This suggests that HAV is transmitted readily within the homosexual communities on a national basis and perhaps on an international basis as well. Whether HAV was transmitted between homosexual communities in the different European countries, is not known. The objective of this study was to determine if these viral outbreaks among homosexual men were related genetically by comparing sequences of HAV outbreak strains from the individual countries, as well as studying the dissemination of these strains in the population. If the HAV strains found among homosexual men are not found in the general population or other risk groups within the individual countries during the same time, this could indicate that these strains circulate among homosexual men exclusively. Phylogenetic analysis of the strains found among homosexual men and other HAV strains is presented, and discussed in relation to endemic HAV transmission among homosexual men.

MATERIALS AND METHODS

An epidemiological and molecular collaborative study of hepatitis A among homosexual men was established between surveillance centres and laboratories in Denmark, Germany, the Netherlands, Norway, Spain, Sweden, and the United Kingdom. Epidemiological data regarding place of infection, age, onset of illness, and sexual orientation was obtained during the time period of outbreaks associated with homosexual men in the individual countries in 1997–2005 by the national surveillance centres. Cases suspected to be associated with the outbreaks among homosexual men were characterized further by sequencing of HAV strains. Based upon the molecular epidemiological data, cases were defined as men ≥17 years of age with acute hepatitis A infection, verified by positive anti-HAV IgM and classified by three case definitions to identify homosexual-related transmissions;

- 1. Confirmed case: HAV outbreak strain confirmed by sequencing and notified as sexually transmitted.
- 2. Probable case: HAV outbreak strain confirmed by sequencing, they had not been notified as sexually transmitted or other known risk factors such as drug use or travel to high endemic regions.
- 3. Possible case: HAV outbreak strain not detected and no other known risk factors had been notified such as drug use or travel to high endemic regions.

Women and children <17 years of age were excluded from the study.

Isolation, Amplification, and Sequencing of HAV RNA

HAV RNA was isolated, amplified, and sequenced by the laboratories in the respective countries according to the protocols detailed below. Table I shows the different extraction and sequencing methods, as well as primers used by each country. The PCR products were subsequently sequenced with second PCR primers.

Denmark

One-step RT-PCR (QIAGEN, GmbH, Hilden, Germany) was used to amplify the N-terminal part of VP1 and the VP1/P2A junction of HAV as previously described [Grinde et al., 1997; Arauz-Ruiz et al., 2001].

Germany

cDNA was synthesised from 5 µl RNA with 1.25 µM HAV5 primer using M-MLV Reverse Transcriptase (Invitrogen, Carlsbad, CA). The VP1/P2A and VP3/VP1 regions were amplified by nested PCR using 0.5 µM primer, 1.5 mM $MgCl_2$, 0.5 U Taq-polymerase and amoniumsulfate buffer (Invitek GmbH, Berlin, Germany). The amplifications were performed for 35 cycles at 94°C in 30 sec, 42°C in 1 min, 72°C in 2 min.

The Netherlands

Isolation, amplification, and sequence analysis of the HAV strains found among Dutch patients were performed as described previously [Bruisten et al., 2001; van Steenbergen et al., 2004; Tjon et al., 2005a].

Norway

cDNA was synthesized and subsequent PCR amplifications were generated with AmpliTaq DNA polymerase (Applied Biosystem, Branchburg, NJ) with 0.5 µM primers, 2 mM $MgCl_2$, and 200 µM dNTP as previously described [Grinde et al., 1997]. The first and second PCR amplifications were performed for 30 and 35 cycles respectively at 94°C for 10 sec, 55°C for 30 sec, and 72°C for 30 sec. In the second PCR (VP1/P2A), the annealing temperature was 60°C.

Spain

Two overlapping fragments were amplified by using two sets of primers: the NH_2-VP1 pair and the COOH-VP1 pair [Sanchez et al., 2002, 2003a,b]. Ten microliters of the extracted nucleic acids were used for the cDNA synthesis in two separate RT reactions using the primers NH2-VP1 or COOH-VP1. Ten microliters of the RT products were added to 50 µl final volumes of PCR mixes. The amino-VP1 PCR was amplified with 53°C annealing temperature using 2 mM $MgCl_2$, while the carboxy-VP1 was amplified with 45°C annealing temperature using 2.5 mM $MgCl_2$. The Expand enzymes from Roche Diagnostics (Basel, Switzerland) were used.

Sweden

cDNA synthesis as described previously [Arauz-Ruiz et al., 2001]. The N-terminal of VP1 and the VP1/P2A region were amplified by PCR as described previously [Grinde et al., 1997; Tallo et al., 2003]. The nested PCR

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TABLE I. Extraction and Sequencing Methods, and Primers Used by Each Country

