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Severe acute respiratory syndrome: update and laboratory findings

As of 9 April 2003, 2722 cases of severe acute respiratory syndrome (SARS), including 106 deaths, have been reported to the World Health Organization (WHO) from 18 countries [<http://www.who.int/csr/sarscountry/en/>](http://www.who.int/csr/sarscountry/en/). The following are classified as affected areas: Toronto (Canada), Singapore (Singapore), Guangdong, Hong Kong Special Administrative Region, Shanxi (Peoples Republic of China), and Taiwan. (An affected area is one in which local chain(s) of transmission of SARS is/are occurring as reported by the national authorities.) Hong Kong and Guangdong remain the affected areas reporting the largest number of new cases. In Hong Kong the large community outbreak that occurred in an apartment block, which has so far has been responsible for 268 cases, appears to be coming to an end (1). The first probable case on the African continent has been reported from Pretoria South Africa on 8 April, although this is awaiting confirmation (2).

In the United Kingdom (UK) two further probable cases were reported during the weekend of 5 to 6 April. Both are currently recovering. This brings the total number of probable cases reported in the UK to five, three of whom have since recovered. Many other suspect cases are being investigated around the country. Advice for those in contact with probable or suspect cases is available on the web at http://www.phls.org.uk/topics_az/SARS/menu.htm.

Available information is being kept under review by the Communicable Disease Surveillance Centre (CDSC) to help in the production of updates for both health professionals and the general public. These include guidance for public health professionals concerning reporting and management of cases, guidance for general practitioners, and guidance for infection control in the community and in hospitals. For the general public there are also answers to frequently asked questions and the latest travel advice for journeys to and from SARS affected countries. All information can be found at http://www.phls.org.uk/topics_az/SARS/menu.htm.

The Influenza Reference Laboratory at the Health Protection Agency's Specialist and Reference Microbiology Laboratory (SRM) has found evidence of coronavirus in samples from people reported as having probable SARS (3). SRM is one of 11 WHO laboratories worldwide that are part of a multi-

centre collaborative network for SARS aetiology and diagnosis. The isolation of coronavirus has previously been reported from other laboratories in the network (4). The isolated virus is unlike any other known member of the genus *Coronavirus*.

The network has recently provided a summary on the major findings in relation to coronavirus. The Hong Kong SARS study group has also published current findings on coronavirus (5). Of 50 patients with SARS, 45 had evidence of infection with the new coronavirus, and no controls tested positive. Although coronavirus is thought to be the main agent causing SARS, other agents have been identified by collaborating laboratories. Human metapneumovirus has been detected in some SARS patients, although its significance is still under investigation.

1. World Health Organization. *Update 23 - Status of the main SARS outbreaks in different countries*. Geneva: WHO, 7 April 2003. Available at <http://www.who.int/csr/sarsarchive/2003_04_07/en/>

2. SARS – worldwide (37): cases. Archive no 20030409.0866. In: *ProMed Mail* [online]. Boston US: International Society for Infectious Diseases, 9 April 2003 [cited 10 April 2003]. Available at <<http://www.promedmail.org>>

3. *Health Protection Agency tests support corona virus link to SARS (press release)*. London: Health Protection Agency, 8 April 2003. Available at <http://www.hpa.org.uk/news/080403_sars.htm>.

4. World Health Organization. *Summary on major findings in relation to coronavirus by members of the WHO multi-centre collaborative network on SARS aetiology and diagnosis*. Geneva: WHO, 4 April 2003. Available at <<http://www.who.int/csr/sars/findings/en/>>

5. Peiris JS, Lai ST, Poon LLM, Guan Y, Yam LYC, Lim W. Coronavirus as a possible cause of severe acute respiratory syndrome. *Lancet* 2003; **361**. Published online ahead of print at <http://www.thelancet.com/journal/vol361/iss9364/early_online_publication>.

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Dramatic increase in ciprofloxacin-resistant gonorrhoea in England and Wales

The Communicable Disease Surveillance Centre (CDSC) of the Health Protection Agency has released preliminary results from the 2002 collection of the Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP) (1), which show marked increases in resistance to ciprofloxacin in England and Wales.

Between June and August 2002, consecutive gonococcal isolates from 26 genitourinary medicine (GUM) clinics were systematically collected for antimicrobial susceptibility testing at one of two central reference laboratories (figure). The minimum inhibitory concentrations (MICs) of five antimicrobials were determined, including ciprofloxacin (range tested 0.002-0.125 mg/L) extended to 32 mg/L as necessary). Clinical, demographic, and behavioural data were collected for each patient included in the collection.

