

ARTICLE 152

"A high level of human health protection shall be ensured in the definition and implementation of all Community policies and activities."

"The Community shall encourage cooperation between the Member States... and, if necessary, lend support to their action."

€uropean surveillance





The International network for the surveillance of Enteric Infections – *Salmonella*, VTEC 0157 and *Campylobacter*

Funded by the European Centre for Disease Prevention and Control

(previously by DG SANCO and DG 12 under Framework 4)



What does Enter-net do?

- Three main strands;
 - International databases and surveillance
 - Urgent enquiries/international outbreaks
 - EQA schemes
 - Salmonella sero-, phage typing and AST
 VTEC serotyping, virulo-typing



Definition of Surveillance

The ongoing systematic collection, collation and analysis of data and the prompt dissemination of the resulting information to those who need to know so that an action can result.

AD Langmuir 1963

ii Information for Action !!



Objectives of Surveillance

By monitoring disease trends to:

- **1. Predict epidemics**
- 2. Detect outbreaks
- 3. Identify risk groups
- 4. Evaluate effectiveness of interventions
- 5. Set priorities for resource allocation
- 6. Provide aetiological clues



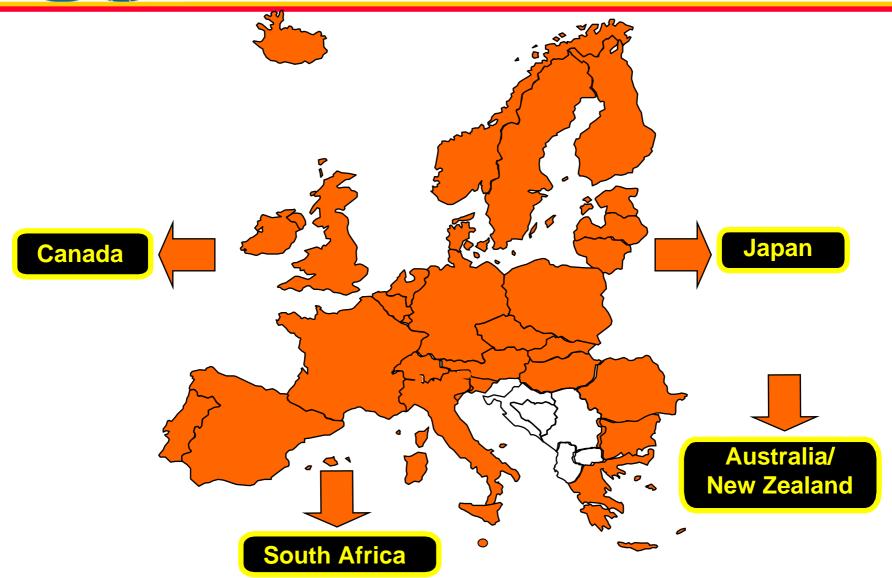
Objectives of Surveillance

By monitoring disease trends to:

- **1. Predict epidemics**
- **2. Detect outbreaks**
- 3. Identify risk groups
- 4. Evaluate effectiveness of interventions
- 5. Set priorities for resource allocation
- 6. Provide aetiological clues
- 7. Recognise and assess emerging issues



Participants

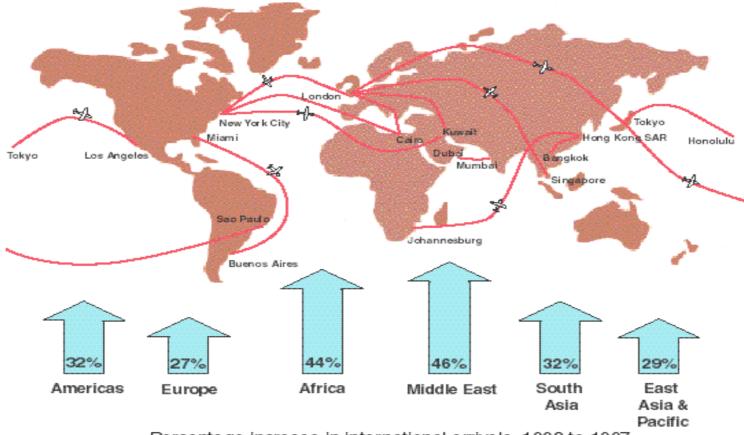




ENTER - NET The impact of international travel.

