms during the past six weeks in a wave of gastrointestinal illness that has swept cities across North America.

"If people are coming to the emergency room on Christmas Day," Barry said, "that suggests to me this illness is more severe than your routine gastrointestinal illness."

"….To Eat or not to Eat, this is the question…"

??

Indagini su epidemie di GE da NoV in cui la "epidemiologia molecolare" ha fornito informazioni sul meccanismo di trasmissione, per la prevenzione e il controllo

Anno	Luogo	Veicolo	Situazione	Novità
1993	Multistato – Lousiana	Ostriche	Epidemia multistato collegata ad ostriche della Lousiana	Sito di coltivazione contaminato da 1 pescatore; sequenze comuni tra i focolai; virus tracciato nelle ostriche
1996	US e Canada	Acqua di pozzo	Epidemie multiple tra turisti USA che si fermavano ad una stazione di bus in Canada	Sequenze comuni tra i diversi casi alla base del tracciamento epidemiologico; primo ritrovamento di NoV nelle acque
1998	Globale	Sconosciuto	Ceppo comune identificato in 6 paesi	Primo ritrovamento di un ceppo epidemico "globale"
1998	Europa e Canada	Lamponi	Epidemia internazionale (5 paesi) legata a lamponi prodotti in Slovenia	Epidemia successiva alla distribuzione di un alimento contaminato
1999	US	"Delicatessen"	Consumatori di un "delicatessen meal"; addetto alla preparazione dell'alimento implicato	Prima identificazione di un alimento contaminato alla superficie; stesso virus nei pazienti

FDA U.S. Food and Drug Administration — U.S. Department of Health and Human Services

FDA News

FOR IMMEDIATE RELEASE
P07-37
March 2, 2007

Media Inquiries:
Michael Herndon, 301-827-6242
Consumer Inquiries:
1-888-SAFEFOOD

FDA Investigating Norovirus Outbreak Linked to Oysters

Consumers Advised To Avoid Raw Oysters Harvested from San Antonio Bay

The U.S. Food and Drug Administration (FDA) is investigating an outbreak of norovirus-associated illness linked to eating raw oysters harvested from San Antonio Bay, TX. FDA advises consumers to avoid eating raw oysters harvested from this area after February 1, 2007, as a result of reports of illnesses in people who attended a Maryland event where these oysters were served. Symptoms of illness associated with norovirus include nausea, vomiting, diarrhea and stomach cramping. Affected individuals often experience low-grade fever, chills, headache, muscle aches and a general sense of tiredness. Most people show symptoms within 48 hours of exposure to the virus. The illness typically lasts one to two days.

FDA U.S. Food and Drug Administration

At Restaurants and other Foodservice Establishments:

- Order oysters fully cooked.

In the Shell:

- Purchase oysters with the shells closed. Throw away any oysters with shells already opened.

To prepare oysters for eating, choose one of the following methods:

- Boil oysters until the shells open. Once open, boil for an additional 3-5 minutes.
- Steamer - add oysters to water that is already steaming and cook live oysters until the shells open; once open steam for another 4-9 minutes.
- Use smaller pots to boil or steam oysters. Using larger pots, or cooking too many oysters at one time, may cause uneven heat distribution, which may cause the oysters in the middle to not get fully cooked.
- Discard any oysters that do not open during cooking.

Shucked Oysters:

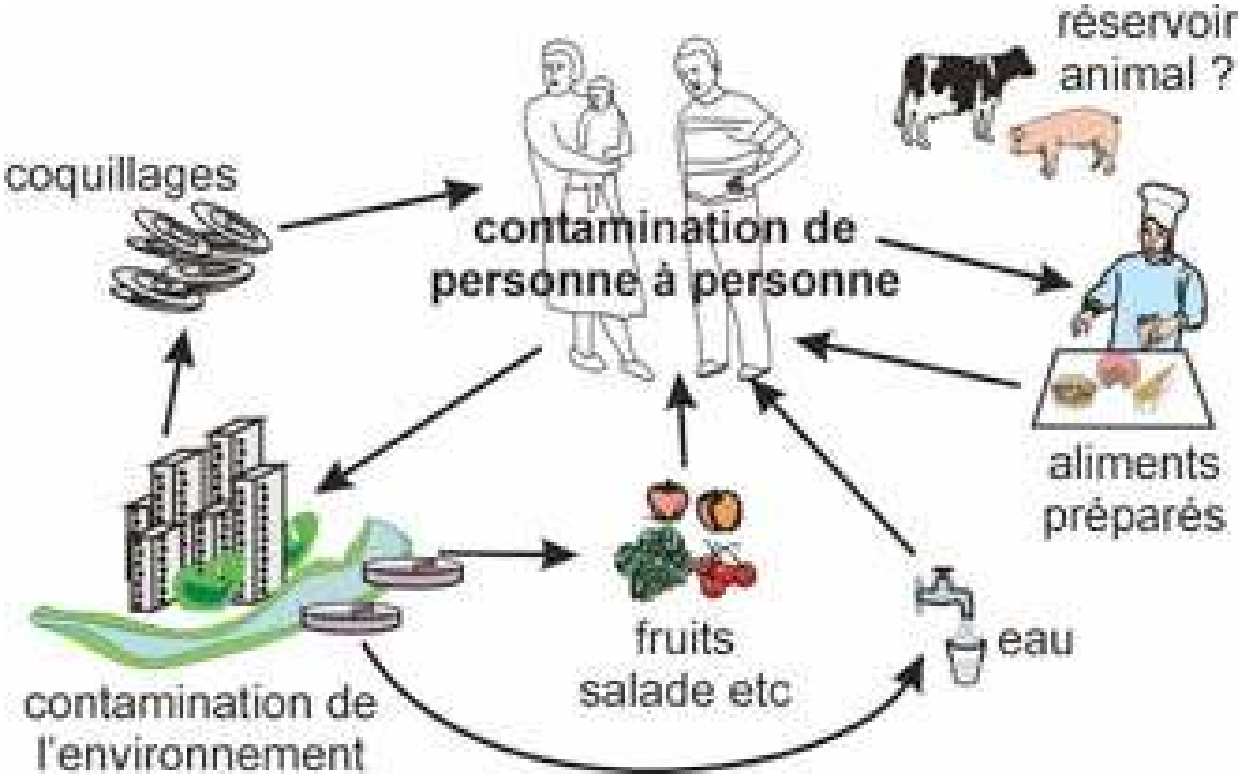
To prepare oysters for eating, choose one of the following methods:

- Boil or simmer shucked oysters for at least 3 minutes or until the edges curl.
- Fry at 375 degrees for at least 3 minutes.
- Broil 3 inches from heat for 3 minutes.
- Bake at 450 degrees for 10 minutes.

For further information contact:

FDA Food Safety Hotline: 1-888-SAFEFOOD
FDA website: www.cfsan.fda.gov

Norovirus cycle



CARATTERISTICHE DEI NOROVIRUS IMPORTANTI AI FINI DELLA PREVENZIONE

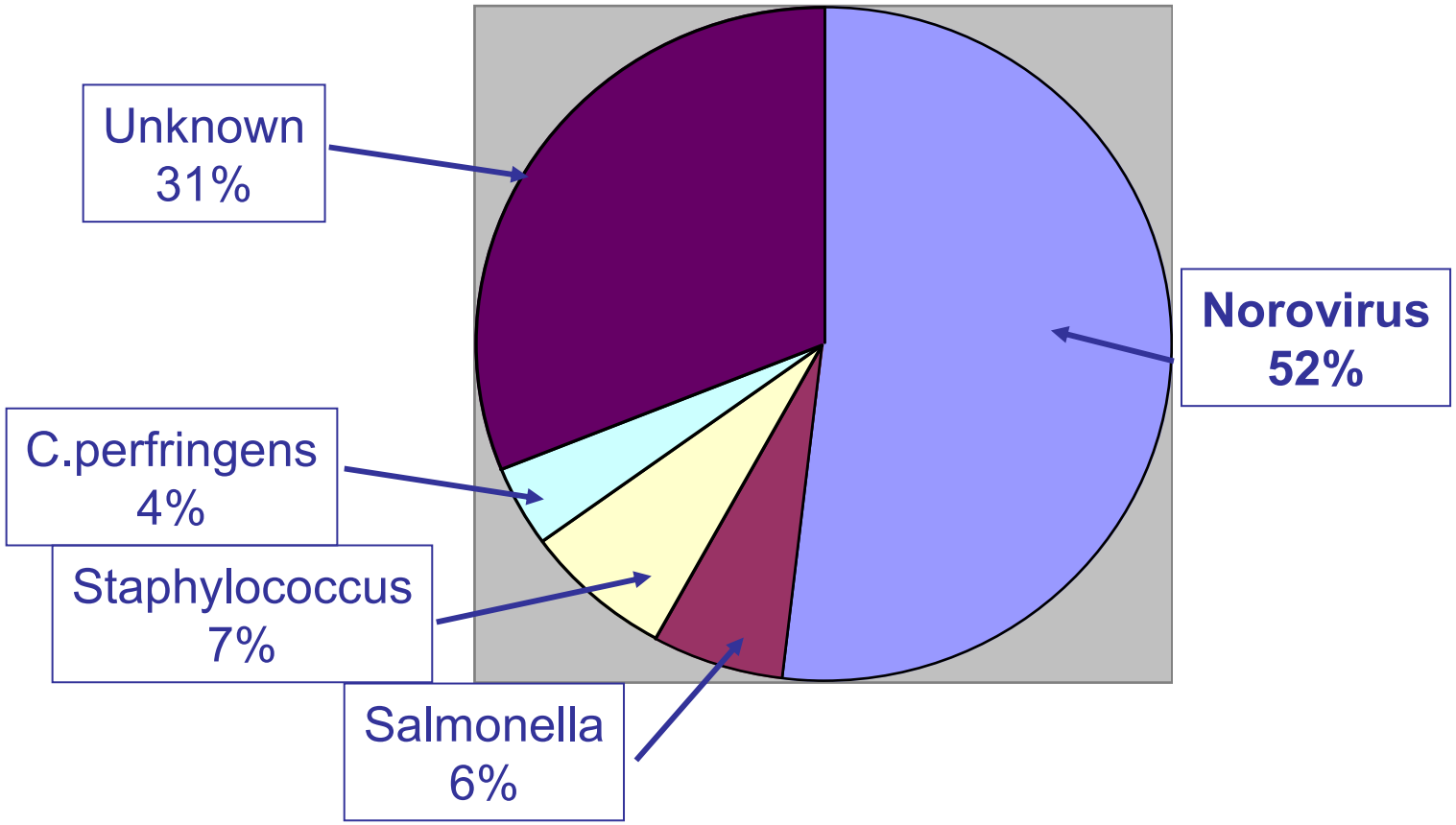
Carattere	Osservazione	Conseguenza
Bassa dose infettante	$<10^2$ particelle virali	Trasmissione per droplets, persona/persona, secondaria
Escrezione asintomatica prolungata	Fino a 2 settimane?	Rischio di infezione secondaria, controllo degli addetti agli alimenti
Stabilità ambientale	10 ppm Cl^*, stabile al congelamento e a 60°C	Difficile da eliminare dall'acqua contaminata; si conserva nel ghiaccio e frutti di mare poco cotti
Grande diversità tra i ceppi	Molti tipi genetici e antigenici (?)	Diagnosi di laboratorio complessa; episodi dovuti a ceppi virali multipli
Mancanza di immunità di lungo periodo	Infezioni sintomatiche ripetute	Esposizione pregressa da bambino non protegge gli adulti
Reservoir	Uomo / animali ?	Recente identificazione di ceppi simili negli animali

Burden of Norwalk-like virus gastroenteritis in US

Agents	Total Illnesses	Foodborne Illnesses	% of all foodborne illness
All Bacteria	5,204,934	4,175,565	30.2
All Parasites	2,541,316	357,190	2.6
Norwalk-like viruses	**23,000,000**	**9,200,000**	**66.6**

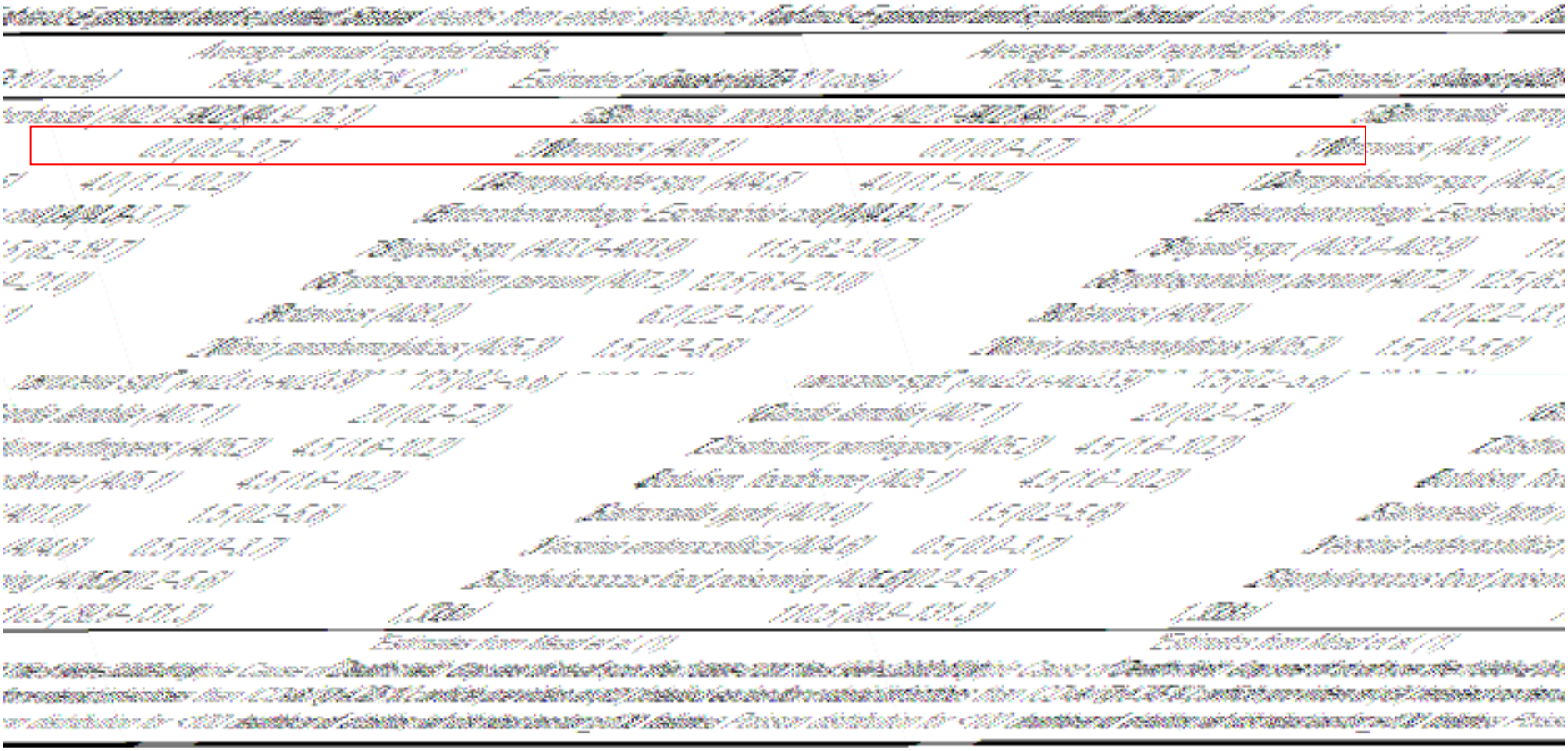
Source: Mead et al, EID, 2000

Conferma di laboratorio in epidemie di GE, US 2001



Jones et al. CID, 2004

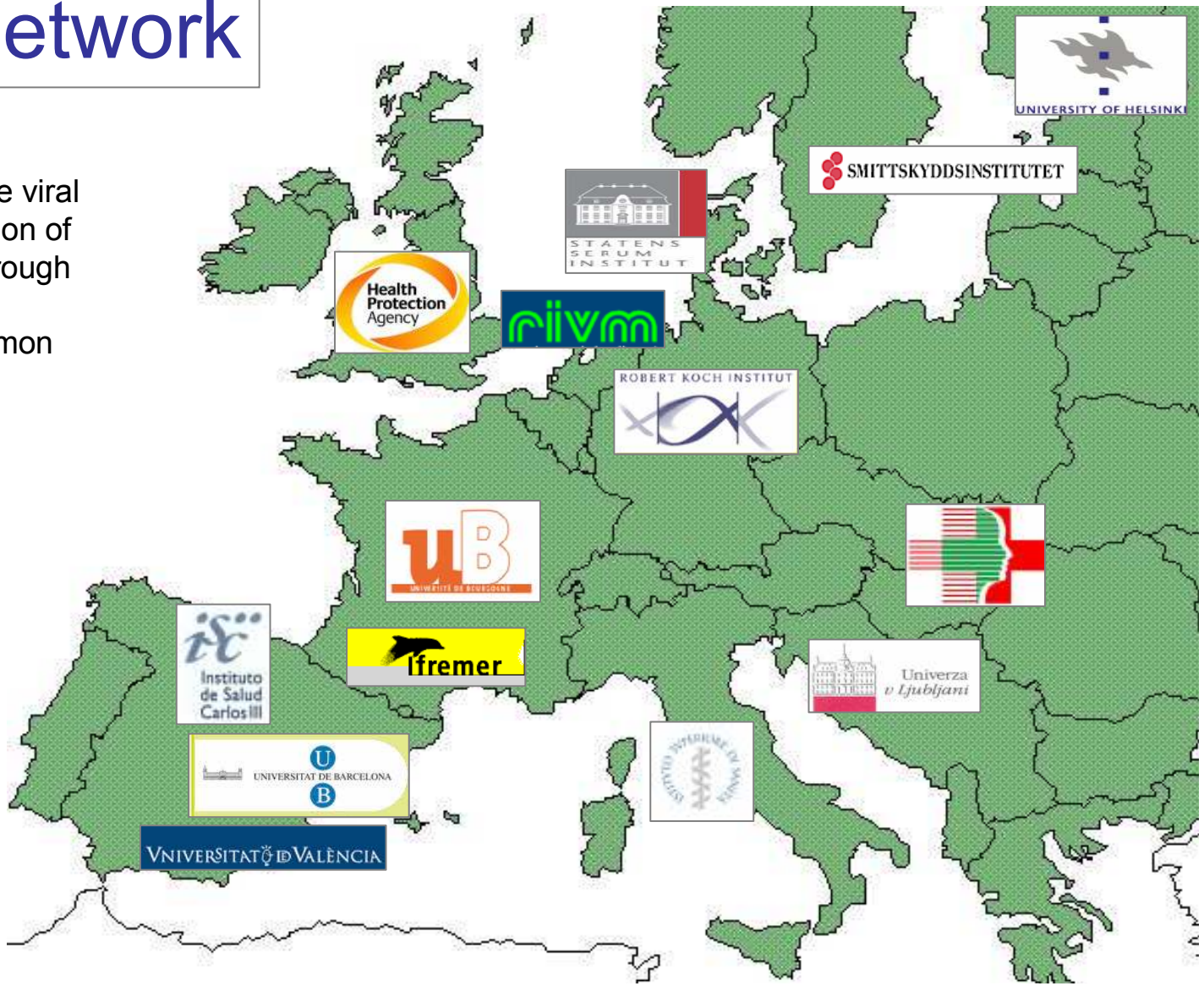
MORTALITÀ DA NOROVIRUS (USA)



P. D. Frenzen. *Emerging Infect Dis.* 10 *2004*

FBVE Network

Rapid detection of transnational foodborne viral infections and elucidation of transmission routes through molecular tracing and development of a common database



A research proposal on “Quality of Life and Management of Living Resources” (1999/C 64/14)

Dipartimento di Sanità alimentare e animale

DIVINE-NET

An EU funded research project under the"Health and Consumer Protection Directorate General"

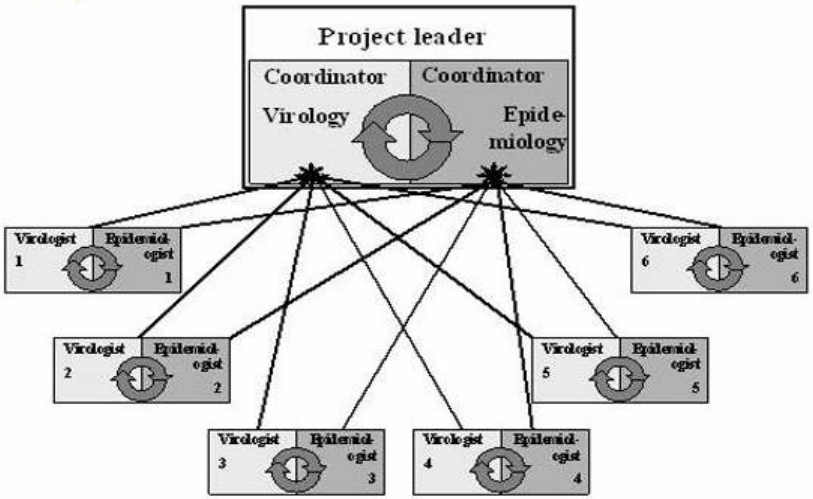
Proposal. no. 790965
Public Health

Organisation charts

An overview of the interactions between DIVINE-NET and other programs is shown in figure 1, with the project organisation structure outlined in figure 2.