Figure Genitourinary medicine clinics participating in GRASP



Over 2200 isolates from GUM clinics were tested in 2002. The overall prevalence of ciprofloxacin resistance ($\text{MIC} \geq 1 \text{ mg/L}$) was 9.8% in 2002, compared to 2.1% in 2000 ($p < 0.0005$). London, which previously had notably low prevalence, saw a marked increase in ciprofloxacin resistance from 0.9% in 2000 to 7.2% in 2002. Prevalence also rose significantly in sentinel clinics outside of London during this period, from 3.7% to 12.4%. Substantial geographic heterogeneity in the prevalence of ciprofloxacin resistance was observed, ranging from 2.8% in the North East to 18.4% in Yorkshire and Humberside. High prevalences were also observed in the South East (13.7%), East Midlands (16.5%), North West (10.1%), Wales (11.8%), and the West Midlands (12.1%). Lower increases were observed in Eastern (7.1%) and South West (6.6%) regions. The increases in ciprofloxacin resistance occurred irrespective of gender, sexuality, and reporting recent sexual contact abroad.

As ciprofloxacin is currently the recommended first line treatment for uncomplicated gonorrhoea (2), there is considerable risk of inappropriate management of this infection and its sequelae. It is a general principle that the chosen treatment regimens should eliminate infection in at least 95% of patients, and it is now clear that ciprofloxacin no longer meets this criterion.

National guidelines (2) recommend alternative treatment with cephalosporins or spectinomycin. Health practitioners should also consider the following advice:

- Ceftriaxone or an oral third generation (3g) cephalosporin is the treatment of choice
- Any patient presenting with a recent travel history should be treated with ceftriaxone
- Spectinomycin resistance is rare and is a treatment option
- Penicillin regimens may be appropriate when resistance levels are less than 5%. The GRASP steering group recommends that a decision to use penicillin should be decided locally
- Azithromycin at either 1g or 2g is not licensed for treatment of genital infections and is not recommended

Further details on GRASP are available on the website of the former PHLS at http://www.phls.org.uk/topics_az/hiv_and_sti/sti-gonorrhoea/epidemiology/grasp.htm
Data from the 2002 collection will be disseminated to clinics and regions shortly.

1. PHLS, GRASP steering group. *The Gonococcal Resistance to Antimicrobial Surveillance Programme (GRASP) Year 2001 report*. London: Public Health Laboratory, 2002. Available at <http://www.phls.org.uk/topics_az/hiv_and_sti/sti-gonorrhoea/epidemiology/grasp.htm>

2. Association for Genitourinary Medicine (AGUM), Medical Society for the Study of Venereal Diseases (MSSVD). 2002 national guideline on the Management of gonorrhoea in adults. London: Association for Genitourinary Medicine (AGUM), Medical Society for the Study of Venereal Diseases (MSSVD); 2002. Available at <<http://www.mssvd.org.uk/PDF/CEG2001/gc%200601.PDF>>

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Emergence of PVL-producing strains of *Staphylococcus aureus*

There is evidence that a new pattern of disease due to Panton-Valentine leukocidin (PVL) - producing strains of *Staphylococcus aureus* is emerging, with a slightly altered pathogenesis and epidemiology. PVL has been described as a marker of virulence, and historically, PVL-producing strains have been strongly associated with necrotising pyogenic cutaneous infections, especially furuncles (1). *Staphylococcus aureus* causes a variety of suppurative, and toxin-mediated infections in humans ranging from superficial skin lesions to potentially life threatening infections such as septicaemia and toxic shock syndrome.

Outbreaks of PVL-producing strains have recently been reported in the United States (US), mainland Europe, and in Scotland. In the US, outbreaks of skin infections (specifically, painful boils and deep skin abscesses) have been reported among prison inmates and the gay community, with smaller outbreaks in athletes, schoolchildren, and newborn babies. Similarly, PVL-producing strains have been identified in the gay community in the Netherlands (2), and small outbreaks of skin abscesses have been documented in Scotland (3). Of further concern are the reports of PVL-producing strains of *S. aureus*, which have been associated with rapidly progressive, haemorrhagic, necrotising, community-acquired pneumonia in young immunocompetent patients with a high fatality rate (4). The majority of strains are methicillin-resistant, but PVL has also been detected in methicillin susceptible strains.