Frequent flyers

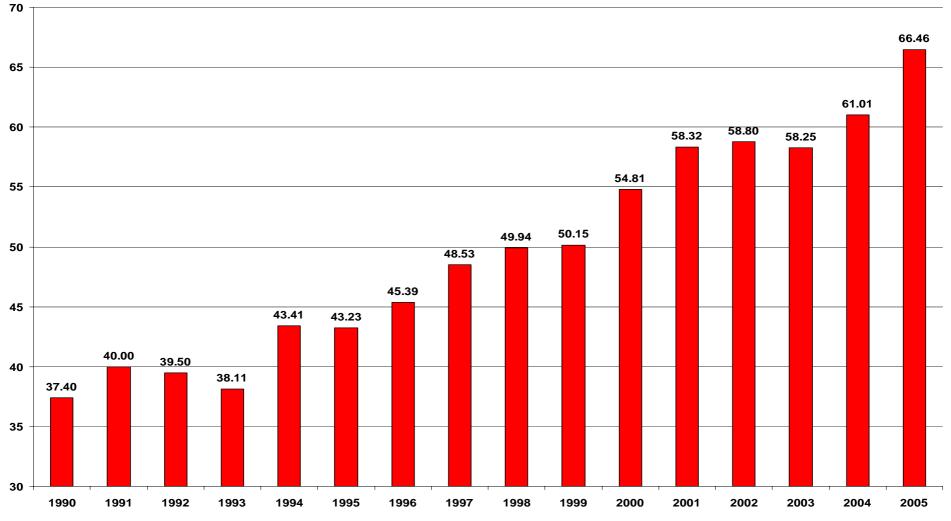
Most popular air routes between continents, 1997



Percentage increase in international arrivals, 1993 to 1997



Imports of agrifoods into the EU-15 (1,000M Euro)



Source: Eurostat yearbook 2005



E. coli O157 Multi-state Outbreak 0609mIEXH-2c – September 2006









Salinas Valley, CA



Pulse Net USA





Objectives

For human isolates:

- Maintain timely international Salmonella and VTEC 0157 databases
- Extend VTEC O157 typing
- Conduct international VTEC O157 Quality Assurance
- Monitor salmonella anti-microbial resistance
- Rapidly recognise and report international outbreaks
- Create international foodstuffs database



Methods

- Harmonisation of reference laboratory procedures
- Standardisation of accompanying data
- Development of collaboration principles
- Rapid data collection and information exchange
- Regular workshops for all participants



Microbiological achievements

- Harmonisation of salmonella phage-typing,
- Countries routinely reporting phage-type data increased from five to 12,
- 14 countries reported phage typing results in 2005
- Study to harmonise results of antibiotic susceptibility testing,
- Encourage the use of VTEC O157 phage-typing.



Epidemiological achievements

- Development and maintenance of the international salmonella database,
- Creation of the international *E. coli* database.
- Application of new software to improve outbreak recognition,
- Expansion of the database to incorporate antibiotic resistance testing results,



VTEC file specification - I

Reference data.

Country Institute Reference number Source Region



VTEC file specification - II

Microbiological data.

Serogroup O157 phage type VT type Presence of intimin gene Specimen type Date of receipt in reference laboratory Date of receipt in source laboratory Antibiotic resistance testing results



VTEC file specification - III

Epidemiological data.

Clinical manifestation Age Ageband Sex Vehicle implicated Travel associated Country of travel

Data are encoded where appropriate according to the full specification.



VTEC file specification - IV

Data transfer

Data format is a flat ASCII (text) file, each record being 194 characters long.

Data are transferred to the co-ordinating centre using standard Internet methods, with encryption, if required.

Data are incorporated into the database and analysed regularly on a monthly, quarterly and ad hoc basis.