Country	Extraction and sequencing method	Region	Primer (sequence or reference)
Denmark	-MagNa-Pure sample extraction	VP1/P2A	HAV6, HAV7, HAV8, HAV9 [Grinde et al., 1997]
	-ABI 3130XL genetic analyzer using BigDye Terminator chemistry (Applied Biosystem)	VP3/VP1	HA1, HA7, 2167, HA3 [Arauz-Ruiz et al., 2001]
Germany	-QIAamp viral RNA Kit (Qiagen)	VP1/P2A	HAV5 3373 5′- CCATTTCAAGAGTCCACACAC-3′*
	-ABI Prism 377 DNA sequencer with Big Dye Terminator chemistry (Applied Biosystem)		HAV6 2791 5′- ATTCAGATTAGACTGCCTTGGTA-3′*
			HAV7 3276 5′- CATTATTTCATGCTCCTCAGT-3′*
			HAV8 2906 5′- GGTTTCTATTCAGATTGCAAATTA-3′*
		VP3/VP1	HAV1 2443 5′- GATCTGATGTATGTCTRGAYTC-3′*
			HAV2 2125 5′- GTTAATGTTTATCTTTCAGCWAT-3*
			HAV3 2407 5′- CAGGAAATGTCTCAGGYACTTTCT-3*
			HAV4 2164 5′- GCTCCTCTTTATCATGCTATGGAT-3*
The Netherlands	-TriPure Isolation Reagent (Roche)	VP1/P2A	BR-5, BR-9, RJ-3, BR-7 [Bruisten et al., 2001; van Steenbergen et al., 2004]
	-ABI Prism 310 genetic analyzer with Big Dye Terminator chemistry (Applied Biosystem)	VP3/VP1	VP1-4 sense, VP-6 antisense, VP1-2 sense, VP1-1 antisense [Bruisten et al., 201; van Steenbergen et al., 2004]
Norway	-QIAamp viral RNA Kit (Qiagen)	VP1/P2A	HAV6, HAV7, HAV8[Grinde et al., 1997]
	-ABI Prism 310 genetic analyzer with Big Dye Terminator chemistry (Applied Biosystem)	VP1	VP1-4 sense [van Steenbergen et al., 2004]
			VP1-anti-sense 2659 3′- AGGCCATGCCATCTACATCAG-5′[?]
			VP1-nested-sense 2170 5′- TTGCTCCTCTTTATCATGCTATG-3′[?]
Spain	-Guanidine thiocyanate [Boom et al., 1990]	VP3/VP1/P2A	NH_2-VP1 primer pair, COOH-VP1 primer pair [Sanchez et al., 2003b]
	-ABI Prism 377 DNA sequencer with Big Dye Terminator chemistry (Applied Biosystem)		
Sweden	-TRIZOL® LS reagent (Invitrogen)	VP1	HA2112S, HA1865AS, HA1369S [Tallo et al., 2003]
	-ABI Prism 3100 genetic analyzer with Big Dye Terminator chemistry (Applied Biosystem)	VP1/P2A	HAV6, HAV7, HAV8, HAV9[Grinde et al., 1997]
United Kingdom	-QIAamp Ultrasens Virus Kit (Qiagen)	VP1/P2A	HAV6, HAV7 [Grinde et al., 1997]
	-CEQ8000 sequencer with GenomeLab™ DTCS Quick Start Kit (Beckman Coulter, Fullerton, CA)		BR-9, BR-5 [Robertson et al., 1992]

*The primers positions are given according to strain HPACG (M20273).
[?]The positions of the primers are according to reference strain HM-175 (M14707).

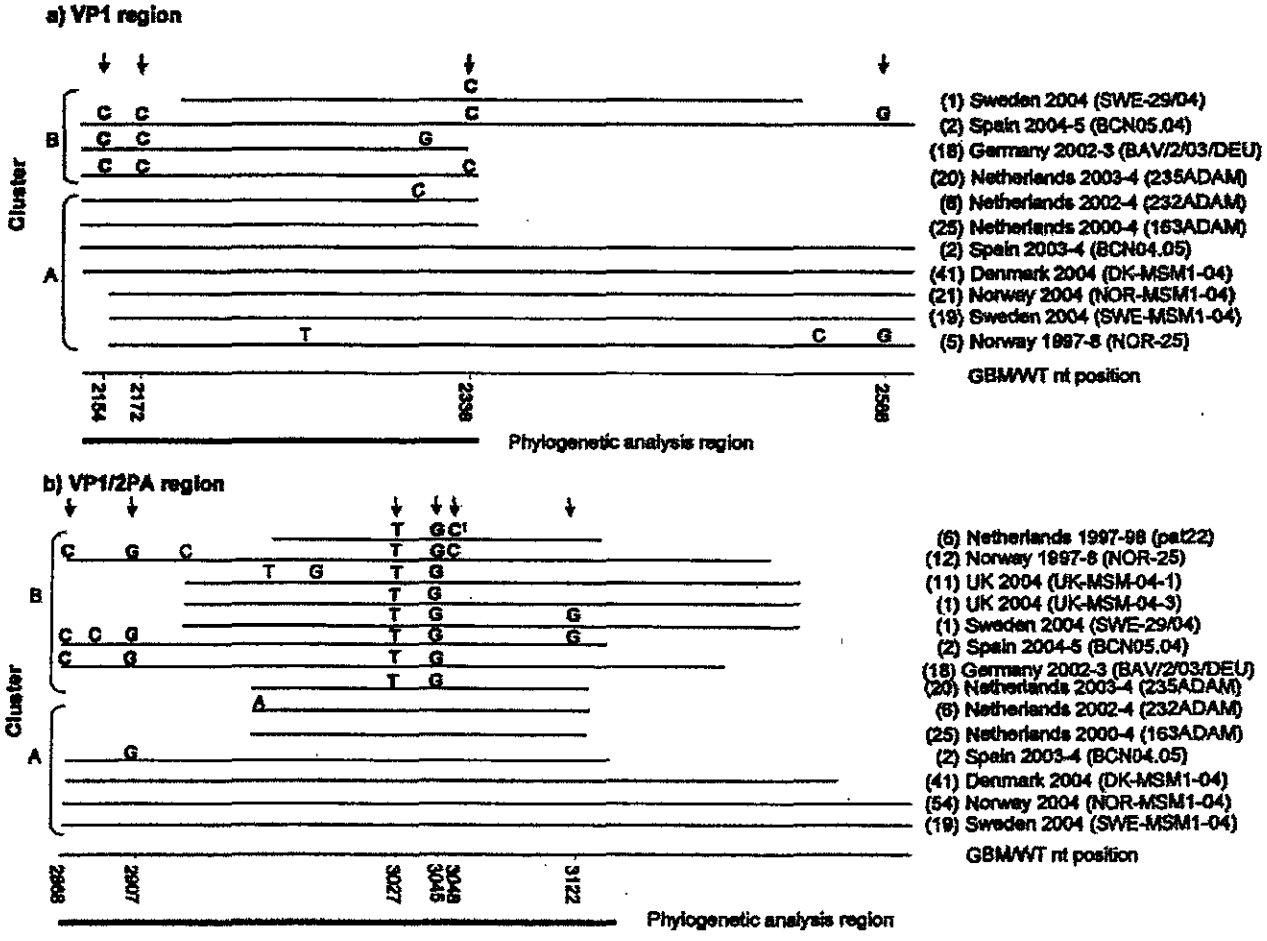
products were purified and sequenced as described previously [Tallo et al., 2003].