These reports have raised the level of interest in PVL-producing strains. It has been suggested (2) that this is a new clone of methicillin-resistant *Staphylococcus aureus* (MRSA) that has emerged in the community, which spreads through skin contact and may also infect healthy people. At present, it is unclear whether the outbreak strains are related and represent a predominant clone world-wide.

The leukotoxic activity of *S. aureus* was first documented in 1894 by Van der Velde. Subsequently, work (5) led to the characterisation of a leukocidin known as Panton-Valentine leukocidin (PVL). Studies have shown that PVL is a bi-component non-haemolytic toxin that induces cytotoxic and cytolytic changes in human and rabbit polymorphonuclear cells, monocytes, and macrophages. In addition, intradermal injection of PVL into rabbits produces a dermonecrotic effect.

PVL is encoded by two genes: *lukS-PV* and *lukF-PV*, which are contiguously located and co-transcribed. Both have been located on several temperate bacteriophage genomes. At least one of the phages can be liberated and is capable of infecting PVL-negative *S. aureus* strains, which then express PVL. Hence, there is potential for horizontal transmission of these genes, although few strains appear to be susceptible to infection with PVL-converting phages (6). This limited host range may account for the relatively low frequency of clinical isolates found to harbour PVL (2-10%) (2,7). Currently, data are lacking on the frequency of PVL-producing strains in England and Wales, and their role in human disease. Studies are under way in the Laboratory of Healthcare Associated Infection in an attempt to gain more insight into the prevalence, microbiological and epidemiological background of these strains and to compare them with isolates from other countries.

If you suspect that recent cases of *S. aureus* infection may be PVL-related (including community-acquired skin infections or pneumonia, originating from the groups outlined above), please contact the Angela Kearns at the Laboratory of Healthcare Associated Infection (LHCAI) at Colindale, tel 020 8200

4400 ext 4227; email: <angela.kearns@hpa.org.uk>. LHCAI would also be pleased to receive isolates for characterisation.

1. Gladstone GP, van Heyningen WE. Staphylococcal leucocidins. *Brit J Exp Path* 1957; **38**: 123-37.
2. Wannet W. Virulent MRSA strains containing the Panton Valentine Leukocidin gene in the Netherlands. *Eurosurveillance Weekly* [serial online] 2003 [cited 10 April 2003]; **7** (10). Available at <<http://www.eurosurveillance.org/ew/2003/030306.asp>>
3. SCIEH. Community MRSA and Panton-Valentine leukocidin. *SCIEH Weekly Report* 2002 [serial online] 2002 [cited 10 April 2003]; **36** (46). Available at <<http://www.show.scot.nhs.uk/scieh/PDF/pdf2002/0246.pdf>>
4. Gillet Y, Issartel B, Vanhems P, Fournet J-C, Lina G, Bes M, *et al.* Association between *Staphylococcus aureus* strains carrying gene for Panton-Valentine leukocidin and highly lethal necrotising pneumonia in young immunocompetent patients. *Lancet* 2002; **359**: 753-59.
5. Panton PN, Valentine FCO. Staphylococcal toxin. *Lancet* 1932; **222** (i): 506-08.
6. Narita S, Kaneko J, Chiba J, Piémont Y, Jarraud S, Etienne J, Kamio Y. Phage conversion of Panton-Valentine leukocidin in *Staphylococcus aureus*: molecular analysis of a PVL-converting phage, ϕ SLT. *Gene* 2001; **268**: 195-206.
7. Prévost G, Couppie P, Prévost P, Gayet S, Petiau P, Cribier B, *et al.* Epidemiological data on *Staphylococcus aureus* strains producing syngohymenotropic toxins. *J Med Microbiol* 1995; **42**: 237-45.

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General outbreaks of foodborne illness, England and Wales: weeks 10-13/03*

DHA	Organism	Location of food prepared or served	Month of outbreak	Number ill	Cases positive	Suspect vehicle	Evidence
Westminster	S.Typhimurium PTU277	Restaurant	January	5	5	None	–

* Preliminary data. Final information will be published in the quarterly report.

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Salmonella infections: England and Wales, reports to the PHLS(salmonella data set*) February 2003

Details of serotypes of the 458 salmonella infections recorded in February 2003 are given in the adjacent table. In March 2003, 483 salmonella infections were recorded and preliminary information was received about one outbreak (see table above).