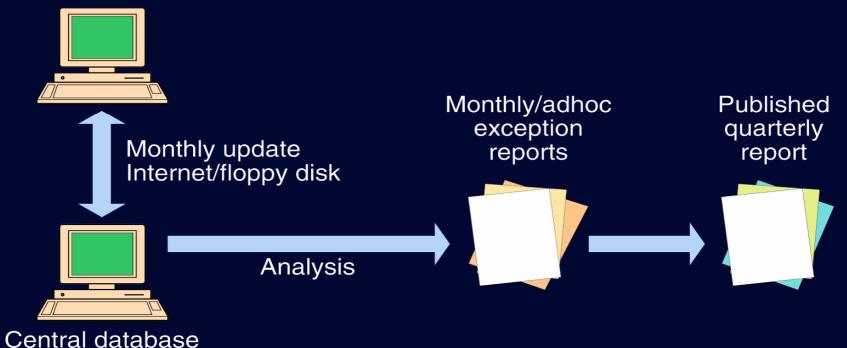
Antimicrobials surveilled

- Aminoglycosides
 - Streptomycin, gentamicin, kanamycin
- ß-lactams
 - Ampicillin, cefotaxime
- tetrahydrofolate inhibitors
 - Sulphonamides, trimethoprim
- Quinolones
 - Nalidixic acid, ciprofloxacin
- Other antimicrobials
 - Chloramphenicol, tetracyclines



Data Collection and Dissemination

Collaborating country





VTEC Reports – II

Contains information on

- 1. Quarterly data major trends
 - Serogroups totals
 - Phage types
- 2. AST results
- 3. Age and gender breakdown
- 4. Clinical manifestation
- 5. Country breakdown
 - Not in public domain report

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•		eeregreeker.								
-		Serogroup	Freq	%	Freq	%	Quarterly data – major trends.			
б •			20	06	20	05				
-		0157	147	41.6	148	35.6	Details in tables 1 & 2 refer to the thirteen			
		026	33	9.3	44	10.6	countries that have supplied data			
-		091	22	6.2	18	4.3	electronically for 2006 and 2005. Tables 3-7			
7		0103	16	4.5	33	7.9	show the results from all cases that are in the database for this year.			
		0146	8	2.3	7	1.7	the database for this year.			
21 ·		0145	7	2.0	12	2.9	The total number of reports in the database			
-		055	4	1.1	8	1.9	shows a decrease of 15.1% over the same			
с С		087	3	0.8	1	0.2	period last year with 353 cases as compared			
-		0111	3	0.8	12	2.9	to 416 in 2005.			
. 14		0113	3	0.8	2	0.5				
-		Untyped/untypable	59	16.7	65	15.6	<i>E. coli</i> O157 was the most commonly			
11		Other	48	13.6	66	15.9	identified serogroup (table 1). Where phage			
-		Total	353		416		typing is performed phage type 21/28 was			
91			Table	1			the predominant strain the same as in 2005			
-		OdE7 Dhawa tawa	Ener	0/	Eren		(table 2). The breakdown of serogroups by			⊻
. 17		O157 Phage type	Preq 20		Freq 20	% 05	country is gi∨en in table 7.			0 7

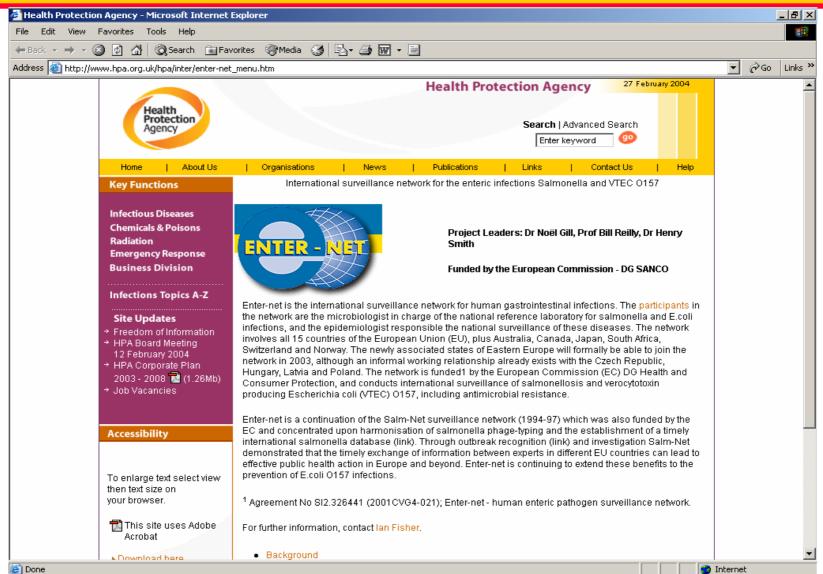
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Web access – I