Figure 2. Organisational structure of DIVINE-NET:

For all partners direct contact between the virologist and epidemiologist is regulated, as is the reporting to the coordinators virology and epidemiology. (Only 6 of 14 partners are shown in the figure as examples).



www.eufoodborneviruses.net/asp

Viral Gastroenteritis Outbreak UPDATE Form

Reporting Institute : NL-National Institute for Public Health and the Environment *

Outbreak Number: EP2002040 * (your unique reference number)

Reporter's Name: Yvonne van Duynhoven * (First Last)

Today's date: 14/03/2002 * dd/mm/yyyy

Transmission

If foodborne, "PREPARED" takes precedence over "SERVED".
If person-to-person "SERVED" takes precedence over "PREPARED".

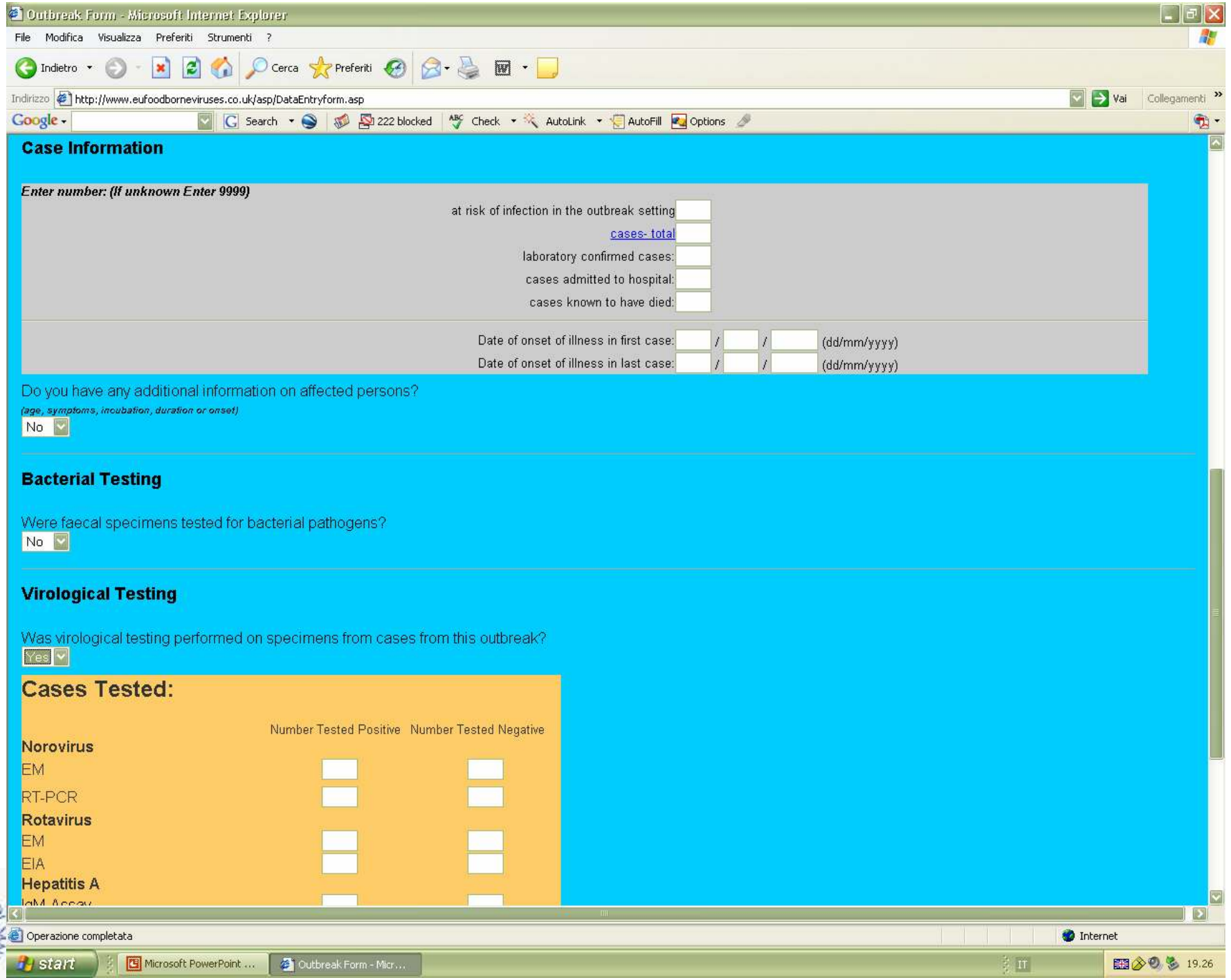
Mode of transmission:
PERSON TO PERSON

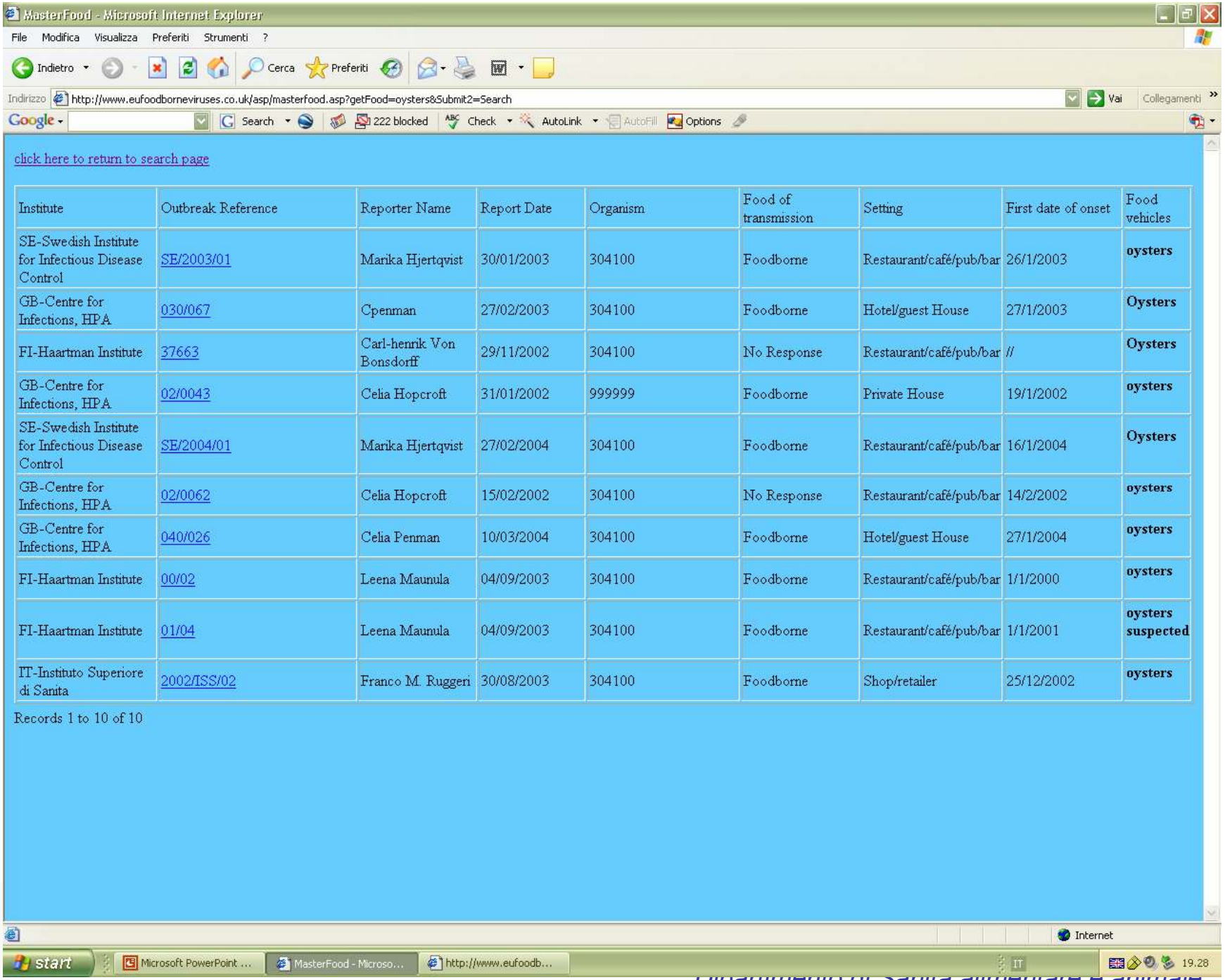
if "other", specify

Place where transmission of infection occurred:
Residential institution

Specify:

Was the outbreak the result of a point source exposure?(e.g. at a function?)
No


Outbreak Form - Microsoft Internet Explorer
File Modifica Visualizza Preferiti Strumenti ?
Indietro Cerca Preferiti
Indirizzo http://www.eufoodborneviruses.co.uk/asp/DataEntryform.asp
Vai Collegamenti
Google Search 222 blocked Check AutoLink AutoFill Options
Case Information
Enter number: (If unknown Enter 9999)
at risk of infection in the outbreak setting
cases- total
laboratory confirmed cases:
cases admitted to hospital:
cases known to have died:
Date of onset of illness in first case: / / (dd/mm/yyyy)
Date of onset of illness in last case: / / (dd/mm/yyyy)
Do you have any additional information on affected persons?
(age, symptoms, incubation, duration or onset)
No
Bacterial Testing
Were faecal specimens tested for bacterial pathogens?
No
Virological Testing
Was virological testing performed on specimens from cases from this outbreak?
Yes
Cases Tested:
Number Tested Positive
Number Tested Negative
Norovirus
EM
RT-PCR
Rotavirus
EM
EIA
Hepatitis A
Operazione completata
Internet
start
Microsoft PowerPoint ...
Outbreak Form - Micr...
IT
19.26

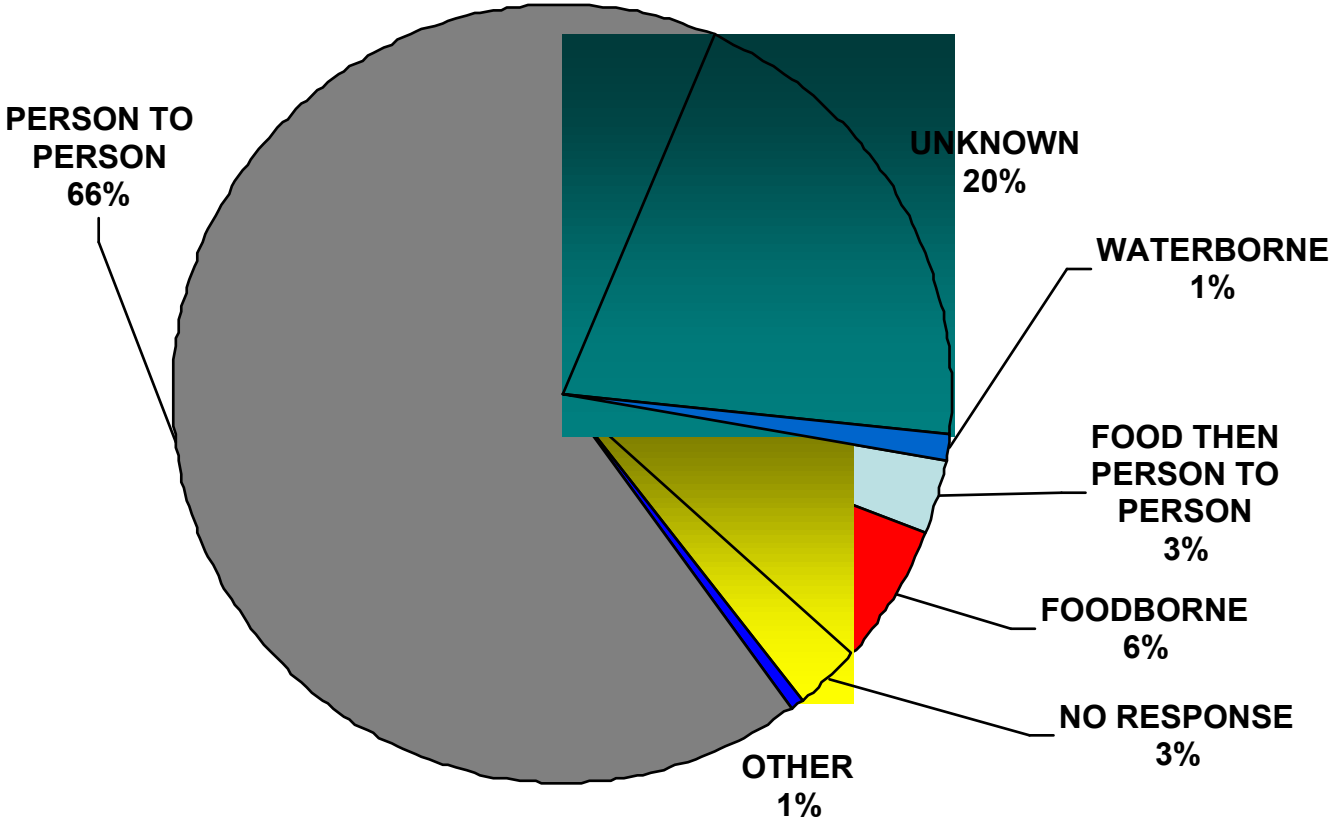


Institute	Outbreak Reference	Reporter Name	Report Date	Organism	Food of transmission	Setting	First date of onset	Food vehicles
SE-Swedish Institute for Infectious Disease Control	SE/2003/01	Marika Hjertqvist	30/01/2003	304100	Foodborne	Restaurant/café/pub/bar	26/1/2003	**oysters**
GB-Centre for Infections, HPA	030/067	Cpenman	27/02/2003	304100	Foodborne	Hotel/guest House	27/1/2003	**Oysters**
FI-Haartman Institute	37663	Carl-henrik Von Bonsdorff	29/11/2002	304100	No Response	Restaurant/café/pub/bar	//	**Oysters**
GB-Centre for Infections, HPA	02/0043	Celia Hopcroft	31/01/2002	999999	Foodborne	Private House	19/1/2002	**oysters**
SE-Swedish Institute for Infectious Disease Control	SE/2004/01	Marika Hjertqvist	27/02/2004	304100	Foodborne	Restaurant/café/pub/bar	16/1/2004	**Oysters**
GB-Centre for Infections, HPA	02/0062	Celia Hopcroft	15/02/2002	304100	No Response	Restaurant/café/pub/bar	14/2/2002	**oysters**
GB-Centre for Infections, HPA	040/026	Celia Penman	10/03/2004	304100	Foodborne	Hotel/guest House	27/1/2004	**oysters**
FI-Haartman Institute	00/02	Leena Maunula	04/09/2003	304100	Foodborne	Restaurant/café/pub/bar	1/1/2000	**oysters**
FI-Haartman Institute	01/04	Leena Maunula	04/09/2003	304100	Foodborne	Restaurant/café/pub/bar	1/1/2001	**oysters suspected**
IT-Instituto Superiore di Sanita	2002/ISS/02	Franco M. Ruggeri	30/08/2003	304100	Foodborne	Shop/retailer	25/12/2002	**oysters**

EUROPE: EPIDEMIOLOGICAL INFORMATION, 1422 ENTRIES: PLACE

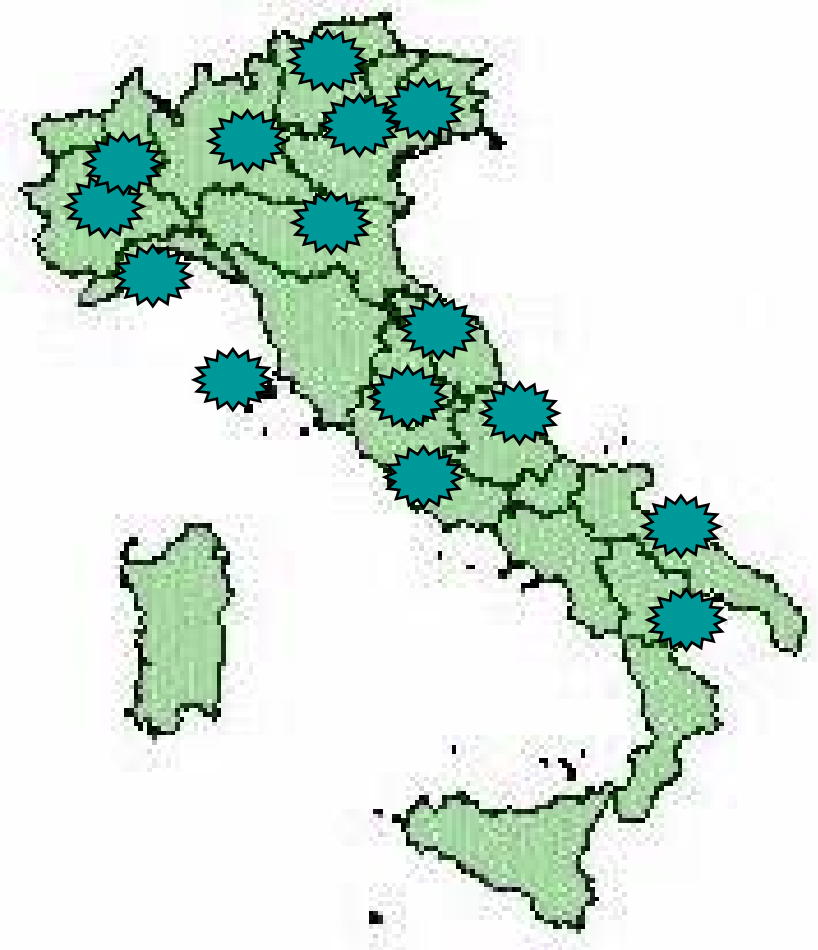
canteen	5
Day-care center	23
farm	1
Food prepared by caterer	13
Hospital	**513**
Hotel/guest house	66
Mobile retailer	1
Private house	12
Residential institution	**508**
Restaurant/Cafe/ Pub/Bar	44
school	77
Shop/Retailer	7
Swimming pool	1
other	126
No info	4