The United Kingdom

HAV RNA was reverse transcribed into cDNA using random hexamers (GE Healthcare, Buckinghamshire, UK) and M-MLV reverse transcriptase (Invitrogen). Primary amplification of the VP1/P2A junction was amplified as previously described [Grinde et al., 1997]. The secondary amplification was performed with primers BR-9 and BR-5 [Robertson et al., 1992] and MegaMix Blue PCR master mix (Microzone Ltd., Ottawa, Canada) using the cycling conditions previously described [Bruisten et al., 2001].

Phylogenetic Analysis

The HAV outbreak strains were sequenced to a different extent by the individual countries and hence the overlapping region for all the sequences was too small to distinguish these strains from other HAV strains. Consequently, not all the sequences could be included in the phylogenetic analysis. A region for phylogenetic analysis was carefully selected that could discriminate between strains, covered most of the informative sites among the MSM1-strains, represented both clusters, and included several strains. Particular emphasis was given to phylogenetically informative sites indicated in Figure 1 as they favor some trees over others. A site was considered informative when there were at least two different nucleotides at the site, each of which was present in at least two sequences from different countries. Only isolates with a nucleotide substitution present in



[1] C in this position is present in two of the six isolate i.e. isolate pat22 and pat23

Fig. 1. Overview of HAV MSM1 sequences from outbreaks among homosexual men in European countries within (a) the N-terminal region of VP1 and (b) the VP1/P2A junction of the HAV genome. The main cluster A outbreak strain is used as a consensus. The number of sequenced isolates from the individual countries is given in parenthesis. The 10 informative sites are indicated by arrows and their positions are numbered according to reference strain GBM/WT. The regions used for phylogenetic analysis are indicated with bars.

more than two sequences from each outbreak were included in the sequence alignment and sequence analysis.

The N-terminal VP1 and/or the VP1/P2A regions, corresponding to nt 2,146–2,341 and nt 2,868–3,144 in reference strain GBM/WT, respectively, indicated by bars in Figure 1 were used for phylogenetic analysis. The sequences included in the distance-matrix were of equal length, sequences partially covering these regions were not included in the analysis. The other sequences were HAV strains found in other risk groups in the population in these countries, as well as sequences obtained by BLAST searches in GenBank with the outbreak strains. The sequences were aligned in BioEdit (http://www.mbio.ncsu.edu/BioEdit) and Molecular Evolution Analysis Software (MEGA) version 3.1[Kumar et al., 2004]. The genetic distances were calculated using the Kimura-2-parameter model and the trees were constructed by using neighbor-joining in MEGA. Reproducibility was tested by performing 1,000 bootstraps in MEGA.

Nucleotide Sequence Accession Numbers

HAV sequences found among homosexual men not included in Figure 2 are obtainable from GenBank; BAV/2/03/DEU (AY656711), 163ADAM (DQ387587), 232ADAM (DQ387654), 235ADAM (DQ387657), 047ADAM/MSM2 (AY343717), 066ADAM/MSM3 (AY343728), 071ADAM/MSM4 (AY343733), pat-21 (DQ469362), pat-22 (DQ469358), pat-23 (DQ469364), pat-24 (DQ469355-6), pat-26 (DQ469352), pat-28 (DQ469365), UK-MSM-04-1–3 (AM260518-20).