Web access – II

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Enter-net outputs

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across the European Union, the number of cases reported to



Peer-reviewed publications – I

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Thumbnails Bookmarks	 Résistance aux antibiotiques d'isolats de Salmonella enterica issus de cas de salmonellose humaine en Europe en 2000 : résultats d'une surveillance multicentrique internationale EJ Threffall¹, IST, Fisher², C. Berghold³, P. Gerner-Smidt⁴, H.Tschäpe⁵, M. Comican⁶, I. Luzzi⁷, F. Schnieder⁸, W. Warnet⁹, J. Machado¹⁰, G. Edwards¹¹ Public Health Laboratory Service, Laboratory of Enteric Pathogens, London, Royaume-Uni ² Enter-net Hub, Gastrointestinal Diseases Division, PHLS-COSC, London, Royaume-Uni ² Enter-net Hub, Gastrointestinal Diseases Division, PHLS-COSC, London, Royaume-Uni ² Enter-net Hub, Gastrointestinal Diseases Division, PHLS-COSC, London, Royaume-Uni ³ Enter J. Status Serum Institut, Copenhagen, Danemark ⁴ Entersity College Hostral, Galway, Hande ⁴ University College Hostral, Galway, Hande ⁵ University College Hostral, Galway, Hande ⁵ University College Hostral, Galway, Hande ⁹ University College Hostral, Luxernbourg ⁹ University College Hostral, Galway, Hande ⁹ University College Hostral, Savay, Hostraloge Hostral, Colege Hostral, Hostral Hostral Galway, Hostral	Antimicrobial drug resistance in isolates of Salmonella enterica from cases of salmonellosis in humans in Europe in 2000: results of international multi-centre surveillance EJ Threfal ¹ , IST, Fisher ³ , C, Berghold ³ , P, Gerner-Smidt ⁴ , H.Tschäpe ⁵ , M. Cormican ⁶ , I. Luzzi ⁷ , F. Schrieder ⁴ , W. Wannet ⁶ , J. Machado ²⁰ , G. Edwards ¹¹ ¹ Public Health Laboratory Service, Laboratory of Enteric Pathogens, London, UnitedKingdom ² Enter-net Hub, Gastrointestinal Diseases Division, PHLSCOBSC, London, UnitedKingdom ³ National Salmonella Reference Laboratory, Graz, Austria ⁴ Dept of Gastrointestinal Infections, Statens Serum Institut, Copenhagen, Denmark ⁵ Robert Koch-Institut, Wernigerode, Germany ⁶ National University of heland, Galway, Ireland ⁷ Istituto Superiore di Sarita, Laboratory of Medical Bacteriology & Mycology, Roma, Italy ⁸ Laboratore National de Sarité, Luzembourg ⁹ National Institute of Public Health and the Envirorment, Diagnostic Laboratory for Infectious Diseases and Perinatal Screening, Bilthoven, the Netherlands ⁹ Instituto Nacional de Saude, Lisbon, Portugal	
	¹¹ Scottish Salmonella Reference Laboratory, Stothill Hospital, Glasgow, Royaume-Uni En 2000, le réseau Enter-net a collecté les résultats d'antibio- grammes pour des isolats issus de plus de 27 000 cas de salmo- nellose humaine, répartis dans dix pays européens. Près de 40% étaient résistants à un antibiotique au moins, 18% étaient multiré- sistants. La résistance à l'ampicilline, à la streptomycine, aux sul- phonamides et aux tétracyclines était fréquente, avec plus de 20 % de résistance à au moins un de ces antibiotiques. La résistance cli- nique à la ciprofloxacine était rare, avec seulement 0,5% de résis- tance (CMI >1,0 mg/l). La résistance à l'acide nalidixique couplée à une sensibilité réduite de la ciprofloxacine (CMI 0,25–1,0 mg/l) était plus fréquente, présente chez 14% des isolats. La résistance aux céphalosporines de troisième génération était rare, avec un taux de résistance de 0,6% seulement à la céfotaxime. Dans tous les pays, le taux de multirésistance était le plus élevé chez Sal- monella enterica Typhimurium, avec 51% d'isolats multirésistance était 13 of 28 ▶ H 8.26×11.68 in □ H HH ≤	¹¹ Scottish Salmonella Reference Laboratory, Stobhill Hospital, Glasgow, UnitedKingdom The Enter-net surveillance system received results of anti- microbial sensitivity tests for isolates from over 27 000 cases of human salmonellosis in 2000 in 10 European countries. Almost 40% of isolates were resistant to at least one antimi- crobial, with 18% multiresistant. Resistance to ampicillin, strep- tomycin, sulphonamides and tetracyclines was common, with over 20% of isolates resistant to at least one of these antimi- crobials. Clinical resistance to ciprofloxacin was rare, with only 0.5% of isolates exhibiting such resistance (MIC > 1.0 mg/l). Resistance to nalidixic acid coupled with a decreased suscep- tibility to ciprofloxacin (MIC 0.25–1.0 mg/l) was more com- mon, with 14% of isolates showing these properties. Resistance to third-generation cephalosporins was rare with only 0.6% of isolates resistant to cefotaxime. In all countries multiple resis- tance was most common in <i>Salmonella</i> enterica serotype Typhi- murium with 51% of isolates multiresistant in total. In England	