Mode of transmission: Norovirus outbreaks

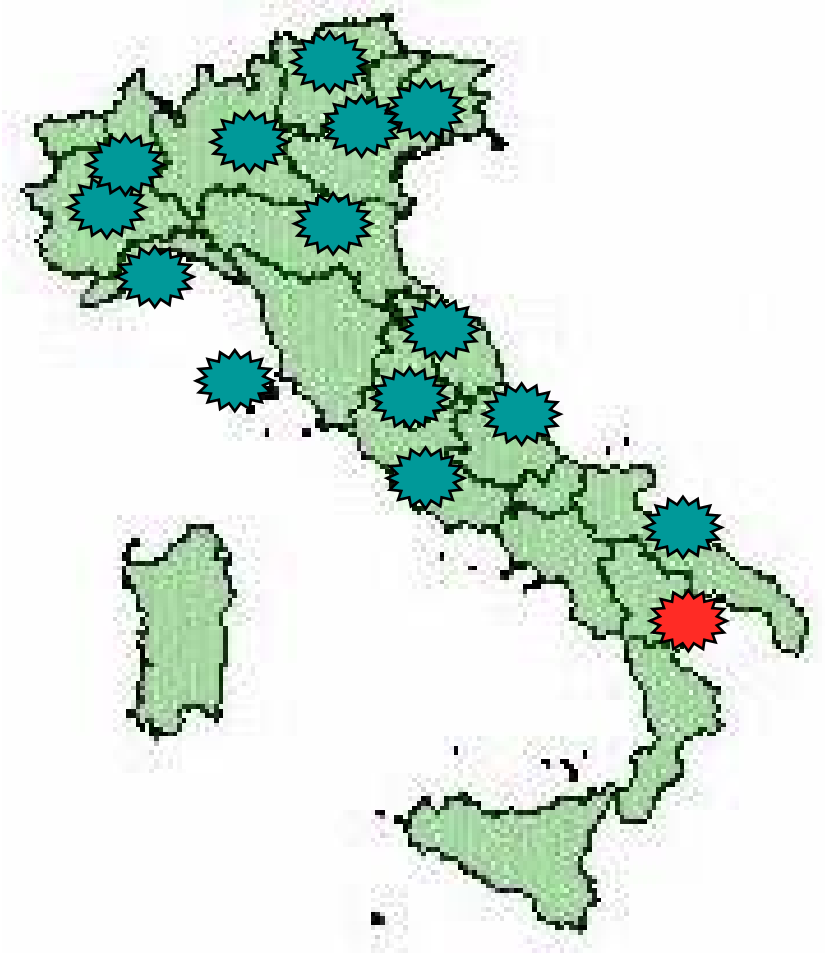


N = 1338

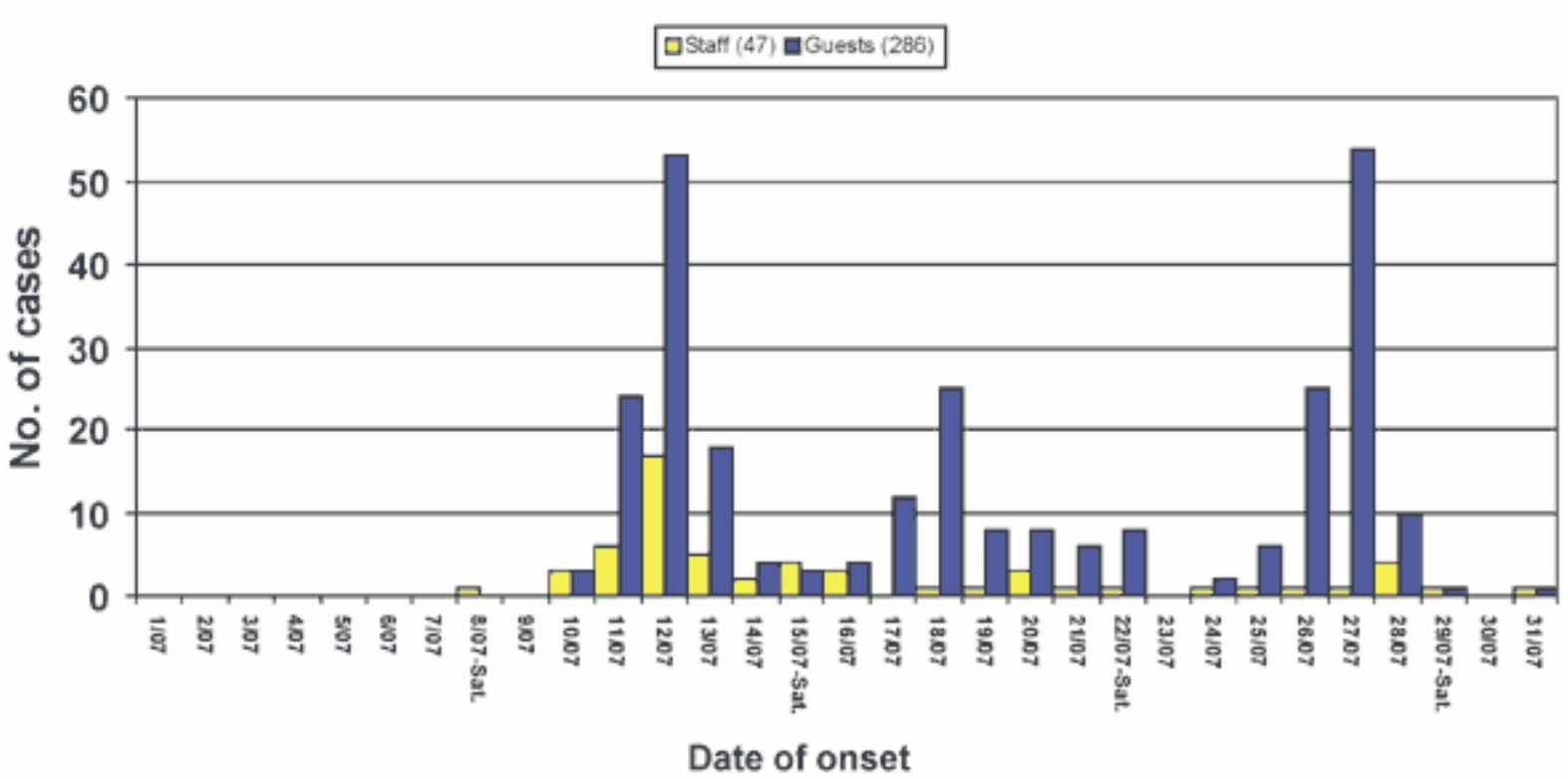
Norovirus outbreaks in Italy



Scanzano J. (PZ), 2000



Waterborne Outbreak of Norwalk-Like Virus Gastroenteritis at a Tourist Resort, Italy

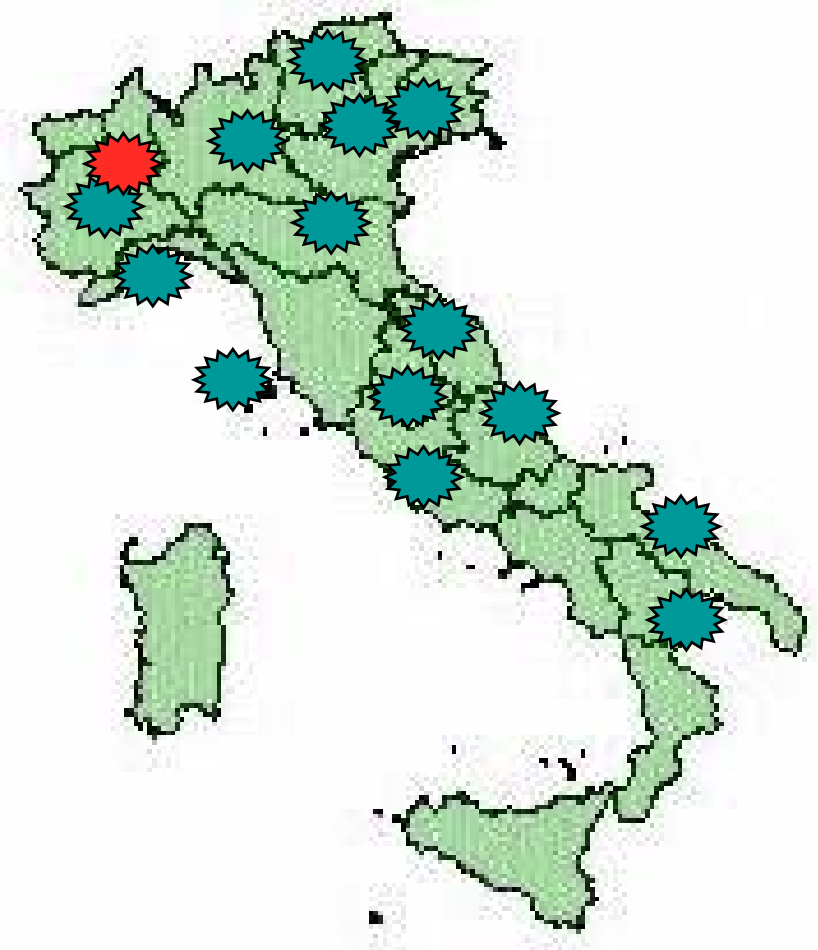


GE outbreak Scanzano J. (TA) July 2000

Experiment: NLV-Polymerase (295 bp)

Rank	Score	Reference number	NLV Pol g.type	Country	Year
1	98.2	01KA223-KOTKA____	Lordsdale	FI	2001
2	96.6	NL-outbreak-2000-27	Lordsdale	NL	2000
3	95.4	2011745	Lordsdale	GB	2000
4	94.5	2039612	Lordsdale	GB	2000
5	94.5	Sensor-1999-3236	Lordsdale	NL	1999
6	94.5	NLV-EUpanel-028	Lordsdale	DE	1999
7	94.5	Nivel-1998-98077	Lordsdale	NL	1998
8	94.5	Sensor-1999-3129	Lordsdale	NL	1999
9	94.4	2114928	Lordsdale	GB	2001
10	93.8	Hun461	Lordsdale		

S. Maurizio C. (TO), 2002



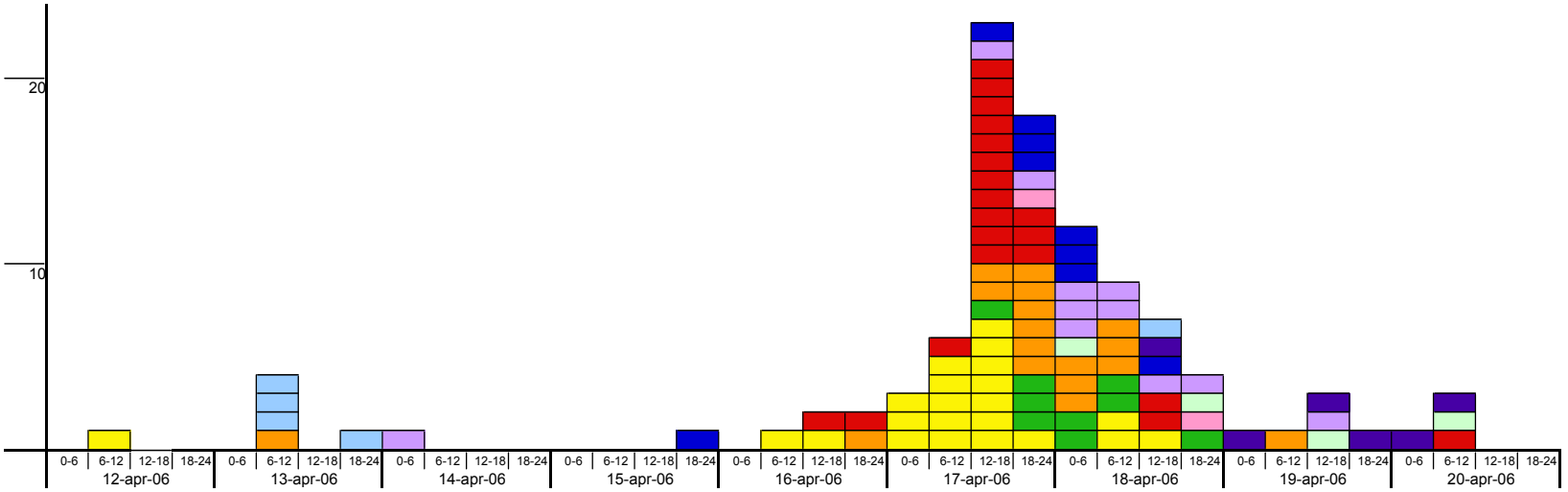
la Repubblica.it

Vota online il gol più bello della storia

Risolto il giallo di San Maurizio Il microrganismo identificato è del tipo Norwalk.

Raro virus la causa dei malori a scuola

… si tratta del virus di Norwalk, rarissimo e poco studiato in Italia. La sua presenza nei cibi delle elementari del Canavese, ipotizzata dal consulente del pm Raffaele Guariniello …



GE outbreak S. Michele (TO) april-may 2002

Experiment: NLV-Polymerase (257bp)

Rank	Score	Reference number	NLV Pol g.type	Country	Year
1	98.9	Fuerstenwalde 809-01-DE	Melksham	DE	2001
2	98.5	Oldenburg 8013-01-DE	Melksham	DE	2001
3	98.4	Siegen 097-02-DE	Melksham	DE	2002
4	98.1	Westerstede 8008-02-DE	Melksham	DE	2002
5	98.0	NL-EP2002007	Melksham	NL	2002
6	97.3	Wolfenbüttel 8001-02-DE	Melksham	DE	2002
7	97.2	NL-OB2001046	Melksham	NL	2001
8	97.2	Siegen 756-01-DE	Melksham	DE	2001
9	97.0	NL-OB2001054	Melksham	NL	2001
10	97.0	NL-EP200125	Melksham	NL	2001

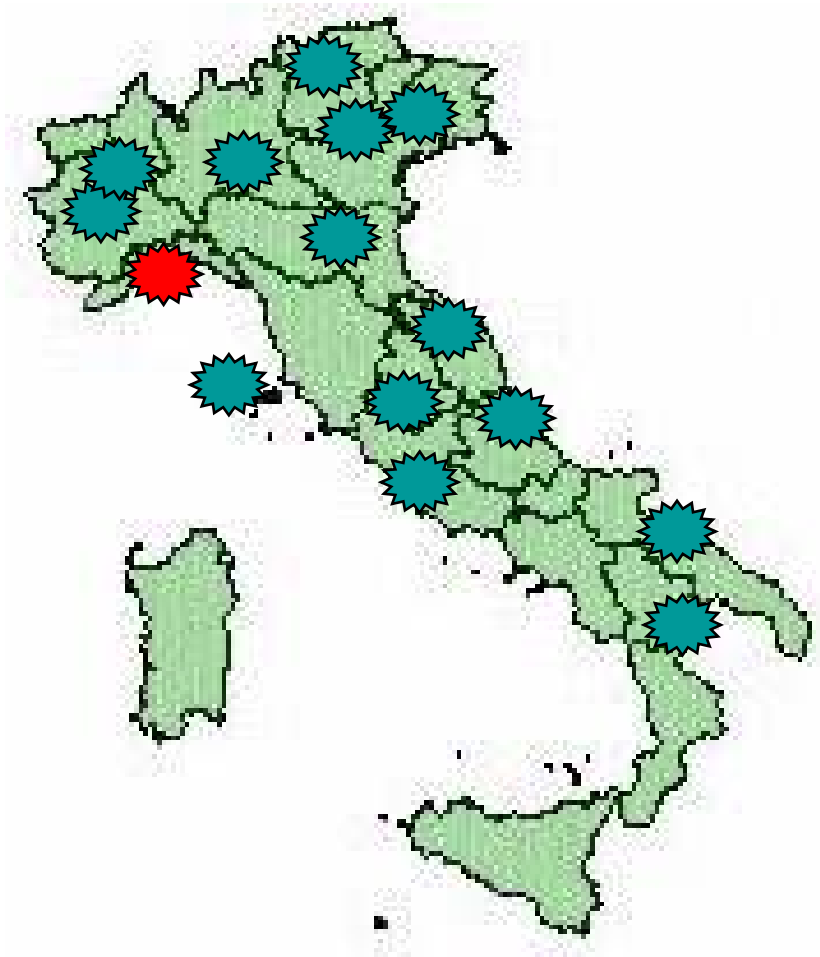
LA SPEZIA OUTBREAK, 2002

AUSL 6 La Spezia:

- 202 cases of GE between December 25-28
- Strong association with consumption of oysters
- High secondary attack rates

41 stools collected
9 stools NoV - pos

4 NoV genotypes



THAU OUTBREAKS, 2002

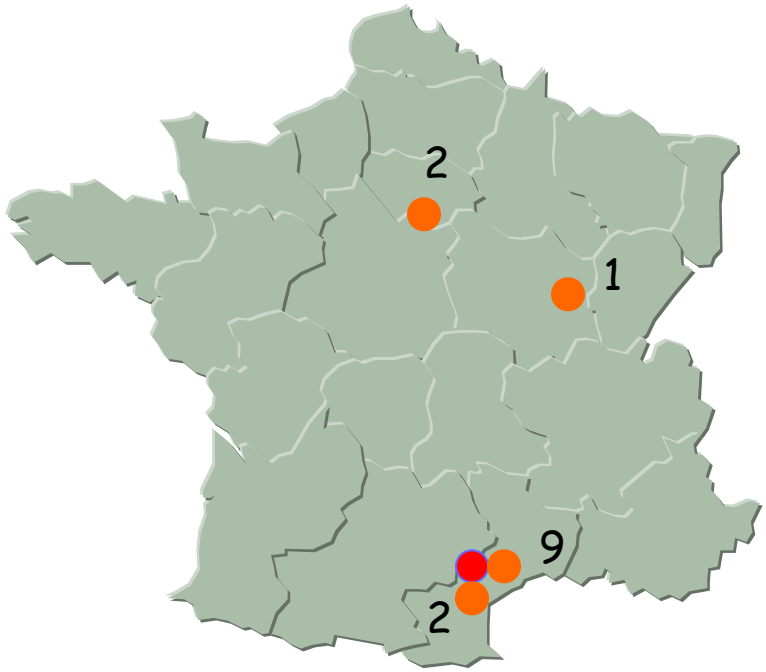
- Setting: private houses and reception
- 14 foodborne outbreaks declared all over France
- 90 sick people in France
- Transmission: oysters
- Origin: pond of Thau

12 stools

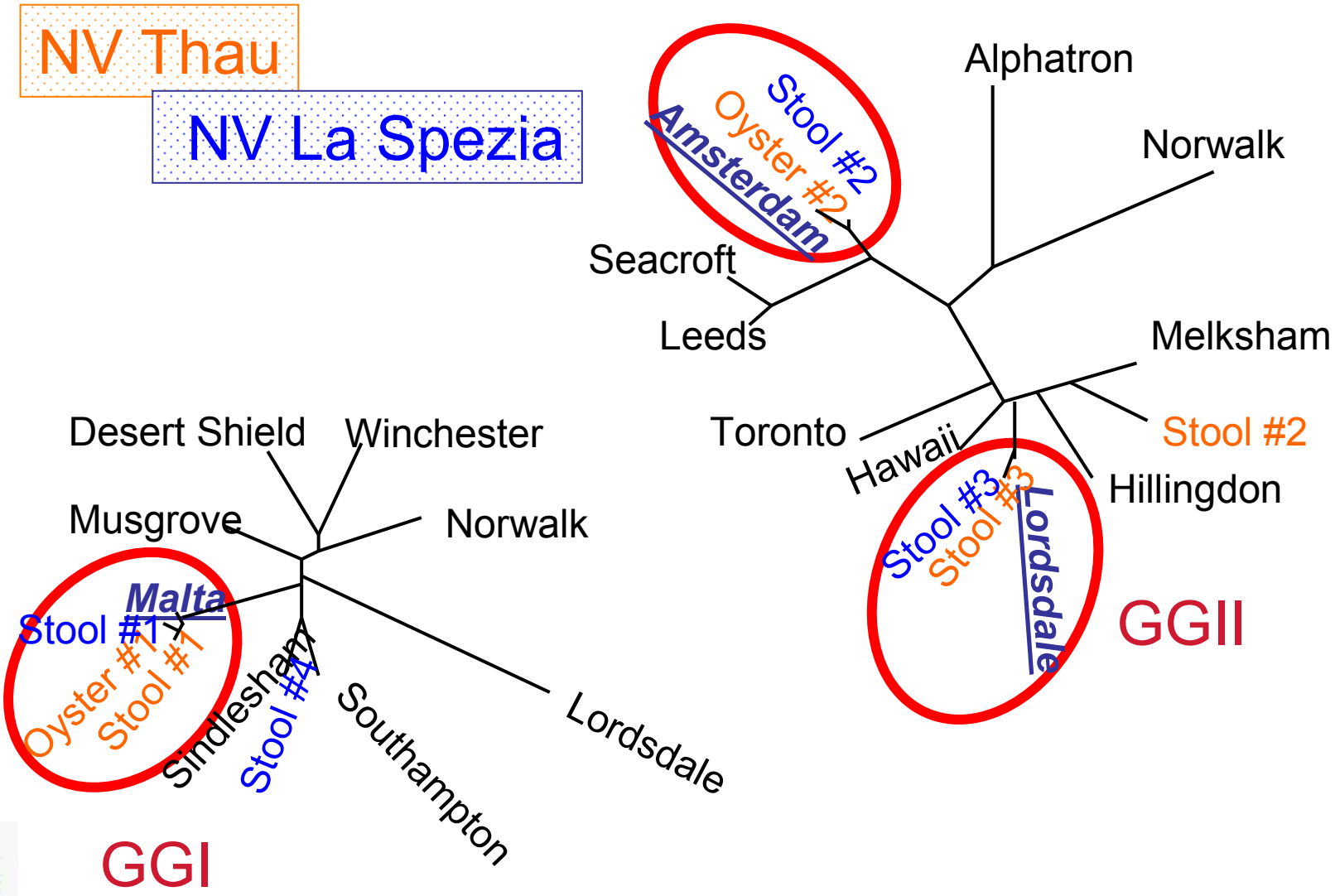
3 NoV genotypes

Oysters

2 Nov genotypes

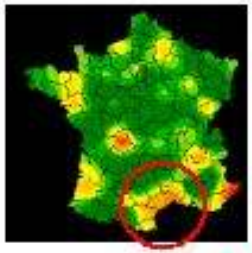


MOLECULAR COMPARISON OF NoVs

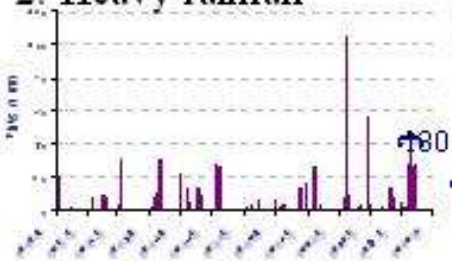


December events leading to shellfish contamination.