RESULTS

Strains Involved in Outbreaks Among Homosexual Men

Hepatitis A virus associated with homosexual men in Denmark, Germany, the Netherlands, Norway, Spain, Sweden, and the United Kingdom over the period 1997–2005 was characterized by sequencing of the N-terminal part of VP1 and/or VP1/P2A regions (Table II). By nucleotide comparison, the majority of strains detected among homosexual men formed a closely related cluster that was named MSM1 (Figs 1 and 2). A few other strains were also detected among homosexual men in some of the countries that were different from the MSM1-strains; the MSM2-MSM4 strains in the Netherlands in 2001–2003 [van Steenbergen et al., 2004], NOR-26 in Norway in 1997–98 [Stene-Johansen et al., 2002], and BCN02 in Spain in 2002 (Fig. 2, Table II). The outbreak strains were of genotype IA, except BCN02 (genotype IB), according to the nomenclature system of Robertson et al. [1992]. The MSM2 and NOR-26 strains were also closely related (data not shown). Phyologenetic analysis of the strains found among homosexual men, among other risk groups in these countries, as well as HAV strains from different geographical regions are shown in Figure 2.

The MSM1 Outbreak Strains

By nucleotide comparison the MSM1-strains could be subdivided further into two sub-clusters, shown as A and B in Figure 1 and Figure 2. Out of the 10 informative sites indicated (Fig. 1), 7 distinguished between clusters A and B. The HAV sequences from outbreaks in the Netherlands (232ADAM and 163ADAM) in the period 2000–2004, Spain (BCN04.05) in 2003–2004, and Denmark (DK-MSM1-04), Norway (NOR-MSM1-04), and Sweden (SWE-MSM1-04) in 2004 were mainly identical, representing cluster A. The outbreak strain (BCN04.05) from Spain 2003–2004 showed one of the substitutions characteristic for cluster B in the VP1/P2A region. The HAV sequences from homosexual men in the Netherlands in 1997–98 (pat-22) and 2003–2004 (235ADAM), Norway in 1997–98 (NOR-25), the United Kingdom (UK-MSM-04-01 and UK-MSM-04-3) in 2004, Sweden (SWE-29/04) in 2004, Spain in 2004–2005 (BCN05.04), and Germany in 2002–2003 (BAV/2/03/DEU) formed cluster B. The NOR-25 outbreak strain from Norway in 1997–98 contained five of six characteristic sites of cluster B in the VP1/P2A region, but only one of the three sites that were covered in the N-terminal of VP1. The outbreak strains; NOR-25, UK-MSM-04-1, BCN04.05, BAV/2/03-DEU, and 232ADAM showed substitutions characteristic for these particular outbreak strains in addition to the common pattern of the clusters. A single substitution in addition to the cluster B pattern was common to one of the Swedish strains (SWE-29/04) and one of the Spanish outbreaks strains (BCN05.04). The strains from the Netherlands (pat-22 and pat-23) and Norway in 1997–98 (NOR-25) showed a common unique substitution.

Characterization of MSM1-Related Outbreaks

An epidemic curve of cases of hepatitis A associated with the MSM1-strains classified by the three case definitions (Table II) for the period 1997–2005 from the seven European countries is shown in Figure 3. The total number of MSM1-related cases is shown on a country basis for the period September 2003 to August 2005 in Figure 4.

DISCUSSION

Several outbreaks of hepatitis A have been reported among homosexual men in low endemicity regions in Europe during the last decade. The dissemination of HAV among homosexual men in European countries was therefore studied by molecular epidemiology including samples from Denmark, Germany, the Netherlands, Norway, Spain, Sweden, and the United Kingdom. These countries were all affected by outbreaks in the homosexual communities in recent years. The majority of these strains formed a cluster of similar HAV strains that were named MSM1 (Figs. 1 and 2). Very few nucleotide substitutions were observed within the cluster of MSM1-strains (Fig. 1). The results of this study suggest that highly similar HAV strains are exchanged among the