Peer-reviewed publications – II

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Thumbnails Bookmarks	CLM 655 ORIGINAL ARTICLE	-
Thumbnails	 definitive phage type 204b in 2000 P. D. Crook¹, J. F. Aguilera^{1,2}, E. J. Threlfall³, S. J. O'Brien¹, G. Sigmundsdóttir⁴, D. Wilson⁵, I. S. T. Fisher⁶, A. Ammon⁷, H. Briem⁴, J. M. Cowden⁸, M. E. Locking⁸, H. Tschäpe⁷, W. van Pelt⁹, L. R. Ward³ and M. A. Widdowson⁹ ¹Gastrointestinal Diseases Division, PHLS Communicable Disease Surveillance Centre, London, UK, ²European Programme for Intervention Epidemiology Training (EPIET), ³PHLS Laboratory of Enteric Pathogens, Central Public Health Laboratory, London, UK, ⁴Division of Infectious Disease Control, Directorate of Health, Reykjavik, Iceland, ⁵County Durham and Darlington Health Authority, UK, 	[Q1] [Q2]
	 ⁶Enter-net Surveillance Hub, PHLS Communicable Disease Surveillance Centre, London, UK, ⁷Robert Koch Institut, Berlin/Wernigerode, Germany, ⁸The Scottish Centre for Infection and Environmental Health, Glasgow, UK and ⁹RIVM, Department of Infectious Disease Epidemiology, Bilthoven, The Netherlands Objective To describe the clinical, epidemiologic and microbiological features of a large outbreak of infection with a multiresistant Salmonella enterica serotype Typhimurium definitive type DT204b infection involving at least 392 people in five European countries. 	
	Methods Icelandic public-health doctors responded to a report on an Internet news site of an outbreak of infection with a multiresistant strain of Typhimurium DT104 in England by contacting the Public Health Laboratory Service (PHLS) Communicable Disease Surveillance Centre (CDSC). An international alert was sent out through Enter-net. All strains from England & Wales, The Netherlands, Scotland and Germany, and 17 of the outbreak isolates from Iceland, were phage-typed, screened for antimicrobial resistance, and subjected to molecular typing. Hypothesis-generating interviews were	



Objectives of Surveillance

By monitoring disease trends to:

- **1. Predict epidemics**
- **2. Detect outbreaks**
- 3. Identify risk groups
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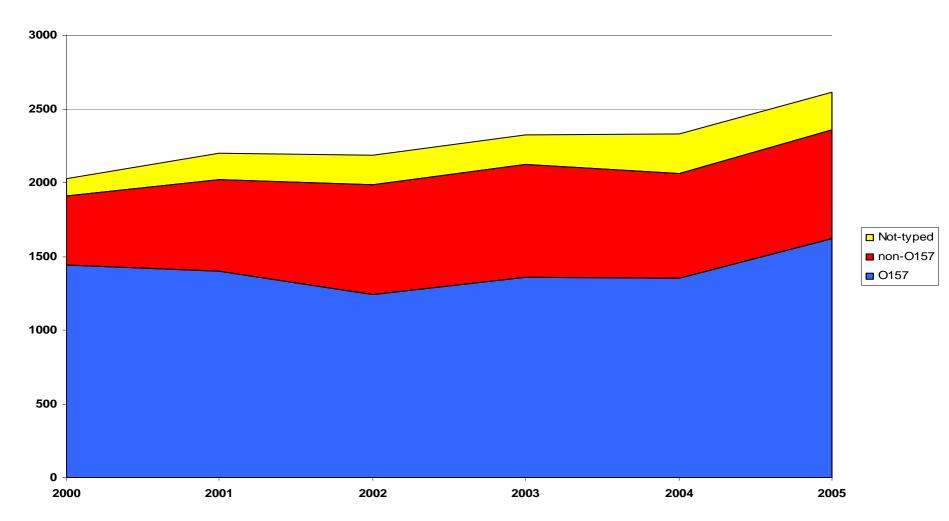
VTEC surveillance results 2000-05

Serotype	Freq	%	Serotype	Freq	%
O157	8,750	61.6	O146	154	1.1
O26	832	5.9	O128	108	0.8
O103	669	4.7	O113	83	0.6
O91	448	3.2	02	78	0.5
O145	296	2.1	Other	2,610	18.2
0111	182	1.3	Total	14,21	<u>0</u>



Trends in VTEC infections

VTEC 2000-2005 (18 countries)





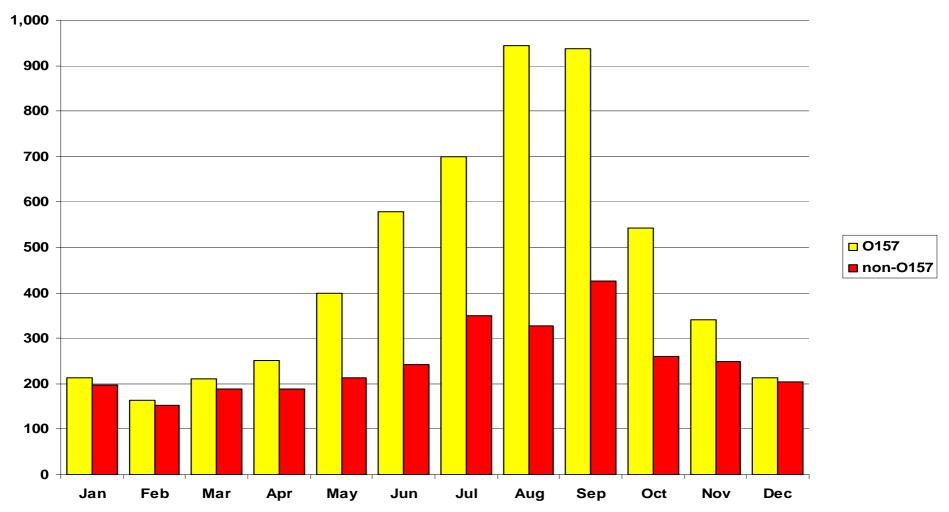
Percent of O157 and non-O157 by country - Enter-net database 2000-05





O157 and non-O157 seasonality

Human VTEC O157/non-O157 by month 2000-04 (n=5,491/2,999)





ENTER - NET VTEC vt1 and vt2 production

O157	VT2 +ve	VT2 -ve	Total
VT1 +ve	1,490	37	1,527
VT1 -ve	1,456	48	1,504
Total	2,946	85	3,031