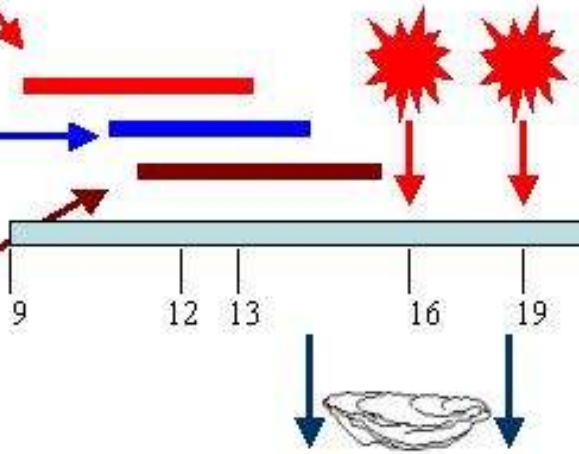
1. Gastroenteritis outbreak



2. Heavy rainfall



Shellfish alert based on *E coli*

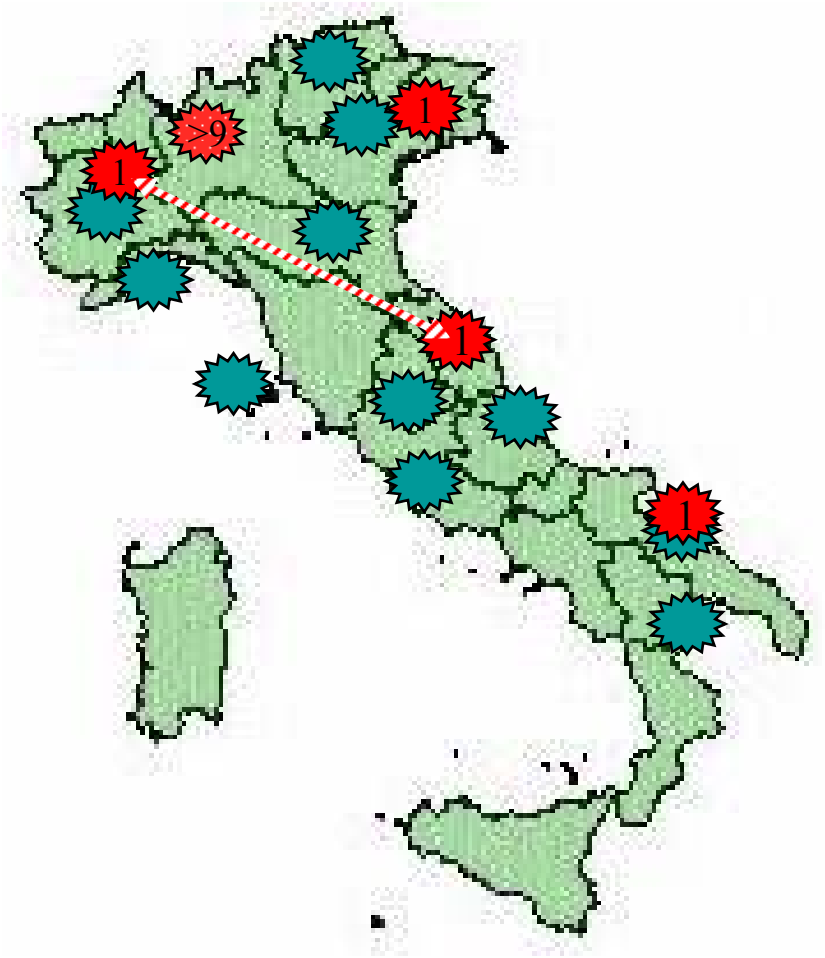


3. STP failure

Oysters send to French or Italian market

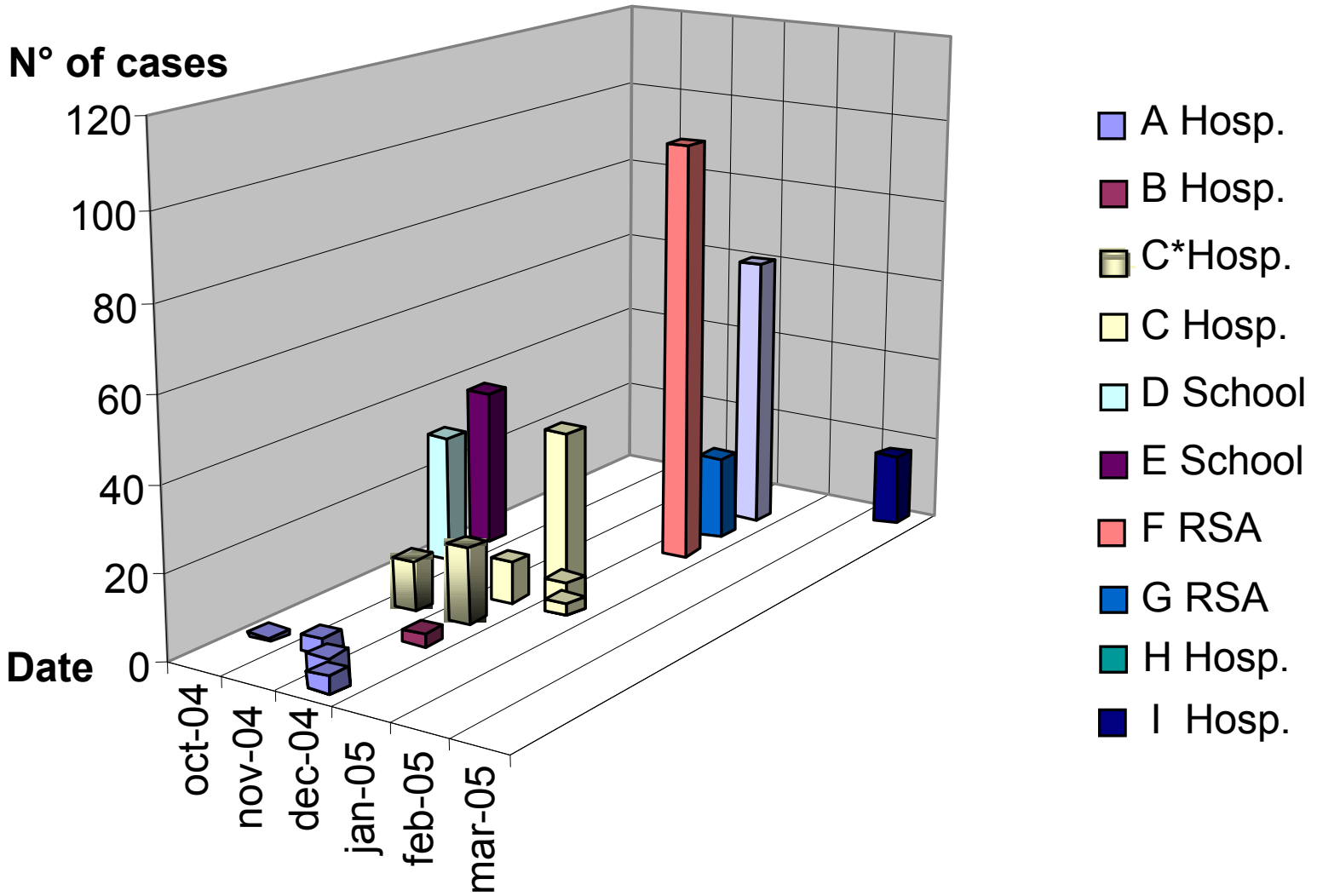
Cases in the population

NoV outbreaks reported, 2004-5

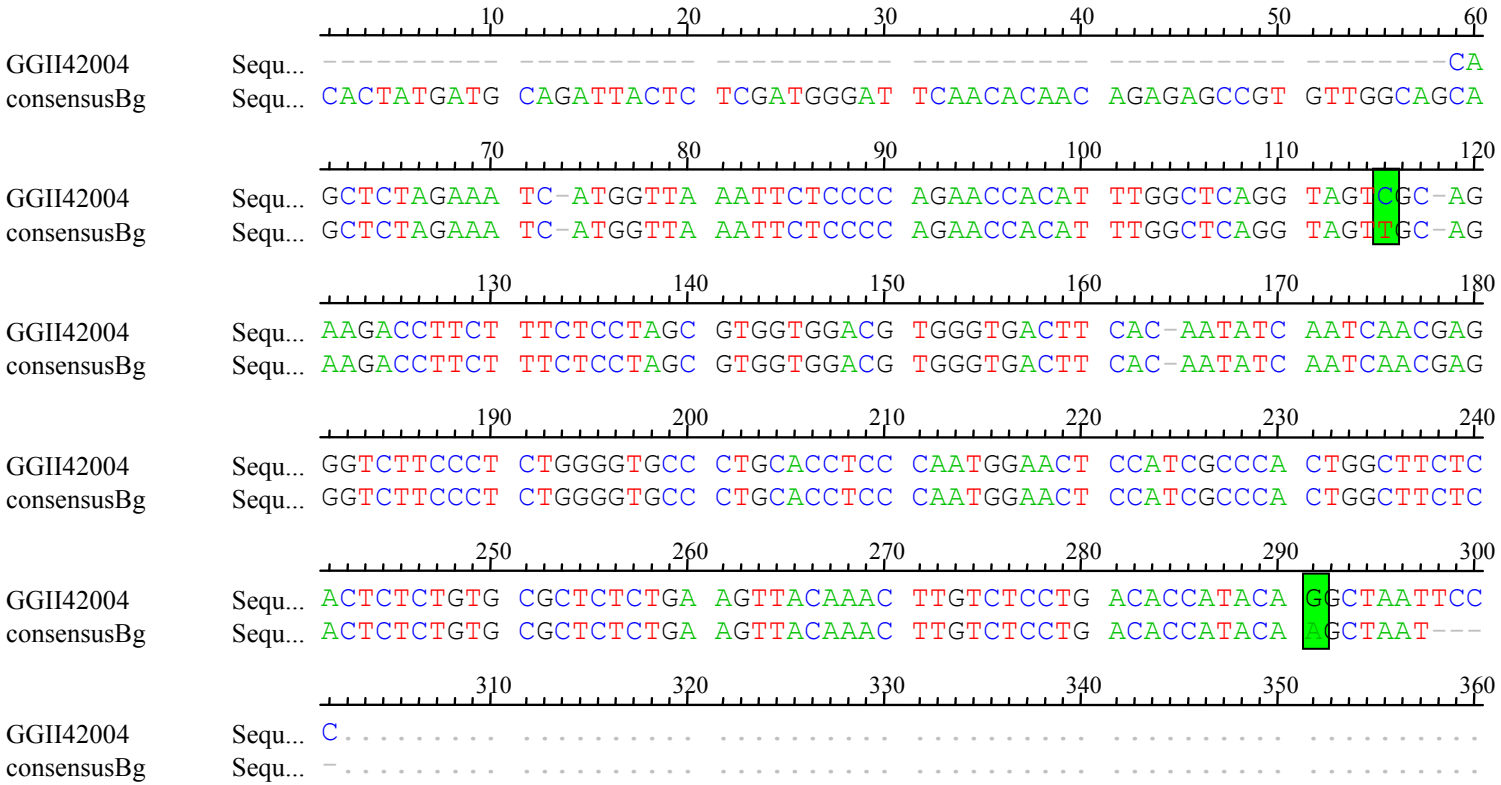


Provincia di Bergamo. Località delle epidemie.

Casi di GE (386 soggetti: degenti, operatori sanitari, alunni, operatori scolastici). Ottobre 2004 - aprile 2005 nella provincia di BG.

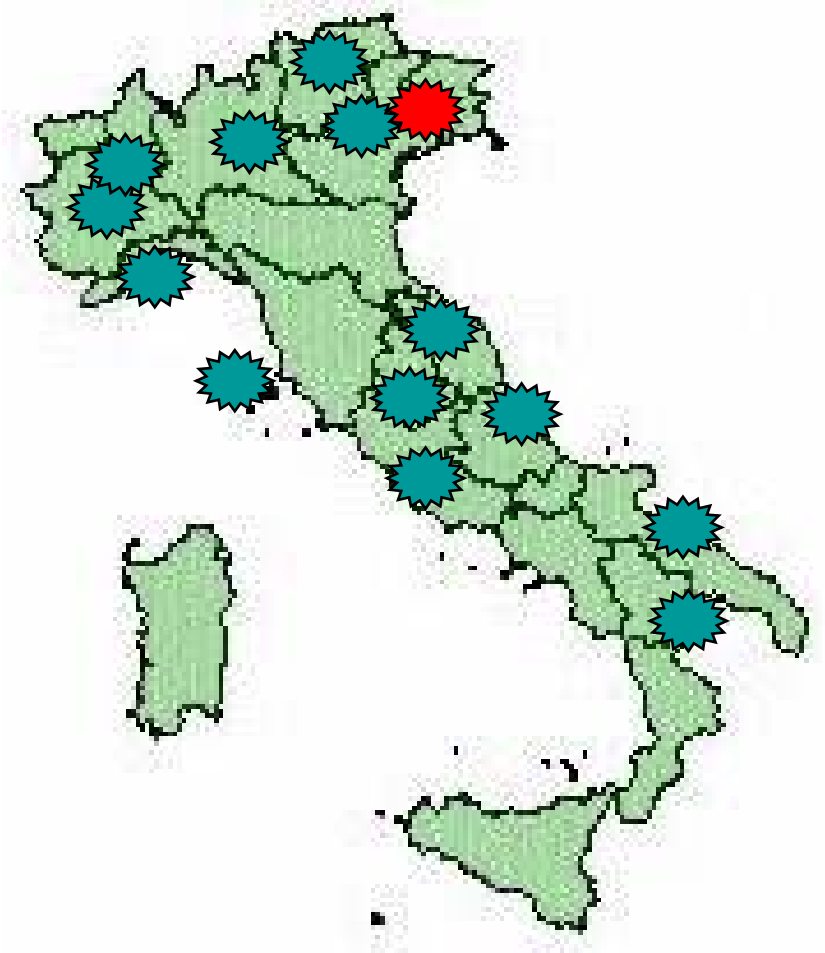


Sequence comparison of NoV strains from Italy, 2004-2005



Evolution of the capsid gene of GGII.4 NoV

Palmanova (UD), 2005



Provincia di Udine - dicembre 2005

VIII PROVINCIA

Appuntamenti natalizi, un salto nel 1600 per riscoprire la fortezza attraverso i registri battesimali

In duecento con il mal di pancia, inchiesta sanitaria

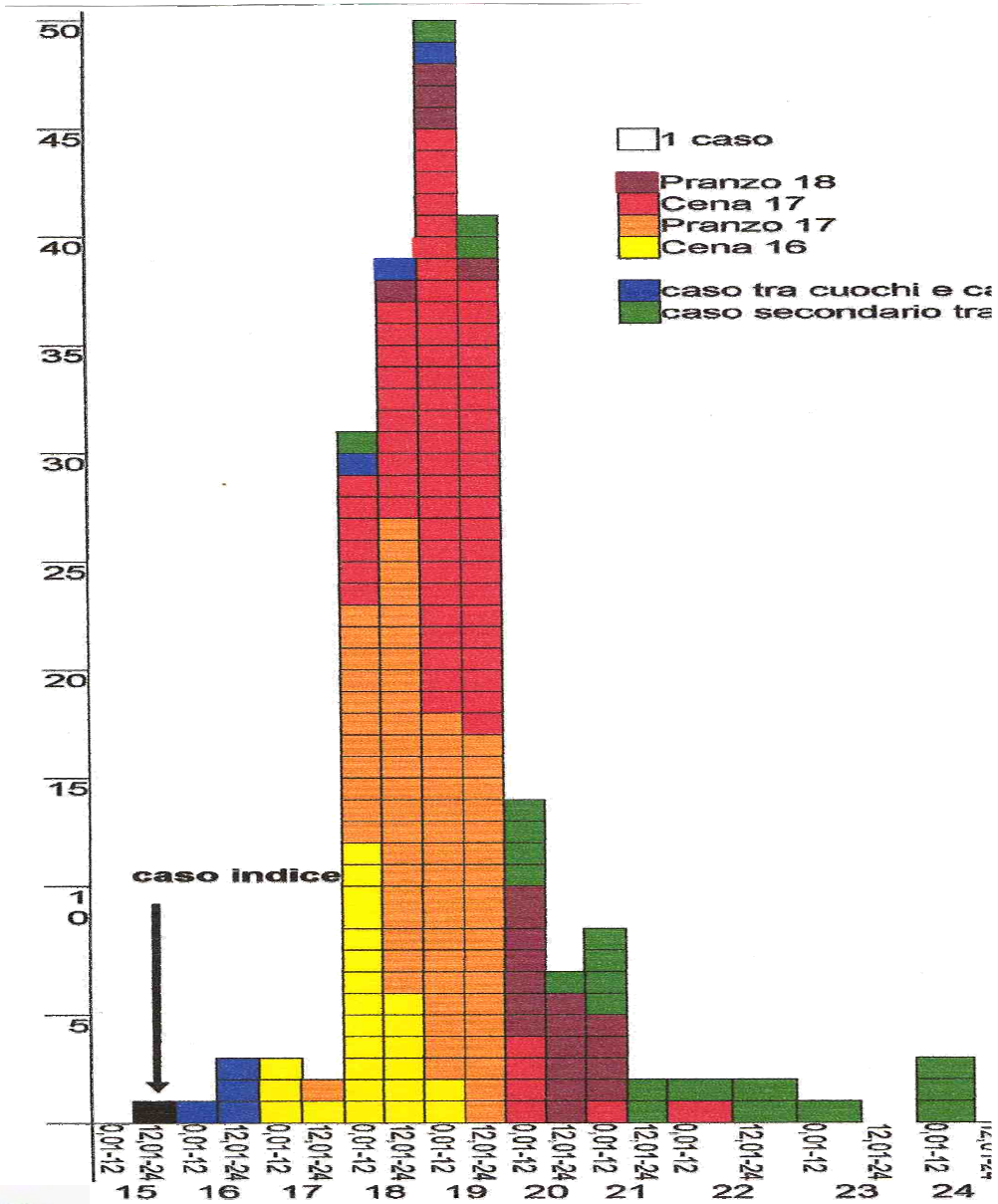
Alla "Europolimeri" metà maestranze in malattia. Squadra di calcio della Bassa ko dopo la cena di Natale

Dopo i furti si pensa alle ronde

IN BREVE

- 16 - 18 dicembre 2005
- 440 persone partecipanti a pranzi e cene prenatalizie organizzate da aziende e gruppi sociali

L. Gallo - Profea **Roma, 13 ottobre 2006**



Ispezione nel ristorante
Cuochi, camerieri (n=15) intervistati:
6 sintomatici

296 intervistati (67%)
Casi: 182 AR=62%

Il 15 dicembre: la figlia del gestore (3 anni) presenta disturbi gastrointestinali con vomito (caso indice)