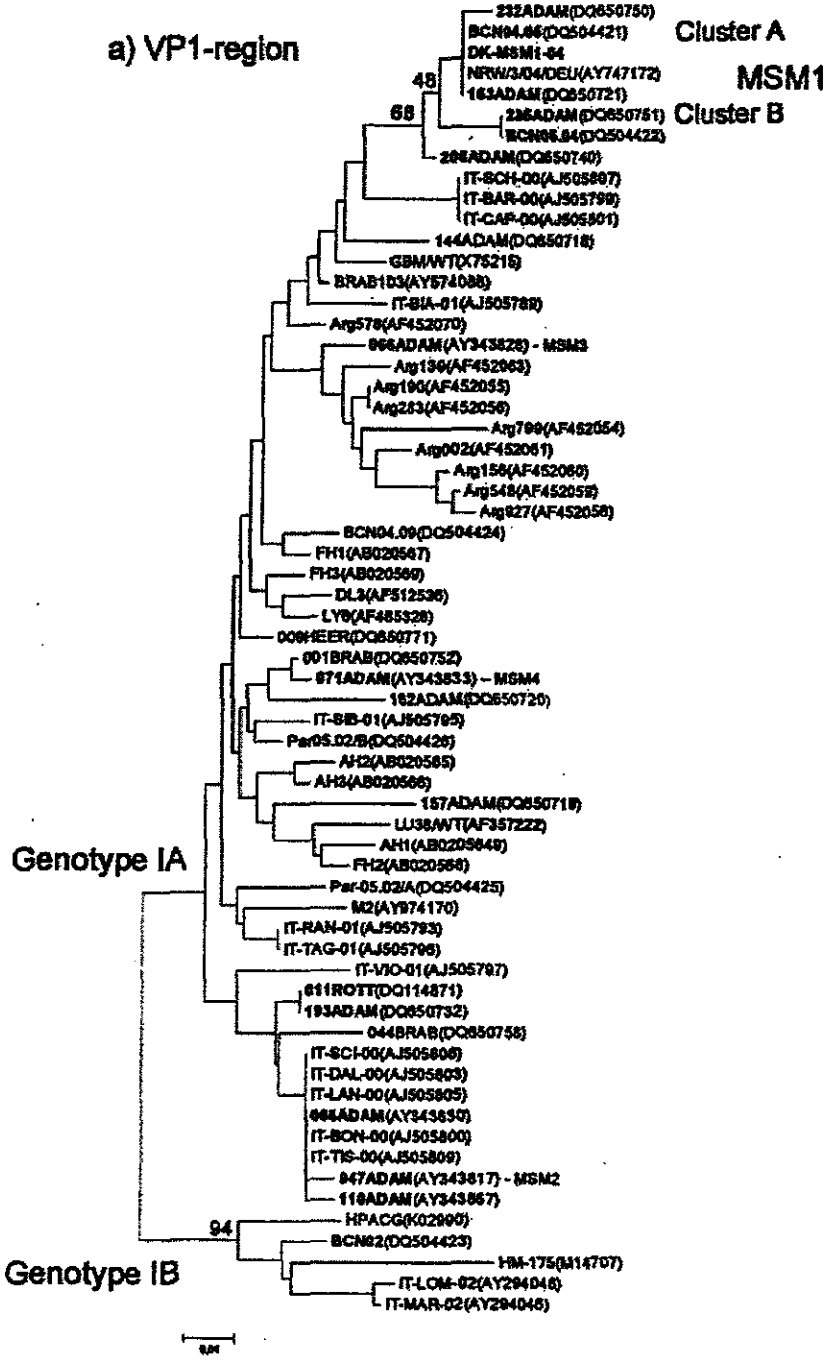


Fig. 2. Phylogenetic trees of the N-terminal of VP1 and the VP1/P2A regions of HAV outbreak strains found among homosexual men in bold in comparison with strains found in other risk groups and strains from different geographical regions. The phylogenetic analysis is based upon the N-terminal part of VP1 and the VP1/P2A junction corresponding to nt 2,146–2,341 and nt 2,868–3,144 in reference strain GBM/WT respectively. Bootstrap values (1,000 replicas) for the clusters of MSM1 are shown. The trees were constructed by use of neighbor-joining of Kimura-2 parameter corrected distances. Accession numbers are shown in parenthesis.

homosexual communities in Europe. HAV is a single-stranded RNA virus that undergoes rapid genetic changes due to the RNA-dependent RNA polymerase that replicates with low fidelity and lack of proofreading activity [Sanchez et al., 2003a]. The nucleotide variation seen between the MSM1-strains were probably caused by natural drift in the HAV population that appears with time, and hence that the MSM1 strains were of the same origin. The circulation of similar HAV strains in the homosexual population on an international basis over