Non-0157	VT2 +ve	VT2 –ve	Total
VT1 +ve	591	2,087	2,678
VT1 -ve	1640	154	794
Total	1,231	2,241	3,472



ENTER - NET VTEC vt1 and vt2 production

O157	VT2 +ve	VT2 -ve	Total	
VT1 +ve	49.2%	1.2%	50.4%	
VT1 -ve	48.0%	1.6%	49.6%	
Total	97.2%	2.8%	100%	

Non-0157	VT2 +ve	VT2 –ve	Total
VT1 +ve	17.0%	60.1%	87.1%
VT1 -ve	18.4%	4.5%	22.9%
Total	35.4%	64.6%	100%



VTEC other virulence factors

Eae gene (n=6,250)	O157	Non-O157	Total
+ve	35.8%	36.7%	72.5%
-ve	0.8%	22.7%	27.5%
Total	37.6%	63.4%	100%

ehly (n=4,959)	0157	Non-0157	Total
+ve	33.3%	48.0%	81.3%
-ve	1.9%	16.8%	18.7%
Total	35.2%	64.8%	100%



Benefits

- Improved outbreak recognition
- More effective outbreak investigation
- Strengthening of national surveillance
- Acceleration of applied research
- Reduction in risks from international food trade
- Interactive network of public health professionals



Benefits – II

- Enter-net is not a "formal" alert system
 It is not the EWRS, GOARN or RASFF
- Its remit is to identify if an international outbreak is occurring
- And if so, it has direct access to the epidemiological and microbiological expertise to respond to and investigate those outbreaks



International outbreaks recognised - I

Organism	Cases	Countries involved (index)	Year	Association
S. Newport	100+	E&W, Finland	1998	None confirmed
S. Livingstone	100+	Austria, Czech Republic, Denmark, E&W, Finland, Germany, Netherlands, Norway, Sweden (identified by data pooling)	1997	Travel to Tunisia
<i>E. coli</i> 0157/ HUS	15	Denmark, E&W, Finland, Sweden	1997	Water
S. Anatum	19	Eire, E&W, France, Scotland	1996	Baby milk (France)
S. Agona	4,000+	Canada, <mark>E&W</mark> , Israel, USA	1996	Kosher snack
S. Dublin	30+	France, Switzerland	1995	Cheese (France)
S. Stanley	200+	Finland, <mark>USA</mark>	1995	Alfalfa Sprouts
S. Tosamanga	28	Eire, E&W, France, Germany, Sweden, Switzerland	1995	None confirmed
S. sonnei	100+	E&W, Germany, Norway, Scotland, <mark>Sweden</mark>	1994	Lettuce (Spain)



International outbreaks recognised - II

Organism	Cases	Countries involved (index)	Year	Association
<i>E. coli</i> 0157	21	E&W, France	2002	Cucumber (Belgium)
S. Cerro	44	Belgium, France	2002	Cream pastries/ powder (Belgium)
<i>S.</i> Oranienburg	500+	Austria, Belgium, Denmark, Finland, Germany, Netherlands, Sweden. (+ve product in Canada, Croatia, Czech Republic)	2001	Chocolate (Germany)
S. Stanley	100+	Australia, Canada, E&W, Scotland	2001	Peanuts (China)
S. Typhimurium DT104	100+	Australia, Canada, E&W, Germany, Norway, <mark>Sweden</mark>	2001	Halva (Turkey)
S. Livingstone	60	Norway, Sweden	2001	Fish Pie (Sweden)
S. Typhimurium DT204b	392	E&W, Germany, Iceland, the Netherlands, Scotland	2000	Lettuce
S. Paratyphi B	309	Denmark, E&W, Finland, Germany, Ireland, <mark>Norway</mark> , Sweden, Switzerland	1999	Turkish holiday resort