T. Gallo; M. Zuliani

Dipartimento di Sanità alimentare e animale

INDAGINE EPIDEMIOLOGICA

Esposizione	% Casi (n)		RRc	RRadj
	Mangiato	Non mangiato		
antipasto pesce gratinato	64% (167)	42% (15)	1,5	==
frittura	81% (90)	50% (92)	1,6	1,3
grigliata di pesce	70% (155)	36% (26)	1,9	==
"volpina"	79% (130)	94% (53)	2,0	1,5
antipasto di pesce freddo	70% (176)	14% (6)	5,1	3,4

INDAGINI VIROLOGICHE

- Feci di 14 persone coinvolte nell'epidemia positive per norovirus (un unico ceppo virale di genotipo GII.6)

- 1 tampone ambientale positivo per norovirus

  (piano di lavoro per la pulitura dei mitili e la preparazione di antipasti di pesce)

CONCLUSIONI

- ✓ Epidemie causate da alimenti:
  - Contaminazione primaria (es. La Spezia)
  - Contaminazione secondaria- manipolazione (es. Udine)

- ✓ In Italia non esiste un sistema di notifica adeguato, la maggior parte delle GE causate da Norovirus non vengono identificate

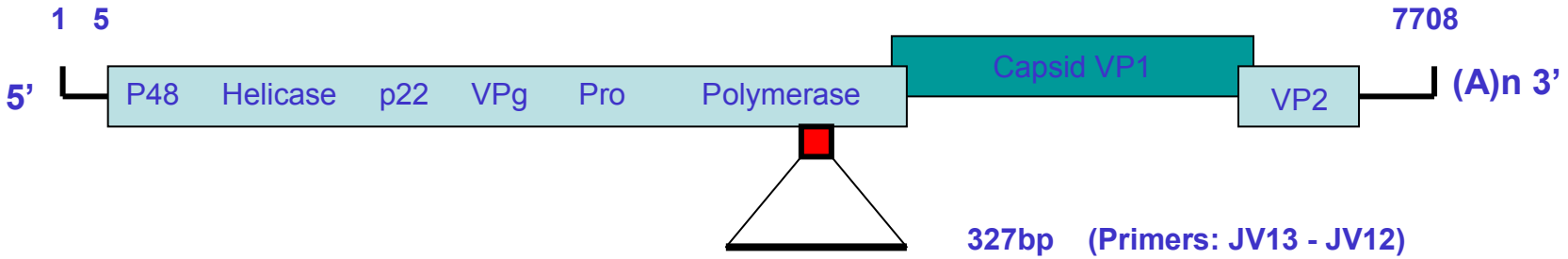
Approcci diagnostici

- EM/IEM (poco sensibile, costoso)
- ELISA (primi kit in commercio)
- RT/PCR (rapido/sensibile/costoso)
  - *Southern Hybridization (conferma)*
  - *Sequencing (confronti, filogenesi)*
  - *RLBH (genotipizzazione)*
  - *nPCR (max. sensibilità)*

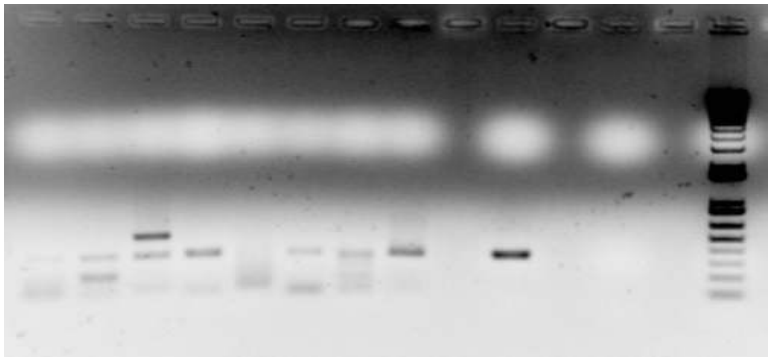
Approcci diagnostici per NoV

	EM	ELISA	Molecular detection
Sensitivity	+	++	++++
Specificity	+++	+++	+++
“Broadness”	+++++	+	+++
Typing possibilities	+	++	++++

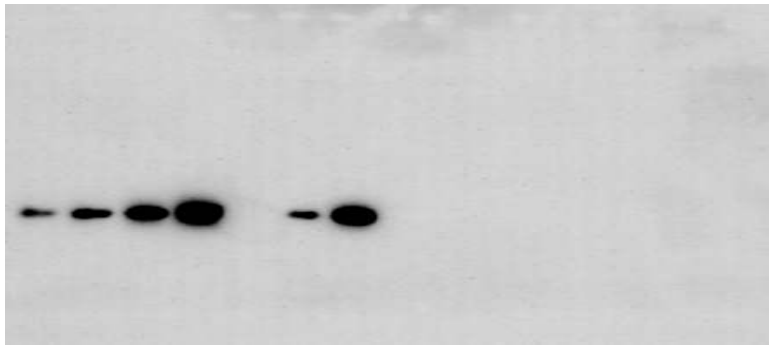
MOLECULAR DIAGNOSIS OF NOROVIRUS



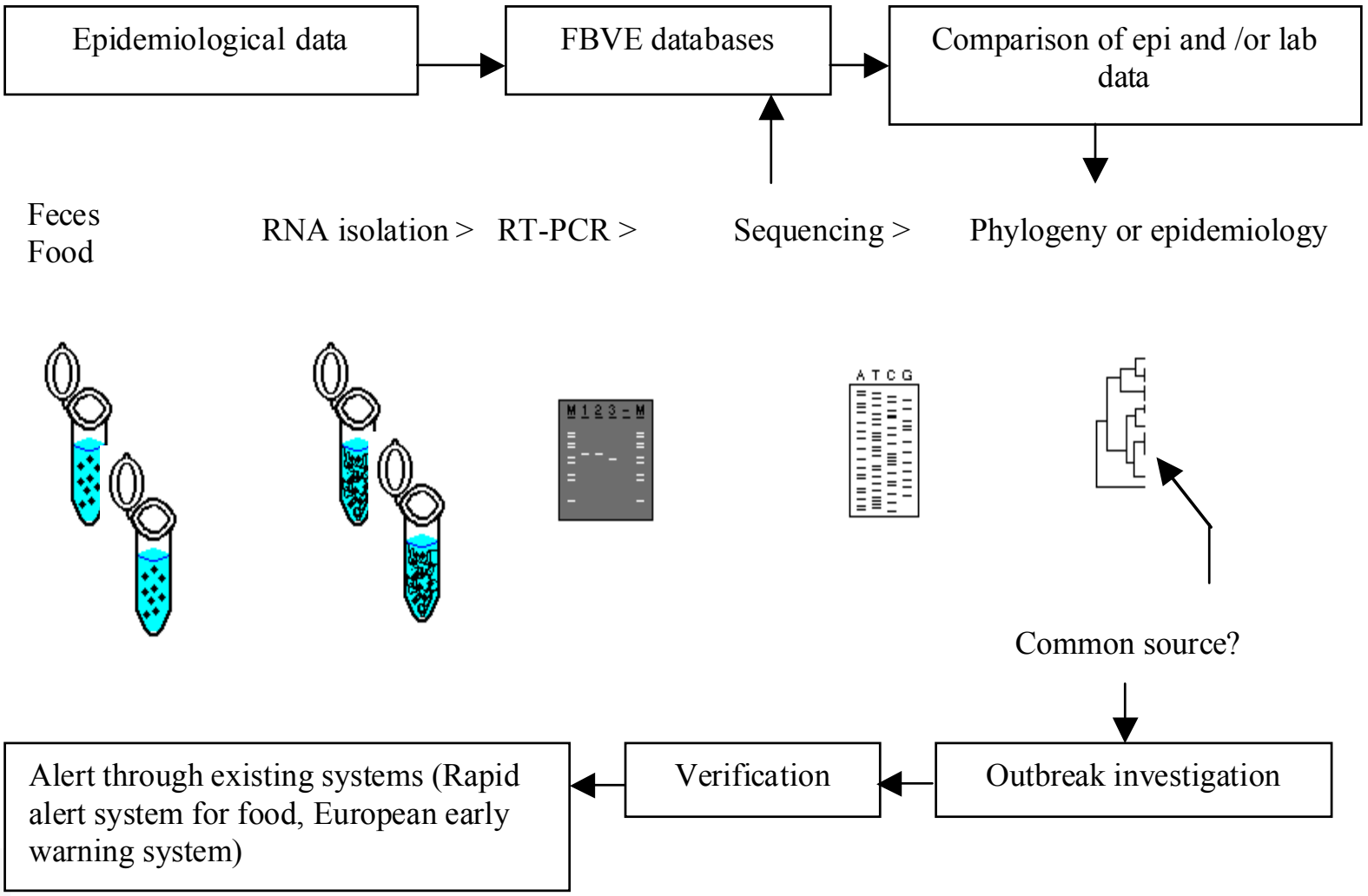
RT/PCR



S. blot



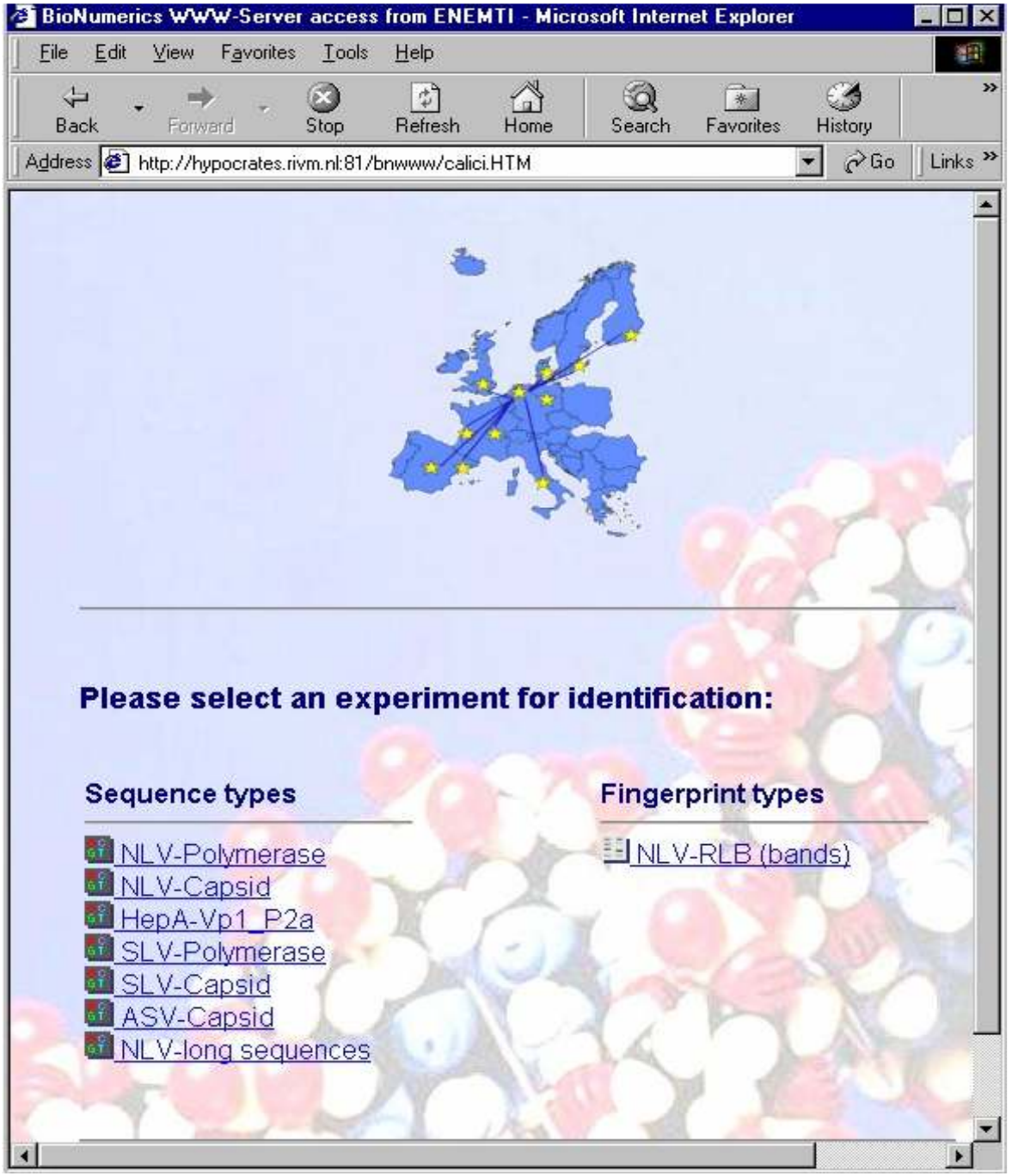
Early detection of common source outbreaks by networking



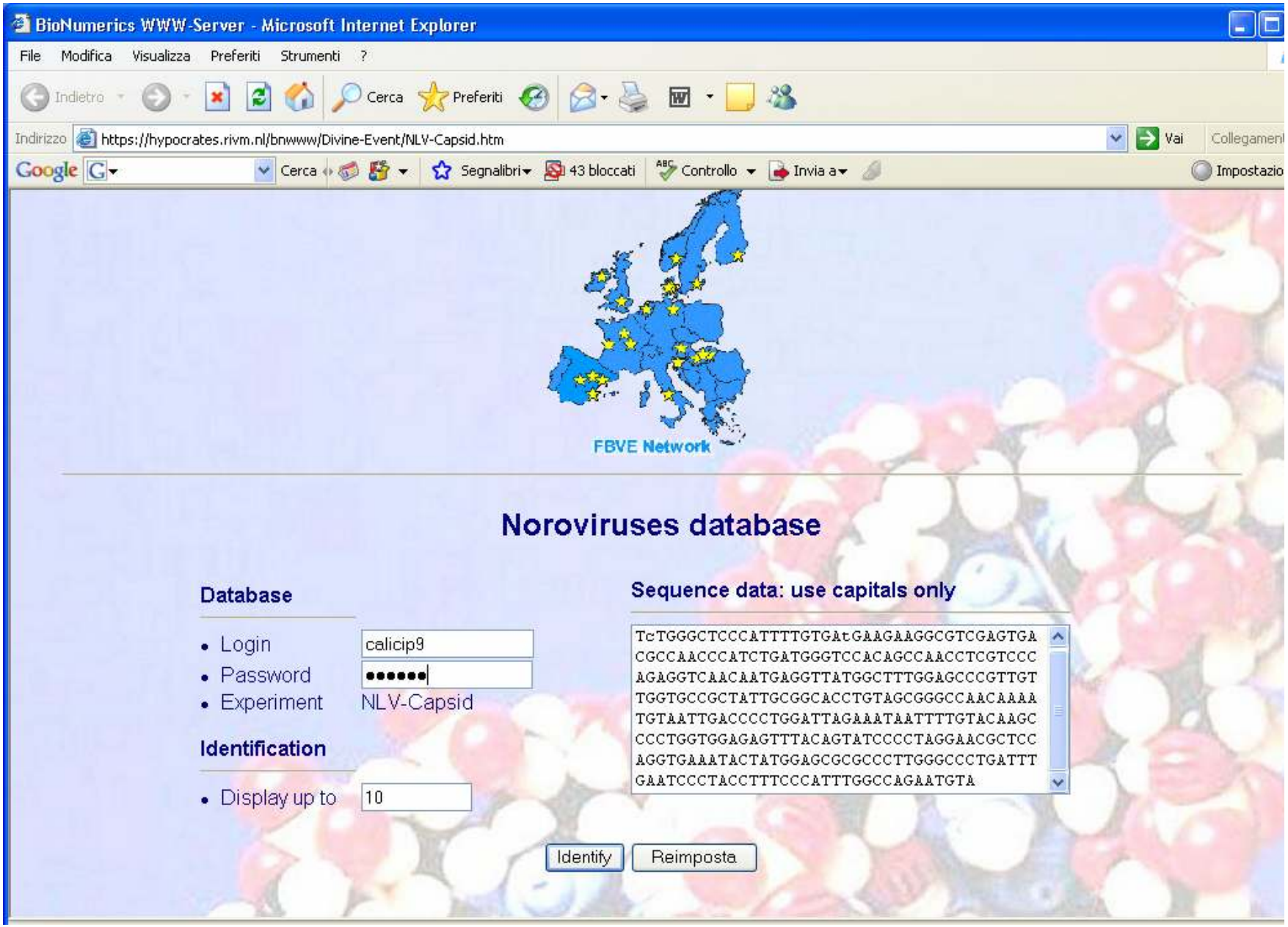
Virological Data - Web-based genetic bank