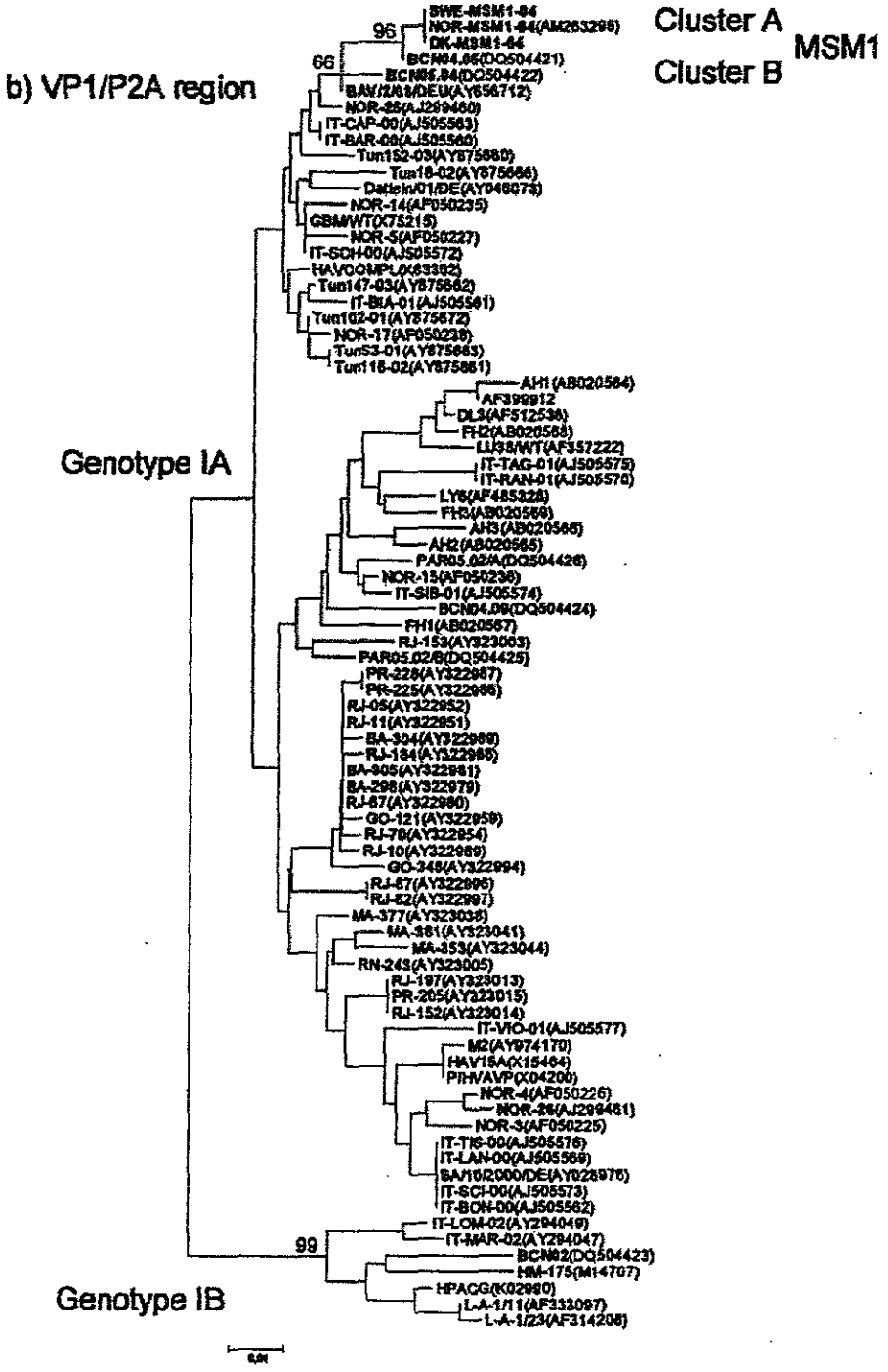


Fig. 2. (*Continued*)

time suggests an endemic HAV population among homosexual men.

The clustering of MSM1-strains was similar for the two regions (N-terminal of VP1 and VP1/P2A), except for the NOR-25 strain from Norway in 1997–98 (Fig. 1a, b). Strain NOR-25 segregated in cluster B in the VP1/P2A junction, whereas it shared two common informative sites with cluster A and one common site with cluster B in the N-terminal region of VP1. Also the bootstrap values could not clearly support clustering of this strain with the other MSM1-strains (data not shown). It is disputable whether this strain should be regarded as an MSM1-strain. The fact that this strain shares the same substitutions as MSM1-related strains from the same

TABLE II. Cases of Hepatitis A Associated With Homosexual Men in Seven European Countries Classified by Case definition in the Period January 1997 to August 2005

Country	Strain	Confirmed cases	Probable cases	Possible cases	Total	Outbreak period (mm.yyyy)
Denmark	MSM1	19	21	95	135	01.2004–12.2004
Germany	MSM1	9	9	59	77	11.2002–07.2003
The Netherlands	MSM1	6			6	01.1997–03.1998
	MSM1	53	7		60	08.2000–10.2004
	MSM2	34	6		40	01.2001–02.2004
	MSM3	3			3	05.2001–08.2001
	MSM4	1	2		3	06.2001–08.2001
Norway	MSM1	12		9*	21	10.1997–03.1998
	NOR-26	5			5	10.1997–03.1998
	MSM1	48	7	25	80	05.2004–12.2004
Spain	BCN02	1		37	38	01.2002–11.2002
	MSM1	2		70	72	07.2003–06.2004
	MSM1	2		6	8	12.2004–08.2005
Sweden	MSM1	14	6	15	35	01.2004–09.2004
United Kingdom	MSM1	10	4	3	17	09.2004–11.2004
Total		219	63	319	601	

*Possible cases could be caused by either of the two co-circulating strains (MSM1 and NOR-26) in 1997–98 in Norway.

time, isolated in the Netherlands (Fig. 1b), supports strongly the notion that these strains are of the same origin. These strains are several years older and might be regarded as ancestral strains or they evolved from the same ancestral strain resulting in evolution of two slightly different clusters. A recombination event in one of the lineages can not be discounted. The outbreak in the United Kingdom involved two different MSM1 strains (Fig. 1b). The major outbreak strain (UK-MSM-04-1) appears to be more distinct than the other MSM1 strains as it differs by two nucleotides from the consensus sequence of cluster B resulting in an amino acid substitution.

An endemic hepatitis A situation requires a continual circulation of strains that are maintained in large populations by continual supply of non-immunized persons. Molecular epidemiological studies show that in high endemic regions there are circulating populations of homologous HAV strains, whereas in low endemic regions strains are highly divergent due to importation from different regions where high endemic transmission occurs [Robertson et al., 1992]. In the homosexual communities across Europe, homologous