Salmonella (provisional data)	February 2003
	458
S.Enteritidis (PT4)	84
S.Enteritidis (other PTs)	106
S.Typhimurium	78
S.Virchow	12
Other (typed)	178

* Data provisional

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Common gastrointestinal infections, England and Wales: laboratory reports, weeks 10-13/03

Laboratory reports	Number of reports received				Total reports 10-13/03	Cumulative total to	
	10/03	11/03	12/03	13/03		13/03	13/02
<i>Campylobacter</i>	457	713	505	459	2152	7798	9037
<i>Escherichia coli</i> O157*	5	3	1	1	10	29	32
<i>Salmonella</i> †	113	136	105	120	474	1823	1836
<i>Shigella sonnei</i>	13	18	2	17	50	143	130
Rotavirus	627	884	837	769	3117	5517	4754
Norovirus	97	122	54	64	337	1354	815
<i>Cryptosporidium</i>	37	58	25	29	149	529	680
<i>Giardia</i>	38	73	41	49	201	664	757

* Vero cytotoxin producing isolates (data from Laboratory of Enteric Pathogens (LEP))

† Data from PHLS LEP

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Less common gastrointestinal infections, England and Wales: laboratory reports, weeks 01-13/03

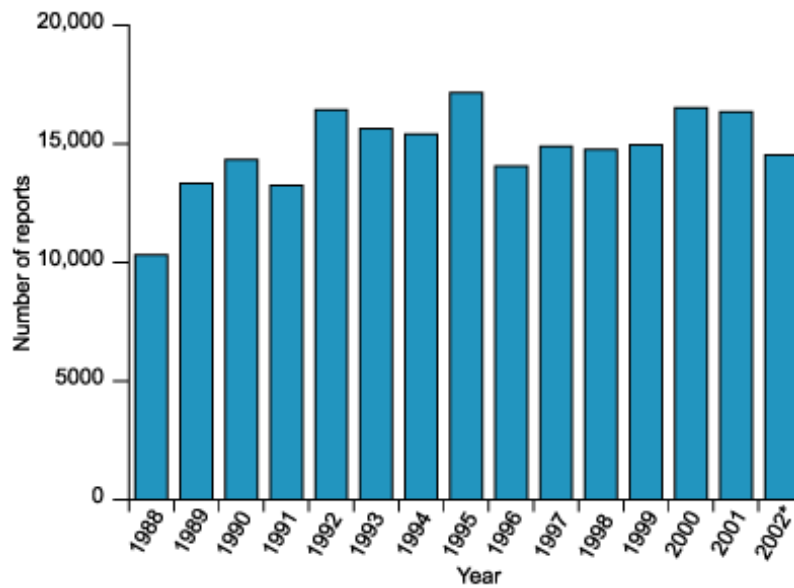
Laboratory reports	Total reports	Cumulative total to	
	03/01-13	13/03	13/02
Adenovirus	23	23	12
Astrovirus	59	59	24
Calicivirus	5	5	15
<i>Shigella boydii</i>	22	22	10
<i>Shigella dysenteriae</i>	5	5	7
<i>Shigella flexneri</i>	47	47	48
Aeromonas	20	20	25
Plesiomonas	3	3	4
Vibrio	8	8	10
Yersinia	8	8	8
<i>Entamoeba histolytica</i>	31	31	36
<i>Blastocystis hominis</i>	85	85	79
<i>Dientamoeba fragilis</i>	31	31	39
<i>Taenia</i> spp	8	8	12
<i>Trichostrongylus</i> spp	–	–	–
<i>Trichuris trichiura</i>	5	5	32

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Rotavirus in England and Wales

Fourteen thousand five hundred and twenty-eight cases infected with rotavirus were reported to the PHLS Communicable Disease Surveillance Centre (CDSC) in 2002 compared with 16,345 in 2001, and 16,528 in 2000 (figure). There is no discernible trend from 1992 to 2002.

Figure Laboratory reports of rotavirus in England and Wales: 1988 to 2002



* Data provisional

Children aged less than 4 years accounted for 87% (12,681) of cases in 2002 and 86% (14,012) in 2001. Cases were evenly distributed across the regions (table)

Table Regional distribution of rotavirus cases in England and Wales, 2002

Region	Number of Cases
Northern and Yorkshire	2285
Trent	1070
Eastern	1840
London	914
South East	1631
South West	1469
West Midlands	2357
North West	1466
Wales	1496
Total	14,528