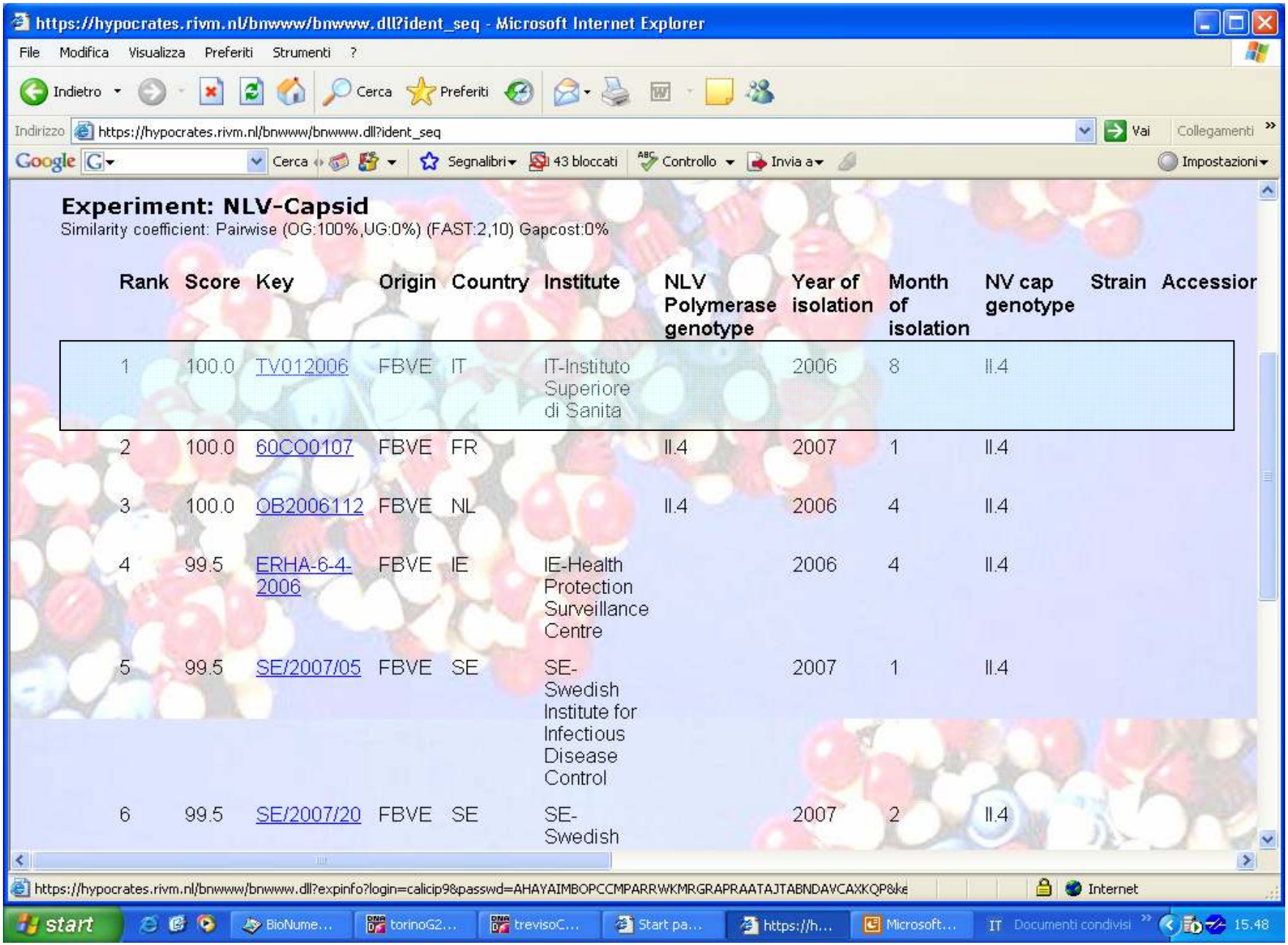
Applied Maths, Ghent, Belgium

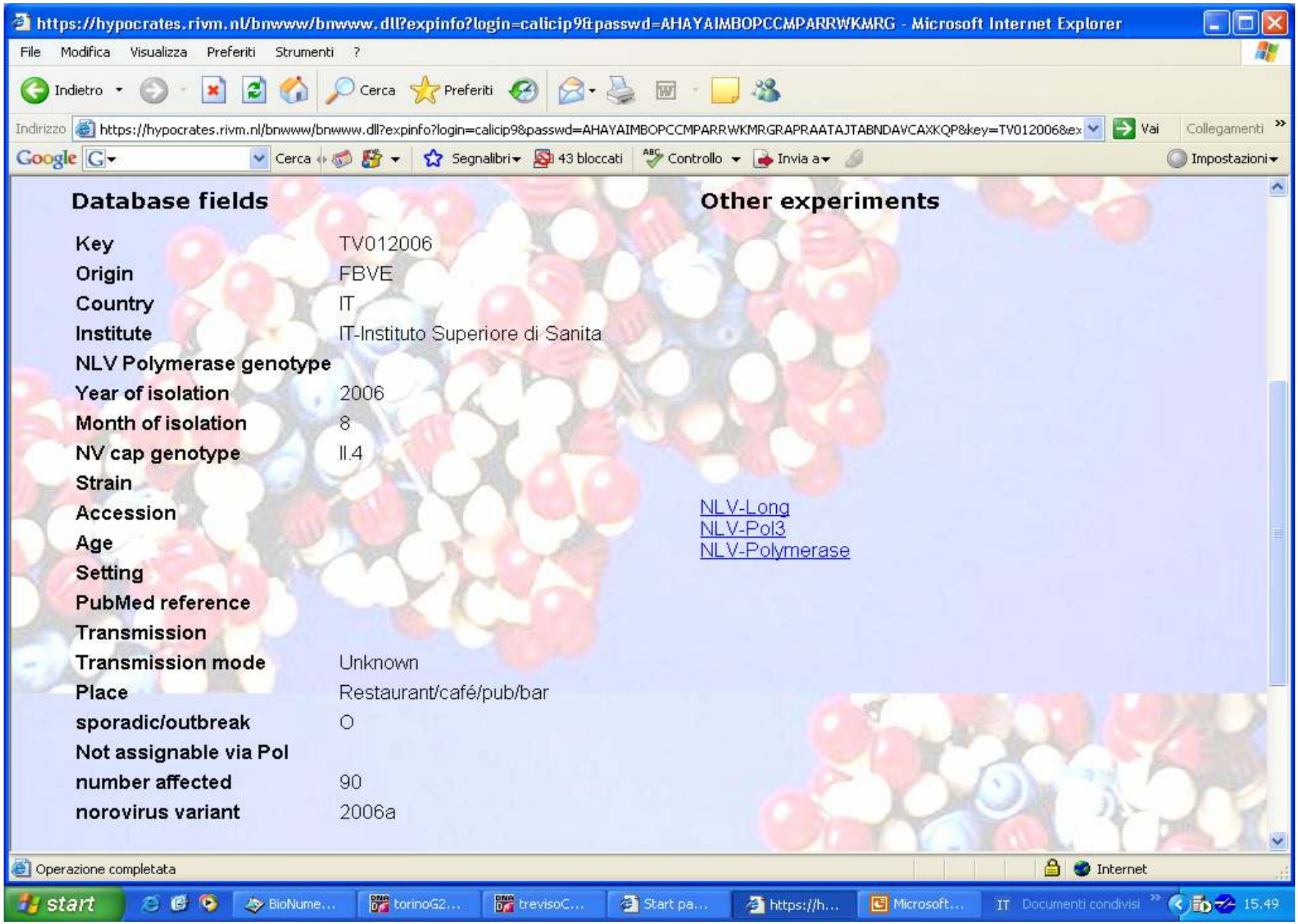
https://hypocrates.rivm.nl/bnwww/



Dipartimento di Sanità alimentare e animale


BioNumerics WWW-Server - Microsoft Internet Explorer
File Modifica Visualizza Preferiti Strumenti ?
Indietro Cerca Preferiti
Indirizzo https://hypocrates.rivm.nl/bnwww/Divine-Event/NLV-Capsid.htm
Vai
Google Cerca Segnalibri 43 bloccati Controllo Invia a
FBVE Network
Noroviruses database
Database
Login calicip9
Password
Experiment NLV-Capsid
Identification
Display up to 10
Sequence data: use capitals only
TcTGGGCTCCCATTTTGTGAtGAAGAAGGCGTCGAGTGA
CGCCAACCCATCTGATGGGTCCACAGCCAACCTCGTCCC
AGAGGTCAACAATGAGGTTATGGCTTTGGAGCCCGTTGT
TGGTGCCGCTATTGCGGCACCTGTAGCGGGCCAACAAAA
TGTAATTGACCCCTGGATTAGAAATAATTTTGTACAAGC
CCCTGGTGGAGAGTTTACAGTATCCCCTAGGAACGCTCC
AGGTGAAATACTATGGAGCGCGCCCTTGGGCCCTGATTT
GAATCCCTACCTTTCCCATTTGGCCAGAATGTA
Identify
Reimposta


https://hypocrates.rivm.nl/bnwww/bnwww.dll?ident_seq - Microsoft Internet Explorer
File Modifica Visualizza Preferiti Strumenti ?
Indietro Cerca Preferiti
Indirizzo https://hypocrates.rivm.nl/bnwww/bnwww.dll?ident_seq
Vai Collegamenti
Google Cerca Segnalibri 43 bloccati Controllo Invia a Impostazioni
Experiment: NLV-Capsid
Similarity coefficient: Pairwise (OG:100%,UG:0%) (FAST:2,10) Gapcost:0%
Rank Score Key Origin Country Institute NLV Polymerase genotype Year of isolation Month of isolation NV cap genotype Strain Accessior
1 100.0 TV012006 FBVE IT IT-Instituto Superiore di Sanita 2006 8 II.4
2 100.0 60CO0107 FBVE FR II.4 2007 1 II.4
3 100.0 OB2006112 FBVE NL II.4 2006 4 II.4
4 99.5 ERHA-6-4-2006 FBVE IE IE-Health Protection Surveillance Centre 2006 4 II.4
5 99.5 SE/2007/05 FBVE SE SE-Swedish Institute for Infectious Disease Control 2007 1 II.4
6 99.5 SE/2007/20 FBVE SE SE-Swedish 2007 2 II.4
https://hypocrates.rivm.nl/bnwww/bnwww.dll?expinfo?login=calicip9&passwd=AHAYAIMBOPCCMPARRWKMRGRAPRAATAJTABNDAVCAXKQP&ke
Internet
start
BioNume... torinoG2... trevisoC... Start pa... https://h... Microsoft... IT Documenti condivisi 15.48


https://hypocrates.rivm.nl/bnwww/bnwww.dll?expinfo?login=calicip9&passwd=AHAYAIMBOPCCMPARRWKMRG - Microsoft Internet Explorer
File Modifica Visualizza Preferiti Strumenti ?
Indietro Cerca Preferiti
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Vai Collegamenti
Google Cerca Segnalibri 43 bloccati Controllo Invia a Impostazioni
Database fields
Key TV012006
Origin FBVE
Country IT
Institute IT-Instituto Superiore di Sanita
NLV Polymerase genotype
Year of isolation 2006
Month of isolation 8
NV cap genotype II.4
Strain
Accession
Age
Setting
PubMed reference
Transmission
Transmission mode Unknown
Place Restaurant/café/pub/bar
sporadic/outbreak O
Not assignable via Pol
number affected 90
norovirus variant 2006a
Other experiments
NLV-Long
NLV-Pol3
NLV-Polymerase
Operazione completata
Internet
start
BioNume...
torinoG2...
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Start pa...
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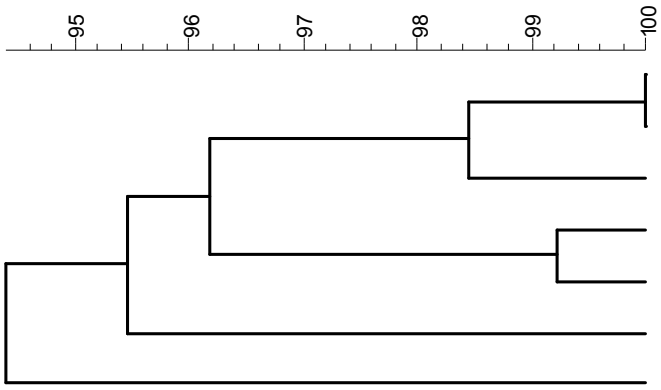
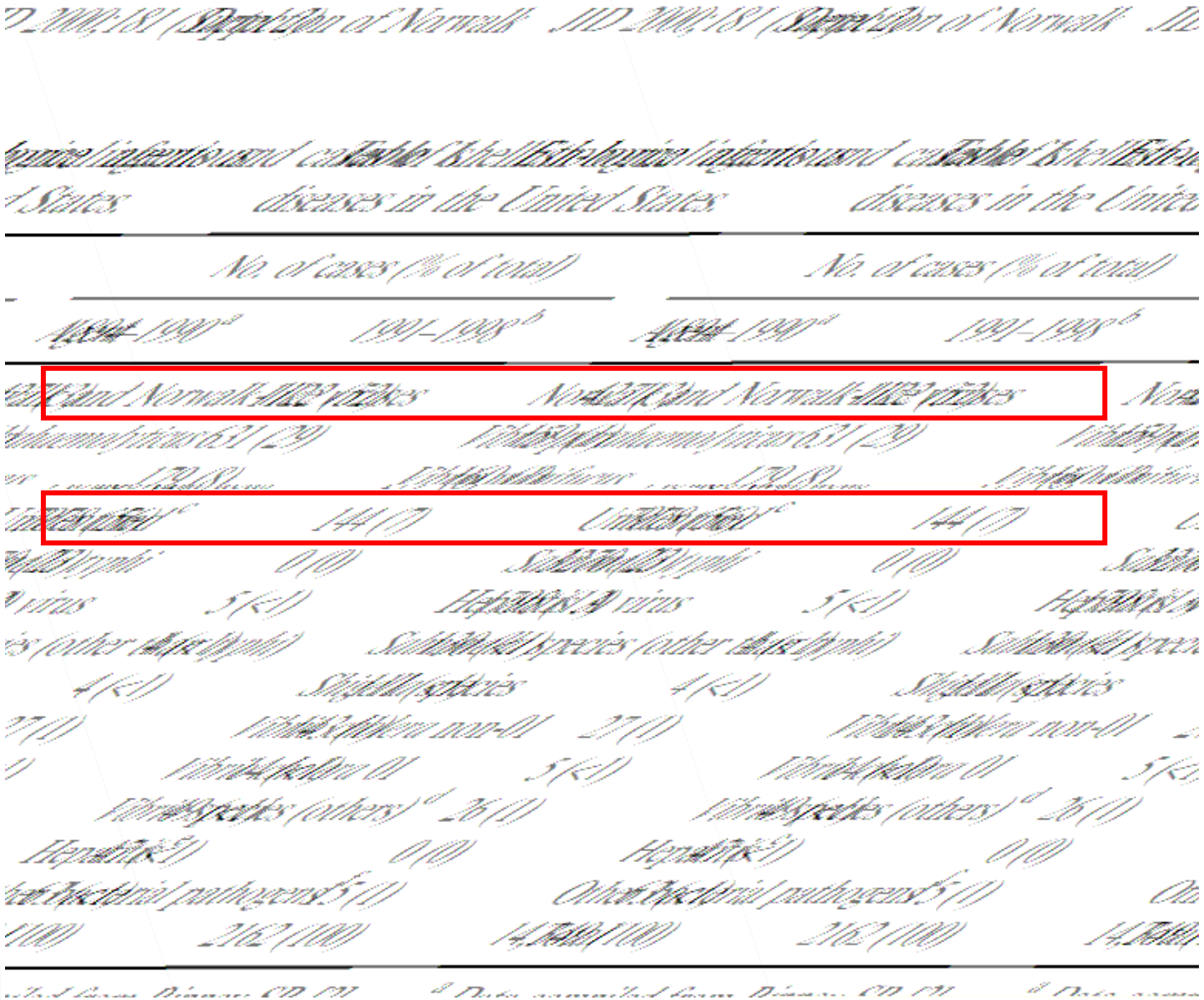
Microsoft...
IT Documenti condivisi
15.49

Varianti Lordsdale (GII.4)

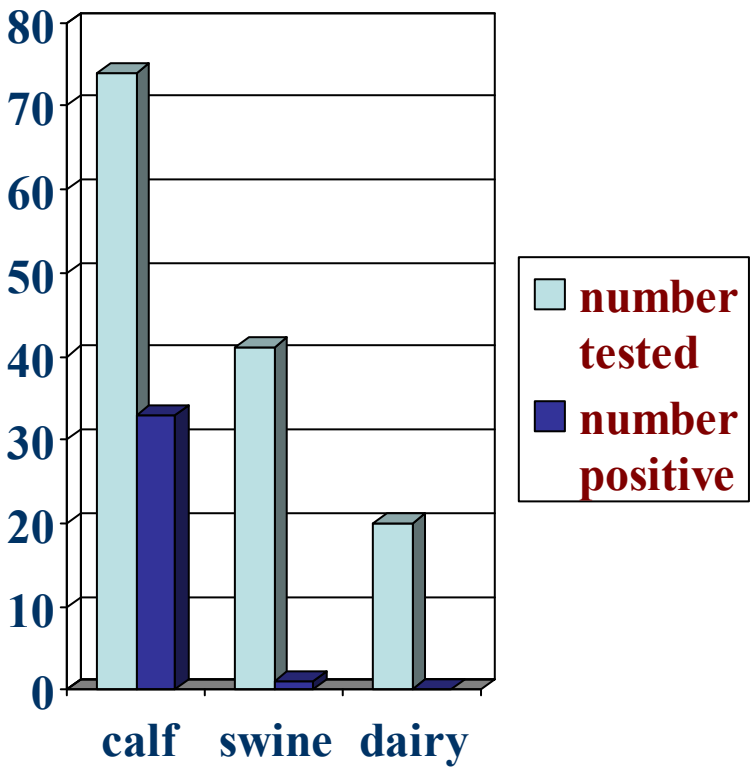
Pairwise (OG:100%,UG:0%) (FAST:2,10) Gapcost:0%
NLV-Capsid



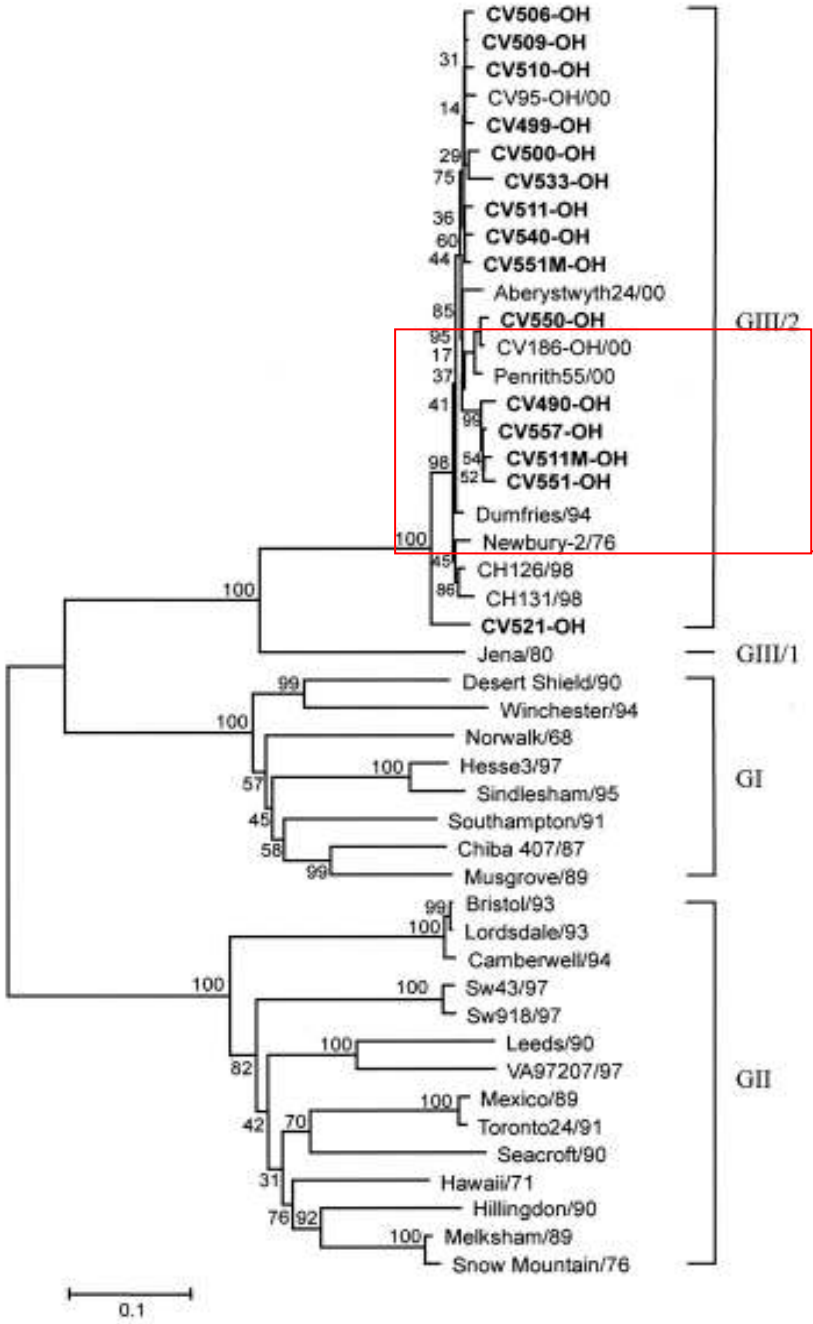
HuNoV/Iordsdale/NL/06a	O.	HuNoV	NL	RIVM	II.406a	2006
HuNoV/TO38/07/IT		HuNoV	IT	ISS	II.406a	2006
HuNoV/TV/06/IT	T.	HuNoV	IT	ISS	II.406a	2006
HuNoV/Lordsdale/HU/07	H.	HuNoV	HU		II.406b	2007
HuNoV/TO/07/IT		HuNoV	IT	ISS	II.406b	2007
HuNoV/Bg/05/IT		HuNoV	IT	ISS	II4 var.2004	2005
HuNoV/Lordsdale/1995	X.	HuNoV	UK		II4	1995

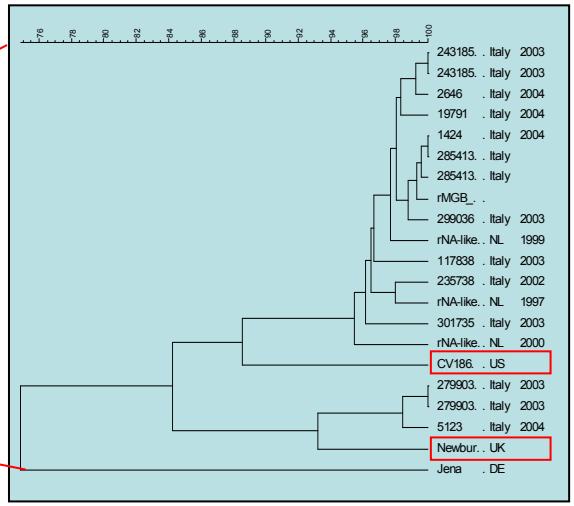


- Do husbandry animals form a reservoir for NLV strains?