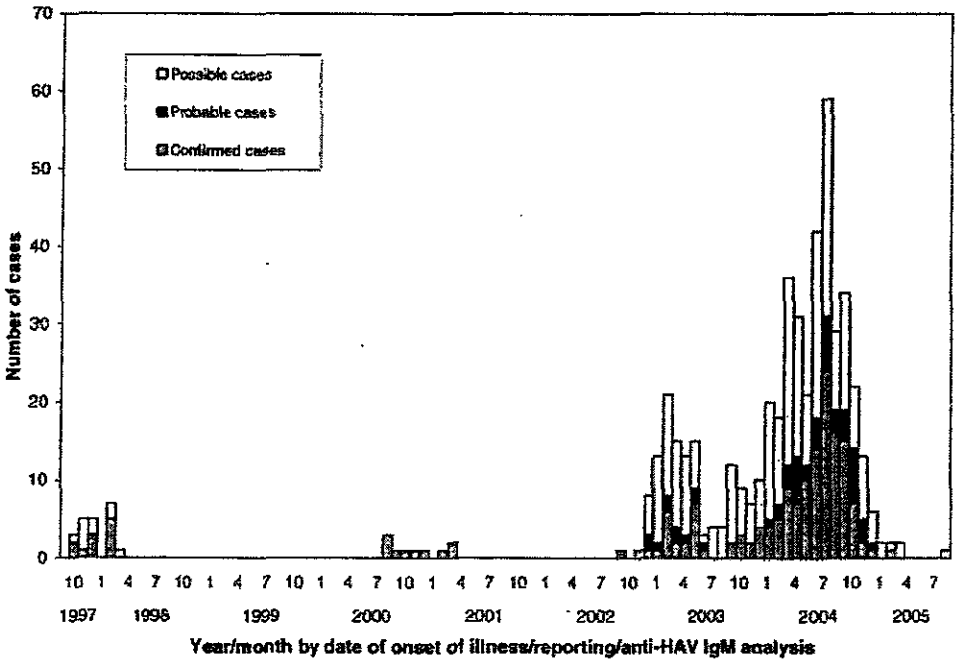


Fig. 3. Epidemic curve of cases of hepatitis A in Denmark, Germany, the Netherlands, Norway, Spain, Sweden, and the United Kingdom from September 1997 to August 2005 classified by case definition. The cases are indicated by month of onset of illness for Denmark, Germany, Norway, and Sweden, month of reporting for the Netherlands, month of testing anti-HAV IgM for the United Kingdom and Spain.

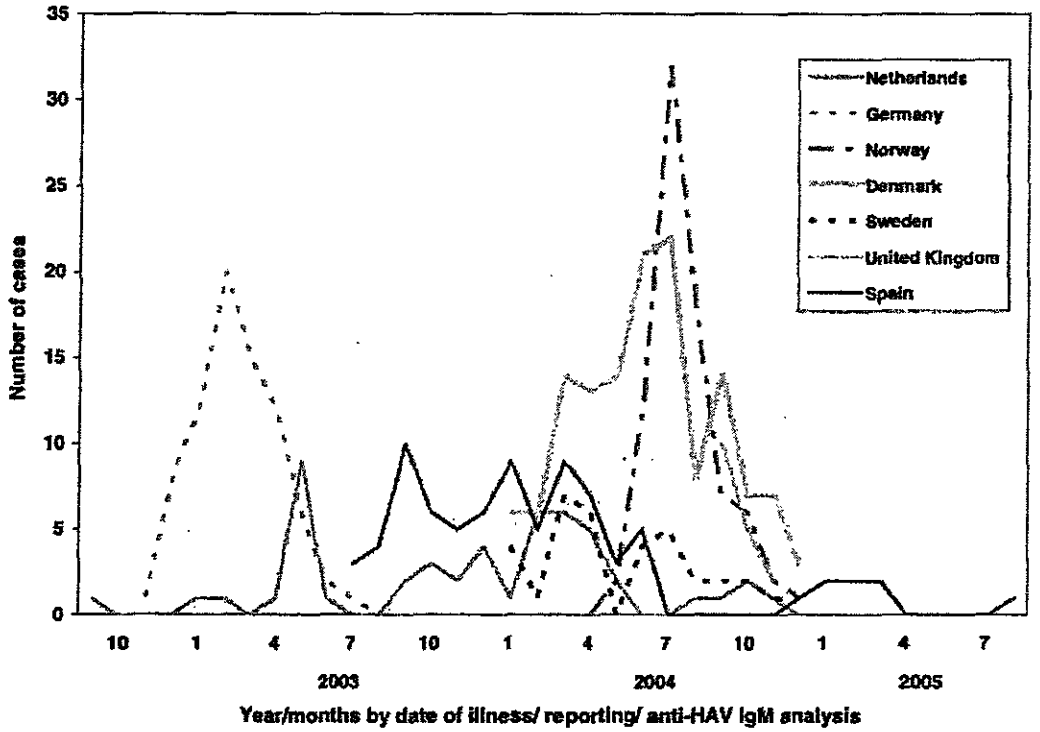


Fig. 4. Cases of hepatitis A associated with the MSM1-outbreak strain in Denmark, Germany, the Netherlands, Norway, Spain, Sweden, and the United Kingdom during the period September 2003 to August 2005. Recorded data as in Figure 3.

strains were found from 1997 until 2004, suggesting interconnected endemic populations of HAV in these communities. In the Netherlands, the strains found among homosexual men appeared as sporadic cases from 2000 to 2004. The detection of MSM1-strains among homosexual men in Norway and the Netherlands in 1997–1998 indicates that this strain has been circulating among homosexual men for a long time. However, no outbreaks were observed in 1998–2000 and 2001–2002 (Fig. 3). Reported cases might have remained unrecognized as homosexual men since not all countries in Europe include sexual orientation in their surveillance data. Also, previously reported outbreaks among homosexual men in London, Berlin, and Paris were not included in the study because no samples could be obtained. Alternatively, the appearance of sporadic closely related strains over time might be due to several independent introductions of HAV strains of the same geographical origin to the homosexual communities in Europe, but this seems less likely.