International outbreaks recognised - III

Organism	Cases	Countries involved (index)	Year	Association
S. Stourbridge	60	Austria, E&W, France, Germany, Luxembourg, Norway, Netherlands, <mark>Sweden</mark> , Switzerland	2005	Unpasteurised goat's cheese (France)
S. sonnei	100	Ireland, Japan,	2005	Travel to Egypt
S. Typhimurium DT104B	60+	Finland, Spain, Sweden	2005	Lettuce
S. Saintpaul		E&W, Scotland	2005	
S. Newport	350	E&W, Scotland	2004	Lettuce
S. Thompson	100	Norway, Sweden (+ve product) [concomitant O/B in E&W]	2004	Lettuce (Italy)
S. Typhimurium DT12	27	Denmark, Norway	2004	None found
S. Typhimurium DT NT (R-AST)	30	Denmark, Norway	2004	None found
S. Typhimurium DT291	100+	Austria, Germany	2003	Eggs (Austria)



International outbreaks recognised - IV

Organism	Cases	Countries involved (index)	Year	Association
S. Hadar PT2	1,500	E&W, France, <mark>Spain</mark>	2005	Cooked chicken (Netherlands)
<i>S.</i> Typhimurium DT 104 MDR	30	Denmark, Netherlands, Norway	2005	Carpaccio (Italy)
S. Goldcoast	150	Denmark, E&W, Finland, Germany, Ireland, Norway, <mark>Scotland,</mark> Spain, Sweden, US	2005	Travel to Majorca
<i>E. coli</i> 0157	100	Norway, <mark>Sweden</mark>	2005	Lettuce (Sweden)
S. Typhimurium NST		Norway, <mark>Sweden</mark>	2005	Salami (Italy)
S. Virchow PT8	50+	E&W, Northern Ireland	2005	Cooked chicken (Thailand)
S. Montevideo	60+	E&W, Scotland	2006	Chocolate (UK)
S. Ajiobo	100+	E&W, Scotland	2006	Spinach (UK)
S. 4, 5, 12:i:-	150+	Luxembourg, Germany	2006	Pork



- Electronic communications have made international networks possible.
- Rapid transfer of data and information allows early recognition of international outbreaks.
- Trend information can quickly be analysed to provide an assessment of intervention measures.
- Meta-surveillance is invaluable in recognising supra-national clusters of infection.



The future - I

- Improved data quality timeliness and completeness
- International extension Candidate/other countries
- Elaboration of liaison procedures for outbreak
- Universal implementation of harmonised typing
- Standard setting for primary laboratories

• Full implementation of foodstuffs database



The future – II



• Funding is being transferred to the ECDC



What is missing – I

- Full link with non-human reference laboratories
 - VTEC phage typing is essential
 - Should we go with PFGE immediately?
- Zoonoses come from animals
 - There must be a link between systems
 - Exactly why I am here!!!!



What is missing – II

- Full implementation of the foodstuffs database!!!!!
 - With the help of your institutes
 - and the Enter-net laboratories
 - Dual access to resultant database
 Under agreed principles



Enter-net Principles of Collaboration between Participants

Prepared by HPA Colindale & Enter-net Co-Ordinator (I Fisher) Version 1.7, June 2004

Introduction

A major aim of Enter-net is the creation of real time international surveillance through a closed network which is fully transparent to all participants. The objective of sharing data and information rapidly is incorporated in the work programme of the surveillance system.

Eurosurveillance 2001; 6: 17-21



An International network for the surveillance of Enteric Infections - Salmonella and VTEC 0157

Funded by the European Commission, DG Health and Consumer Protection (previously by DG 12 under Framework 4)



Acknowledgements

Project team;

ON Gill, WJ Reilly, EJ Threlfall,

Austria; Australia; Belgium; Bulgaria; Canada; Cyprus; Czech Republic; Denmark; England, Wales and Northern Ireland; Estonia; Finland; France; Germany; Greece; Hungary; Iceland; Ireland; Italy; Japan; Latvia; Lithuania; Luxembourg; Malta; the Netherlands; New Zealand; Norway; Poland; Portugal; Romania; Scotland; Slovakia; Slovenia; South Africa; Spain; Sweden; Switzerland;

Administrator; F Stalham



Acknowledgements – II



European Commission DG SANCO