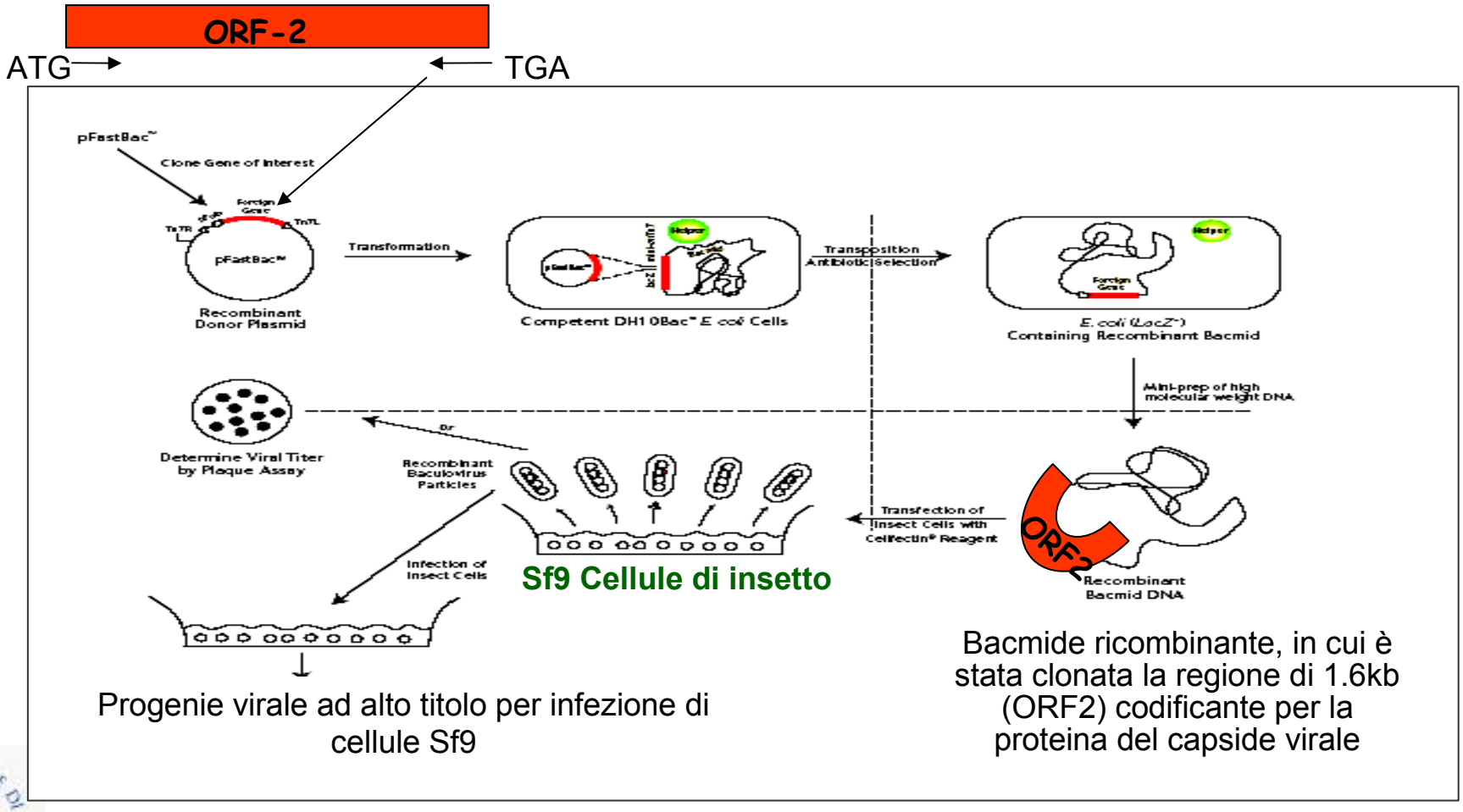


Norovirus da bovini in Italia, 2002-2004





Baculovirus ricombinante BacBECORF2 per la proteina del capside virale (ORF2) di ceppi umano e bovino di Norovirus



Progenie virale ad alto titolo per infezione di cellule Sf9

Bacmide ricombinante, in cui è stata clonata la regione di 1.6kb (ORF2) codificante per la proteina del capside virale

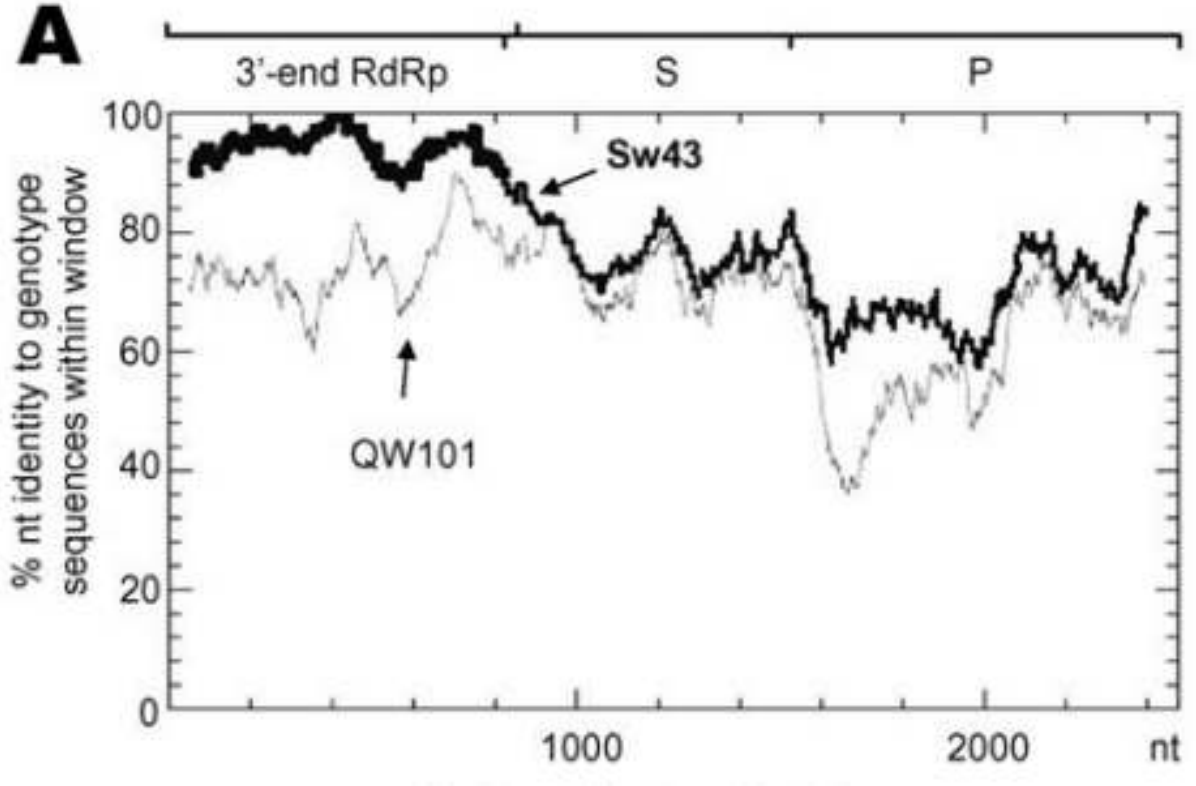
Sieroprevalenza

- Le VLPs del ceppo umano e del ceppo bovino sono state utilizzate in esperimenti ELISA per la ricerca di anticorpi in sieri umani (categoria a rischio: veterinari) e in sieri bovini

- Primi risultati:
- Sieri Veterinari: 58 sieri su 84 riconoscono VLP-Hu, 5 dei quali riconoscono anche VLP-BEC. 1 siero riconosce solo VLP-BEC
- Sieri Bovini:nessuno dei 48 sieri di vitelli americani testati riconoscono VLP-Hu o VLP-BEC Italia

Porcine Noroviruses Related to Human Noroviruses

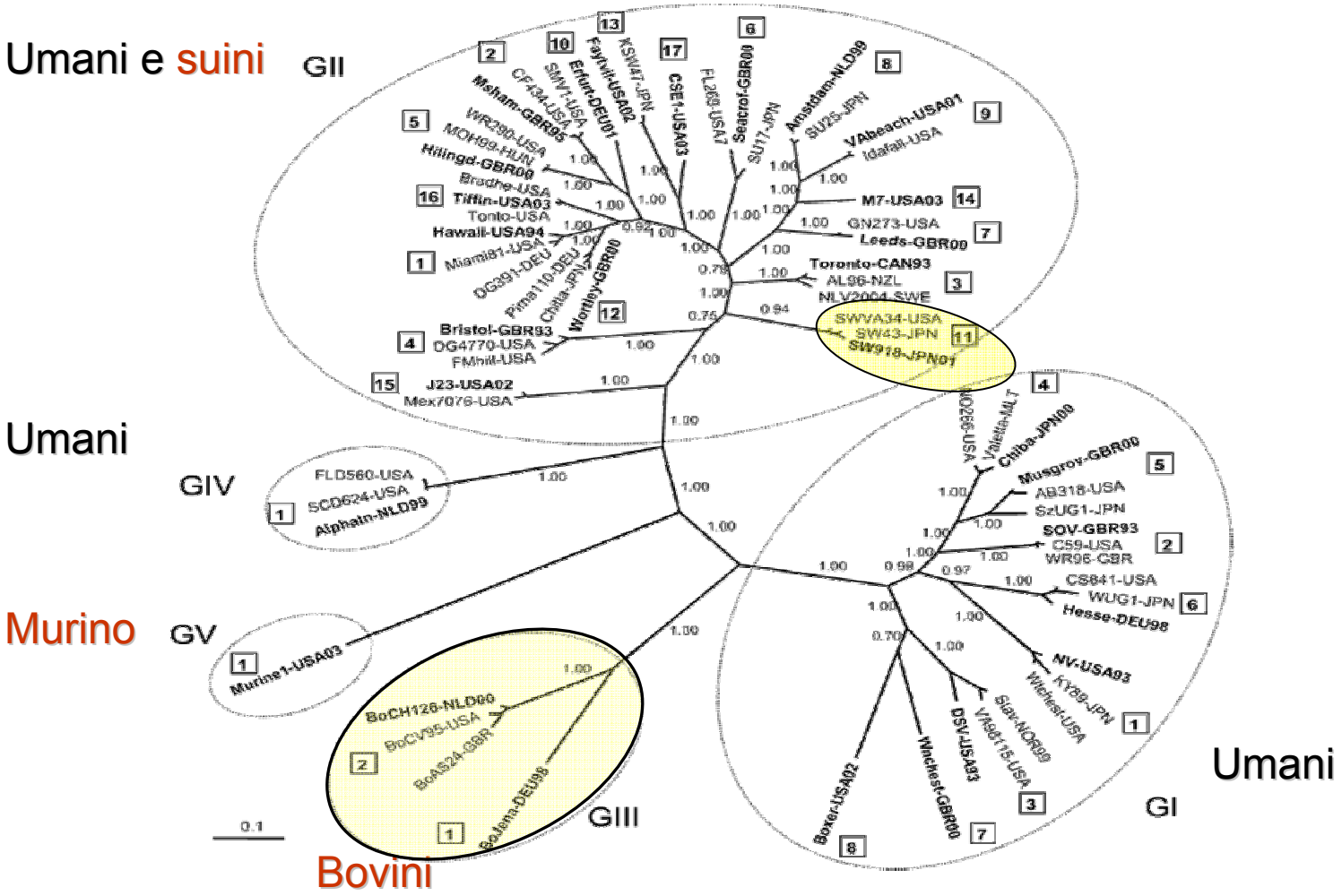
Qiu-Hong Wang,* Myung Guk Han,* Sonia Cheetham,* Menira Souza,* Julie A. Funk,† and Linda J. Saif*



Emerging Infectious Diseases • www.cdc.gov/eid • Vol. 11, No. 12, December 2005

FILOGENESI DEI NOROVIRUS

Elevata variabilità; classificati in 5 genogruppi



JOURNAL OF VIROLOGY, Nov. 2006, p. 10372–10381 Vol. 80, No. 21
0022-538X/06/$08.00+0 doi:10.1128/JVI.00809-06

Pathogenesis of a Genogroup II Human Norovirus in Gnotobiotic Pigs

Sonia Cheetham,[1] Menira Souza,[1] Tea Meulia,[2] Sheila Grimes,[3] Myung Guk Han,[1] and Linda J. Saif[1]*

APPLIED AND ENVIRONMENTAL MICROBIOLOGY, Mar. 2006, p. 1800–1809 Vol. 72, No. 3
0099-2240/06/$08.00+0 doi:10.1128/AEM.72.3.1800–1809.2006

Human and Animal Enteric Caliciviruses in Oysters from Different Coastal Regions of the United States

Veronica Costantini,[1] Fabienne Loisy,[2] Lynn Joens,[3] Françoise S. Le Guyader,[2] and Linda J. Saif[1]*

MED-VET-NET

Welcome to the partner workplace for the virtual institute of Med-Vet-Net!

WP31 - ZOOVIR-NET

Food producing animals as a potential source of emerging viral zoonoses (ZOOVIR-NET)

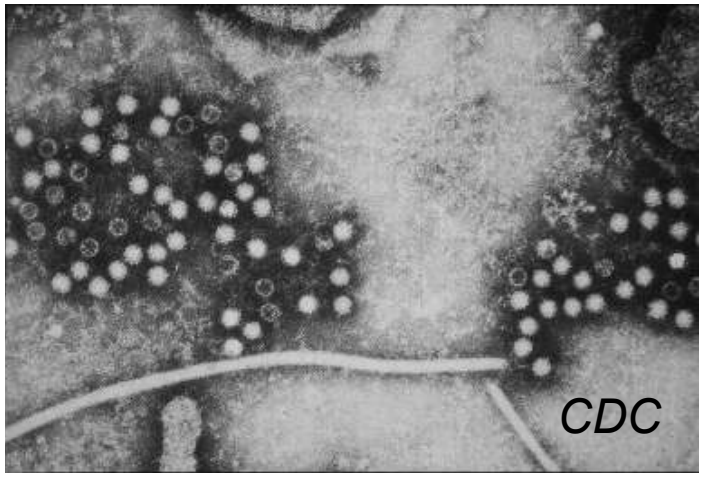
Objectives

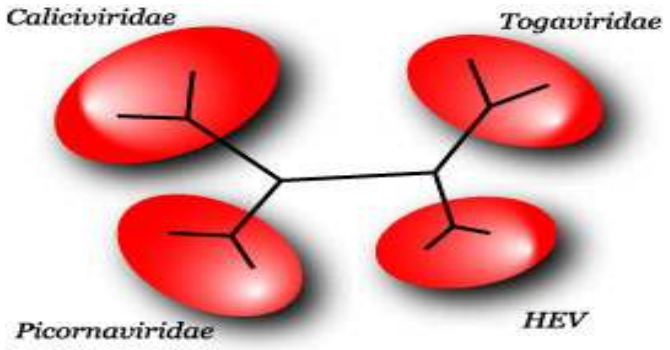
- To evaluate existing reagents and technologies; develop improved tests.
- To identify possible cell culture systems for HEV, EMCV and Anellovirus.
- To investigate the host/cell growth restriction of virus variants and produce antigens for immunological studies.
- To establish the presence and genomic and/or antigenic characteristics of HEV, Anellovirus and EMCV in swine populations in different countries. Comparative analyses of the genomes of swine/human strains.
- To establish a centralized database allowing WP31 and other interested Med-Vet-Net scientists to access standardized data on viral strains and genomic sequences characterized during the study.
- To assess TBEV milk transmission. To adapt available serologic TBEV ELISA kits to investigating dairy animal infection. To establish recommendations for milk production control in endemic regions.
- To contribute to the integration of research on the detection, monitoring and risk factor analysis of new/emerging food-borne zoonoses in production animal reservoirs.
- To develop joint (epidemiological and microbiological) strategies for research of emergence of
food-borne pathogens from various reservoirs.
- To improve quantitative PCR technology and primer specification for:
i) HEV in swine blood and faecal samples, and water and food samples
ii) EMCV in blood and tissues and food
iii) Anellovirus in the food chain
iv) TBEV in milk.
- To develop novel immune reagents and implement knowledge on selected viral antigens.
- To adapt MAbs to user friendly diagnostic tests to be assayed by the WP partners.
- To investigate the tissue/organ sites of virus replication and persistence of swine viruses in production animals, for assessing possible risks in the food chain.
- To extend knowledge developed within the WP activity to MVN, institutions and collaborating networks in order to target risks, and address possible control measures.

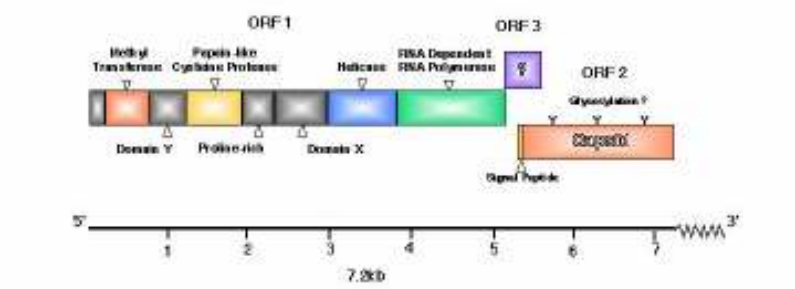
Deliverables

1. Database of relevant contacts/expertise/reagents available on selected zoonotic and emerging viruses (TTV, HEV, EMCV, TBEV) within MedVetNet and in Europe by month 6
2. Validated diagnostic protocols for emerging viruses in pig populations and TBEV in farm

Virus dell'Epatite E (HEV)