The homosexual communities within the individual countries in Europe are probably too small to maintain HAV in their population over time due to a limited number of susceptible individuals. Following outbreaks, small communities develop herd immunity that gradually will decline with the recruitment of non-immunized individuals to the communities [Widell et al., 1982, 1983; Gust, 1992; Melnick, 1995]. Consequently, in smaller communities, outbreaks may occur with a cyclic appearance. Seen on a more global basis, the homosexual communities across Europe are probably so large and interconnected that HAV may circulate for years resulting in an endemic situation among homosexual men. Notified cases of HAV in these European countries are mainly seen in certain risk groups whose habits or lifestyle put them at high risk of infection, and not in the general population. Other distinct strains were detected among travellers to endemic regions and intravenous drug users [Grinde et al., 1997; Stene-Johansen et al., 1999, 2002; Bruisten et al., 2001; van Steenbergen et al., 2004; Sunqvist et al., 2005; Tjon et al., 2005b] suggesting that the MSM-related characterized strains in this study were found among homosexual men exclusively.

The molecular data suggest transmission of HAV among men in homosexual communities in the European countries. The epidemiological data alone could only indicate transmission between homosexual men in the different European countries to a very small extent [Mazick et al., 2005] emphasizing the need of molecular epidemiology in outbreak investigations. The sexual practices among homosexual men place them at high risk of infection, and increased travel with visits to gay clubs contribute to a wide spread of HAV among homosexual men in Europe. HAV infection seems to be endemic in this risk group and new outbreaks among homosexual men may be expected soon. Vaccination of homosexual active men in Europe is therefore necessary

to prevent further outbreaks in these communities. A local vaccination policy based upon distribution of vaccine to homosexual active men during outbreaks may provide only limited preventive measures when HAV spreads on a global basis.

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医薬品
医薬部外品　研究報告　調査報告書
化粧品

識別番号・報告回数		回	報告日 年　月　日	第一報入手日 2007年2月7日	新医薬品等の区分 該当なし	総合機構処理欄
一般的名称			研究報告の公表状況	BSE confirmed in Alberta. Canadian Food Inspection Agency website: www.inspection.gc.ca/english/toce.shtml	公表国 カナダ	
販売名(企業名)						

研究報告の概要	使用上の注意記載状況・その他参考事項等
カナダ食品検査庁によって発表された本報告書は,アルバータ州で見つかった9例目のウシ海綿状脳症(BSE)症例に関するものである。当該雄ウシは2000年に生まれ，死亡時は約6.5歳であった。また，発見された農場にて出生・生育した。カナダで反芻動物由来の飼料禁止が実施された1997年以後の出生であるため，当該ウシは，おそらく非常に少量の感染物質に，おそらく生後1年以内に曝露したことが示唆される。当該ウシの飼料が何であったかを調査し，当時の同じ群の他のウシを追跡するために，詳細な調査が進行中である。当該ウシは，これまでのカナダにおける全BSE症例と同様，全国監視プログラムによって同定された。このプログラムでは2003年に北米で最初のBSE症例が出現して以来，高リスクのウシ150,000頭を検査してきた。これらのデータから，実際にはカナダにおけるBSEの発現率は非常に低く，飼料禁止の強化が2007年7月12日に発効されることからさらに低くなることが期待される。	BYL-2007-0271

報告企業の意見	今後の対応
カナダで9例目のBSE症例は,高リスクのウシ150,000頭の中から体系的な調査によって同定された。この新規症例が報告されたが,カナダにおけるBSEリスクは非常に低いという結論は変わらない。	現時点で新たな安全対策上の措置を講じる必要はないと考える。

Canadian Food Inspection Agency / Agence canadienne d'inspection des aliments

BYL-2007-0

BSE CONFIRMED IN ALBERTA

OTTAWA, February 7, 2007 - The Canadian Food Inspection Agency (CFIA) has confirmed the diagnosis of bovine spongiform encephalopathy (BSE) in a mature bull from Alberta. The animal's carcass is under CFIA control, and no part of it entered the human food or animal feed systems.

Preliminary information indicates that the age of the animal falls well within the age range of previous cases detected in Canada under the national BSE surveillance program. This signifies that the animal was exposed to a very small amount of infective material, most likely during its first year of life.

An epidemiological investigation directed by international guidelines is underway to examine what the animal was fed early in its life and to identify its herdmates at the time. All findings will be publicly released once the investigation concludes.

Under Canada's enhanced feed ban, which comes into effect on July 12, 2007, BSE should be eliminated from the national cattle herd within approximately 10 years. The CFIA expects the periodic detection of a limited number of cases to continue as the level of BSE continues to decline.

The finding of a mature animal should not impact Canada's BSE country categorization submission to the World Organization for Animal Health (OIE). The science-based BSE risk-level determination process requires that a country is able to demonstrate a full understanding of the pathways that resulted in BSE exposure and expression, as well as the implementation of appropriate comprehensive measures to block those pathways and protect human and animal health, leading to the eradication of the disease over time.

The animal was identified at the farm level by the national surveillance program, which has detected all cases found in Canada. The program targets the highest risk cattle populations and has tested roughly 150,000 animals since 2003. The surveillance results reflect an extremely low incidence of BSE in Canada.

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