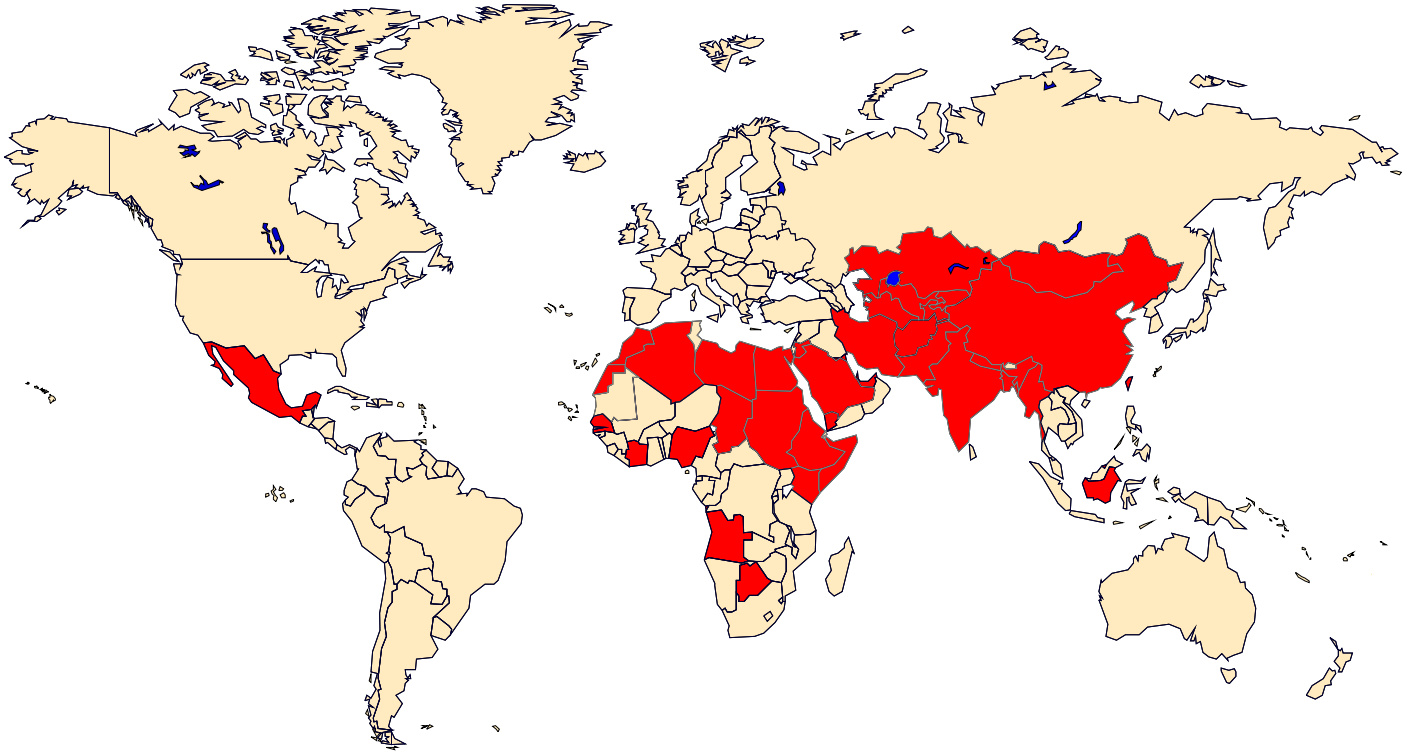






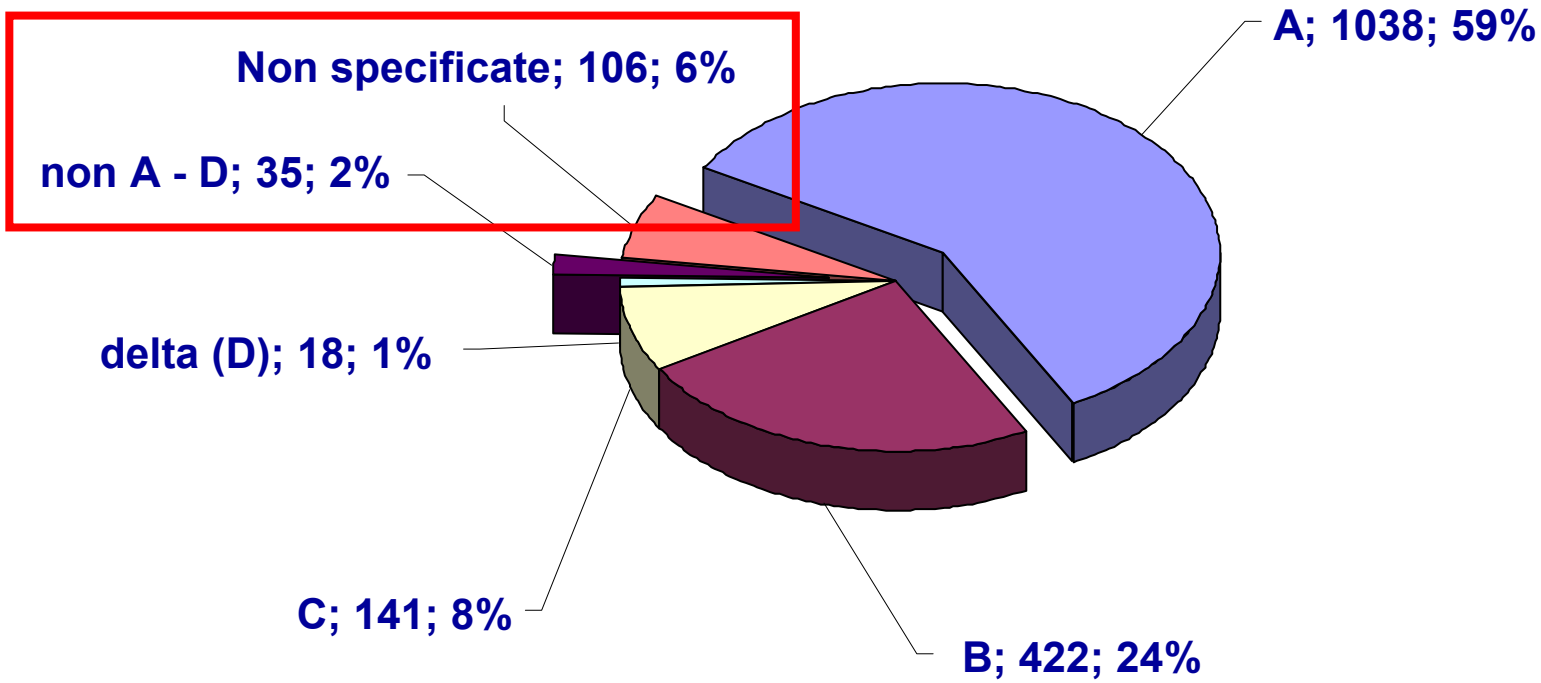
- Unenveloped, ssRNA virus, small (27-34 nm)
- Formerly associated with *Caliciviridae*, recently assigned to the new genus *Hepevirus*

Distribuzione dell'Epatitie E nel mondo



- The largest outbreak was reported in northeast China, with 100,000 people affected between 1986 and 1988
- The overall case fatality rate is 4% (much higher in pregnancy)

Epatiti virali in Itala
(SEIEVA, 1997-2003)



Hu-HepE incidence in Italy, 2003: 0.4/100,000

HEV sieropositivi, Italia

NORD

Milano (0.95)
Genova (1.3)
Venezia (2.6)

CENTRO

Firenze (1.4)
S.Marino (2.3)

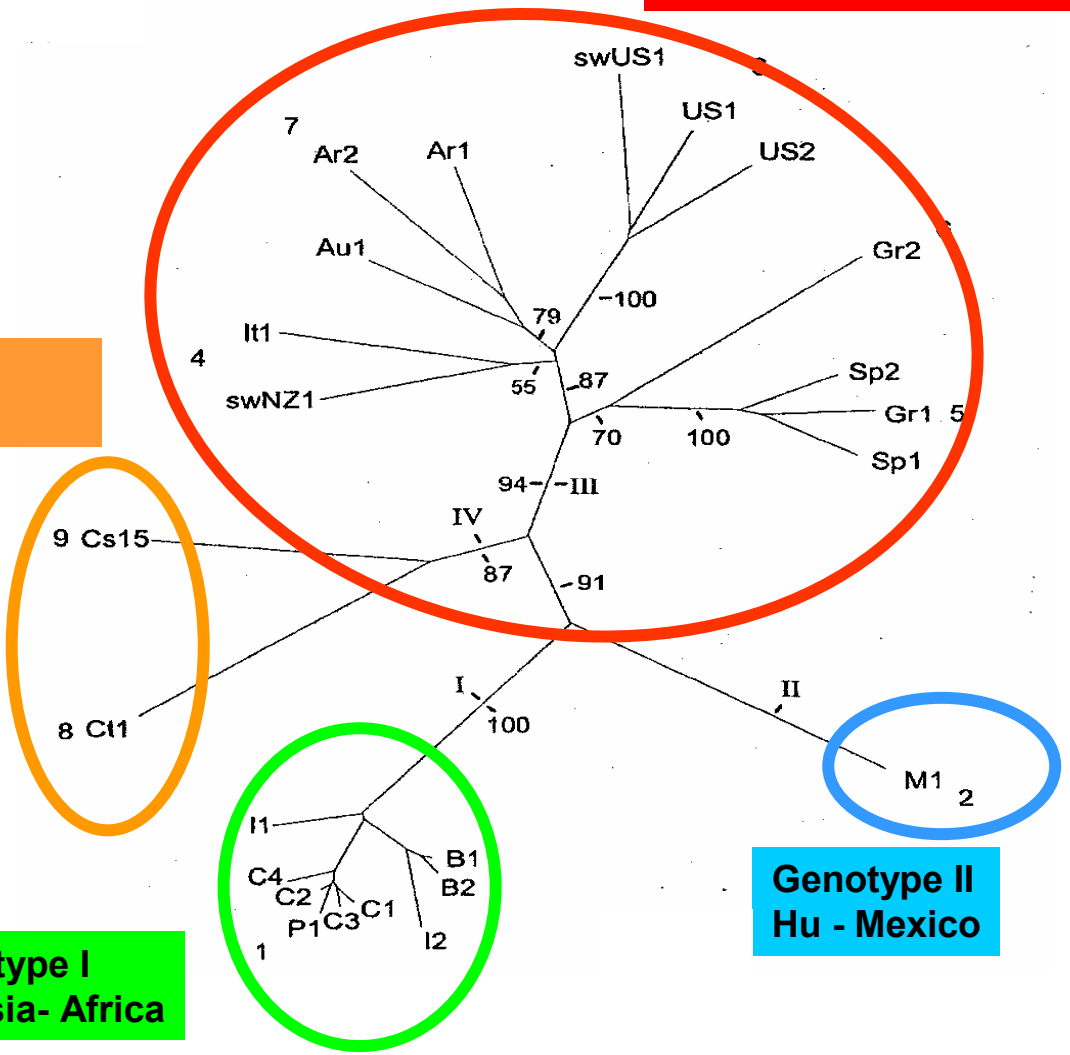
SUD

Bari (1.5)
Foggia (3)
Catania (3)
Cagliari (5.4)

Genotipi di HEV

- 1 sierotipo
- 4 genotipi
- Genotipi 3 e 4 sono identificati nell'uomo e negli animali

Genotype III
Industrialized countries

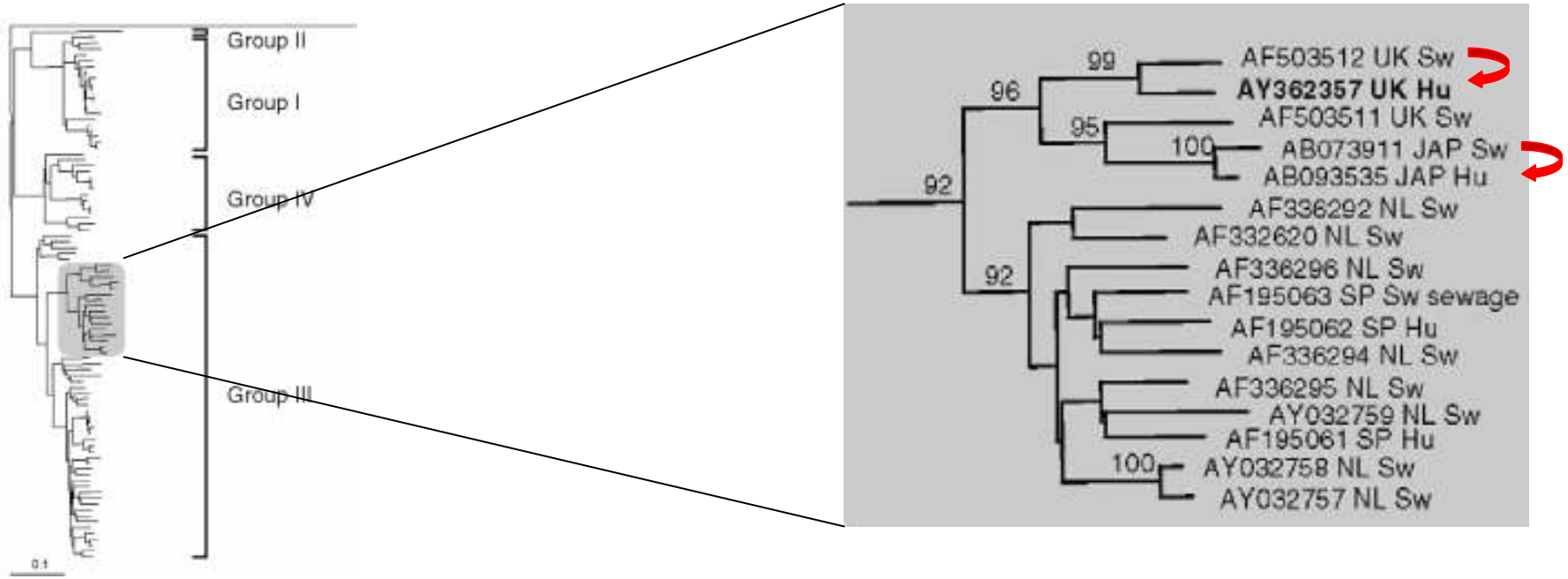


Genotype IV
Asia

Genotype I
Hu Asia- Africa

Genotype II
Hu - Mexico

Ceppi zoonotici di HEV dal suino?



… a case of acquired infection of a strain of hepatitis E virus (HEV) with a 100% amino acid identityto the analogous region in strains of HEV circulating in a United Kingdom pig herd. This case further supports the theory that autochthonous HEV infection in industrialized countries is zoonotic…

Banks *et al. Emerging Infect Dis* 10, 2004

Ceppi zoonotici di HEV dal suino?

- Anti-HEV antibodies in numerous animal species *(pigs, rodents, chickens, dogs, cows, sheep, goats)* from both developing and industrialized countries
- The first (1997) US swine HEV is genetically correlated to US human strain.
- Recently, other human and swine HEV strains from same geographic areas have been shown to be genetically correlated
- Recent seroepidemiological studies indicate that individuals working with swine have higher risk of HEV infection

Il suino come *reservoir di* HEV?

J Infect Dis. 2006 Jun 15;193(12):1643-9. Epub 2006 May 10.

Related Articles, Links

The University of Chicago Press

Swine as a Principal Reservoir of Hepatitis E Virus that Infects Humans in Eastern China.

Zheng Y, Ge S, Zhang J, Guo Q, Ng MH, Wang F, Xia N, Jiang Q.

Department of Epidemiology, School of Public Health, The Key Laboratory on Public Health Safety, Ministry of Education, Fudan University, Shanghai, China.

Background and methods. Genotype IV hepatitis E virus (HEV) has been isolated from humans and swine. To study the relationship between the human and swine reservoirs, we estimated their respective viral burden, analyzed the genetic makeup of the virus populations, and assessed the risk of infection associated with swine farming.Results. In 2 swine-farming districts of eastern China, 9.6% of swine and 0.3% of healthy human subjects excreted HEV in stool, as did 68.8% of patients with confirmed HEV infection. The virus population circulating in humans consisted of genotype I and at least 4 phylogenetically distinct subgroups of genotype IV viruses, 2 of which concurrently circulated among swine. Persons engaged in occupations related to swine farming were found to have a 74% higher risk of infection than those engaged in other occupations, and persons living in communities downstream of the swine farms were found to have a 29% higher risk of infection than persons living in communities upstream.Conclusions. Genotype IV HEV is freely transmitted between humans and swine. Because the size of the swine population and its viral burden are much larger than those of humans, transmission of the virus most likely is directed from swine to humans. Infection can be acquired through contact with swine and their waste.

PMID: 16703507 [PubMed - in process]

HEV come agente zoonotico alimentare?

- Consumption of uncooked deer meat (*sashimi*) is a risk factor for exposure to HEV in Japan.
- HEV RNA was isolated from a sample of uncooked deer meat eaten by a patient who developed acute hepatitis E.
- In Japan, a proportion (1.9%) of packaged raw pig livers for sale were contamined with HEV.

Tei et al. 2003. Lancet, 362: 371-373
Tamada et al., 2003. J. Hepatol., 38: 827-32.

Journal of General Virology (2003), **84**, 2351–2357 DOI 10.1099/vir.0.19242-0

Short Communication

Sporadic acute or fulminant hepatitis E in Hokkaido, Japan, may be food-borne, as suggested by the presence of hepatitis E virus in pig liver as food

Yasuyuki Yazaki,[1] Hitoshi Mizuo,[2] Masaharu Takahashi,[3] Tsutomu Nishizawa,[3] Nobuhiko Sasaki,[4] Yuhko Gotanda[5] and Hiroaki Okamoto[3]

Journal of General Virology (2007), **88**, 912–917 DOI 10.1099/vir.0.82613-0

Short Communication

Detection and characterization of infectious *Hepatitis E virus* from commercial pig livers sold in local grocery stores in the USA

A. R. Feagins,[1] T. Opriessnig,[2] D. K. Guenette,[1] P. G. Halbur[2] and X.-J. Meng[1]

HEV in suini allevati, Italia

Rilascio medio con le feci:

42%

Range (6 allevamenti)

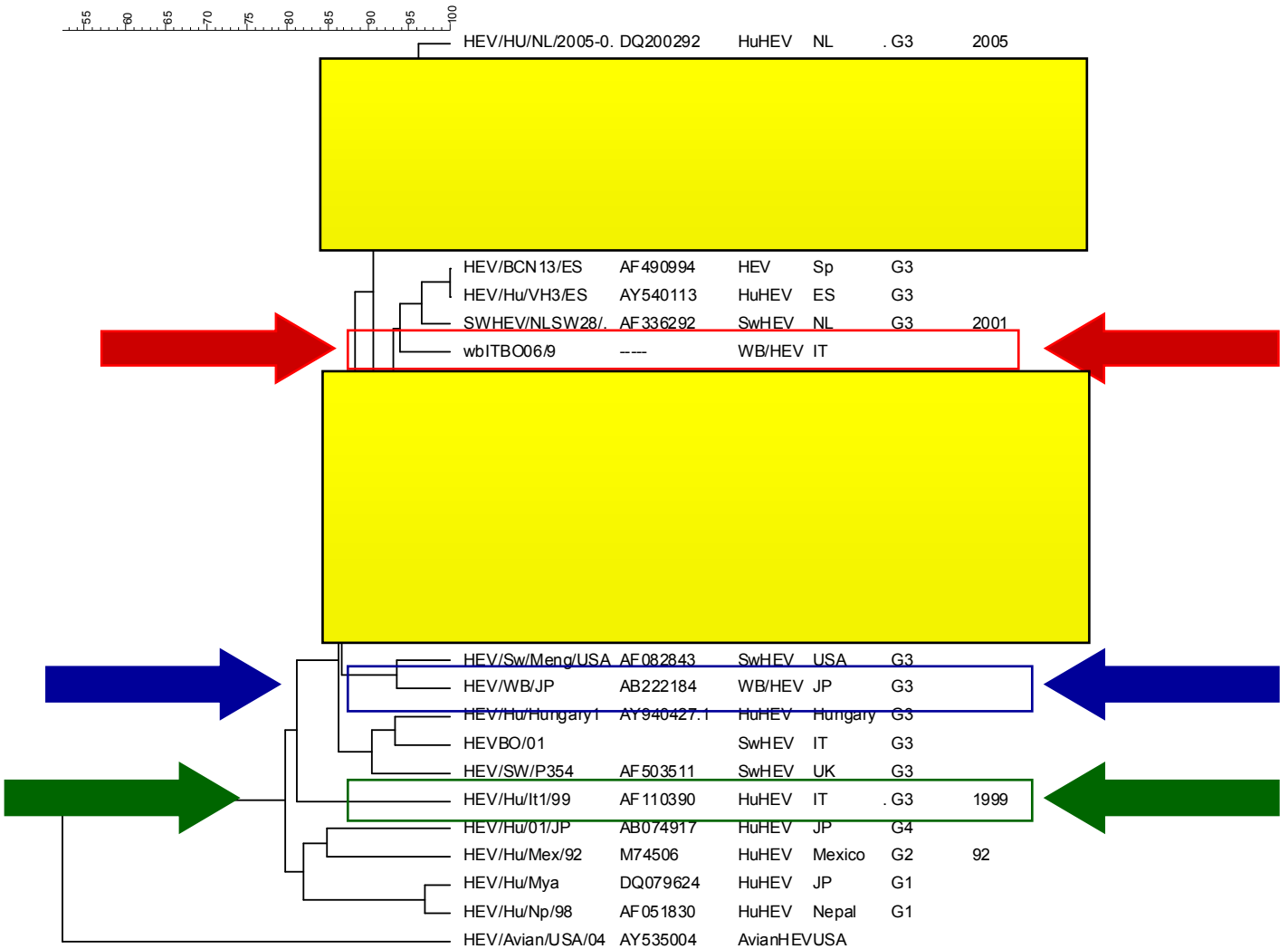
(12.8 – 72.5%)

HEV Infezione da HEV nei cinghiali

(Parco Gessi-Bolognesi, BO)

Sex class	Age class	Estimated total population	Total examined	HEV positive	HEV prevalence	Estimated prevalence in the whole population (95% CI)
All animals	<12 months	172	23	8	34.8	20.4 - 51.7
	13-24 months	87	53	11	20.8	14.9 - 27.6
	> 24 months	20	12	3	25.0	15.0 - 40.0
	Total	279	88	22	25.0	18.6 - 32.6
Male	<12 months	74	8	4	50.0	25.7 - 74.3
	13-24 months	39	20	3	15.0	7.7 - 28.2
	> 24 months	6	6	2	33.3	-
	Total	119	34	9	26.5	16.8 - 38.7
Female	<12 months	98	15	4	26.7	12.2 - 46.9
	13-24 months	51	33	8	24.2	17.7 - 33.3
	> 24 months	11	6	1	16.7	9.1 - 36.4
	Total	160	54	13	24.1	16.3 - 33.7

Caratterizzazione genomica di HEV da cinghiali in Italia



Genotipi P e G di rotavirus comuni nell'uomo e negli animali

G type	P serotype [genotype]										
	1A[8]	1B[4]	2A[6]	2C[6]	3[9]	4[10]	5A[3]	6[1]	8[11]	11[14]	12[19]
1	Wa	AU64	M37	AU19	K8						
2		DS-1	1076								
3	P	107E1B	McN13		AU-1		HCR3		157C		
4	Hochi		ST-3								
5	Br1054										
6					PA151					PA169	
8		MW333	MW023			69M				HAL1166	
9	WI61		US1205						116E		Mc323
10									I321	Mc35	
12			US585								

Globally common
Regionally common
Uncommon
Neonates

JID 2005:192 (Suppl 1) • Gentsch et al.

GRAZIE

PER L'ATTENZIONE