

Summary

- Relatively few H1 viruses isolated and relatively little influenza activity associated with H1 viruses
- No new antigenic or genetic variants of H1 HA have been detected
- In HI tests using post infection antiserum to the A/New Caledonia/20/99 vaccine strain, recently isolated H1 viruses are well inhibited
- The NA genes of N1 and N2 subtype viruses are similar to those of viruses circulating a year ago

Influenza A(H3N2)

HI REACTIONS OF INFLUENZA H3 VIRUSES (02/06/03)

REFERENCE ANTIGENS	REFERENCE FERRET ANTISERA						Date collected
	A/MOS110	B/PN2007	FUJ1140	CU6416	HK1560	NY185	
1 A/MOSCOW/10/99	640	320	80	320	320	320	01/16/99
2 A/PANAMA/2007/99	160	320	160	320	320	320	07/12/99
3 A/FUJIAN/140/2000	80	160	320	160	160	160	07/26/00
4 A/HK/156/01	160	160	80	320	160	320	08/14/01
5 A/HONG KONG/1560/2002	640	640	320	640	640	640	01/19/02
6 A/NEW YORK/66/2001	640	320	160	640	320	1280	11/21/01
7 A/GUANGZHOU/405/2002	80	160	80	160	160	80	08/21/02
TEST ANTIGENS							
8 A/NEW JERSEY/4/2002	1280	640	640	1280	1280	1280	11/04/02
9 A/THAILAND/117/02	320	640	640	1280	640	1280	10/21/02
10 A/EGYPT/19441/2002	1280	640	320	1280	640	1280	11/07/02
11 A/DAKAR/60/02	320	640	160	1280	320	1280	04/01/02
12 A/THAILAND/1169/2002	640	320	160	640	320	640	10/17/02
13 A/CALIFORNIA/09/2002	160	160	320	320	320	160	12/03/02
14 A/BELUNG/178/2002	160	160	320	320	320	160	11/21/02
15 A/BELUNGER/12/2002	160	160	320	160	320	160	12/20/02
16 A/PARIS/02/02	320	160	160	320	320	640	12/01/02
17 A/KOREA/2/10/02	160	160	320	320	320	160	12/12/02
18 A/KOREA/2/2/02	160	80	160	80	160	80	12/10/02
19 A/HAWAII/2/2002	160	80	160	160	160	80	12/18/02
20 A/BELUNGER/01/2002	160	80	160	160	80	160	12/20/02
21 A/ANNAM/580/2002	80	60	320	80	160	80	12/01/02
22 A/EGYPT/19606/2002	160	80	160	160	320	160	11/16/02

HI REACTIONS OF INFLUENZA H3 VIRUSES (01/30/04)

REFERENCE ANTIGENS	REFERENCE FERRET ANTISERA						Date collected
	A/PN2007	FUJ1141	KO/77/03	HYV/03	KUM/102	T240	
1 A/PANAMA/2007/99	1280	160	160	320	160	640	07/12/99
2 A/FUJIAN/141/2002	320	320	2560	2560	1280	2560	08/11/02
3 A/KOREA/2/2002	160	1280	1280	2560	1280	1280	12/03/02
4 A/WYOMING/02/2003	320	1280	1280	2560	1280	2560	02/13/03
5 A/KUMAMOTO/102/2002	320	1280	1280	2560	1280	2560	12/25/02
6 A/TEXAS/04/2004	640	2560	2560	2560	320	2560	10/03/03
7 A/HONG KONG/1186/2003	48	160	320	320	160	640	04/04/03
8 A/TANJANG/138/2003	88	320	320	640	320	640	09/07/03
TEST ANTIGENS							
9 A/OWA/06/2003	320	1280	1280	1280	2560	640	12/12/03
10 A/NEW YORK/09/2003	320	640	640	1280	640	1280	12/18/03
11 A/NEW YORK/05/2003	80	160	320	320	160	160	12/01/03
12 A/RHOADES/131/04/2003	160	320	320	320	160	80	12/29/03
13 A/NEW YORK/103/2003	160	160	320	320	640	80	12/29/03
14 A/ARIZONA/47/2003	40	160	160	320	160	80	12/14/03
15 A/PERUS/04/2003	80	320	640	640	320	320	09/20/03
16 A/PERUS/31/2003	160	640	640	1280	320	320	10/11/03
17 A/INDONESIA/03/2003	320	1280	2560	2560	1280	640	10/11/03
18 A/THAILAND/02/2003	320	1280	2560	5120	2560	1280	04/01/03
19 A/HONG KONG/187/2003	160	1280	1280	1280	2560	1280	04/01/03
20 A/GA/1/04/03	80	1280	1280	2560	1280	640	12/15/03
21 A/KOREA/4834/2003	320	1280	1280	2560	640	1280	12/18/03
22 A/THAILAND/0332/2003	320	1280	1280	1280	640	1280	04/01/03
23 A/HONG KONG/152/2003	80	640	640	1280	640	160	11/02/03
24 A/INDONESIA/02/2003	80	640	1280	640	640	320	11/25/03
25 A/JAPAN/584/2003	160	640	640	1280	640	320	12/15/03
26 A/KOREA/5937/2003	80	320	640	640	320	160	11/25/03
27 A/PANAMA/2007/99	80	320	320	640	320	160	12/04/03
28 A/BELUNGER/178/2002	80	320	320	640	320	160	12/05/03
29 A/ANNAM/580/2002	80	320	320	640	160	160	12/05/03
30 A/JAPAN/5486/2003	20	160	320	320	160	80	12/05/03
31 A/KYRGYZ/1/AN5863/2003	160	320	320	640	320	1280	160

Influenza A(H3N2) Isolates Characterized by CDC

	U.S.A	North America	Europe	Asia	Central America	Africa	Total
April 2002 - September 2002							
A/Panama/2007/99-like	16	1	3	108	28	12	167 (89%)
A/Panama/2007/99-like (low)				8	3	9	20 (11%)
Total: 187							
October 2002 - March 2003							
A/Panama/2007/99-like	101	8	22	128	7	16	282 (72%)
A/Panama/2007/99-like (low)	3			19			22 (6%)
A/Fujian/411/2003-like	16	7	8	47	6	2	86 (22%)
Total: 350							
April 2003 - September 2003							
A/Panama/2007/99-like	41	13		29	171	1	255 (86%)
A/Panama/2007/99-like (low)	1			3			4 (1%)
A/Fujian/411/2003-like	31	10	1	79	48	14	183 (41%)
Total: 442							
October 2003 - February 2004							
A/Panama/2007/99-like	106	1	3	1	1		112 (16%)
A/Fujian/411/2003-like	444	3	19	60	6	14	546 (76%)
A/Fujian/411/2003-like (low)	36			16	4	1	57 (8%)
Total: 720							
Total: 784 43 66 601 276 70 1739							

Influenza Strain Characterization (VRBPAC, CBER, FDA, February 18-19, 2004)

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Influenza A(H1N1) and A(H1N2)



HI REACTIONS OF INFLUENZA H1 VIRUSES

REFERENCE ANTIGENS	REFERENCE FERRET ANTISERA							Date collected	NA
	A BJ/262 NC/20	B CU8885 HI/10	C PE/3135 NE/52	D HI/15	E	F	G		
1 A/BEIJING/262/95	640	640	320	320	80	320	80	01/09/95	N1
2 A/NEW CALEDONIA/20/99	160	1280	320	160	160	320	80	06/09/99	N1
3 A/CHILE/8885/02	80	640	160	80	20	160	80	07/03/02	N1
4 A/HAWAII/10/02	160	640	160	320	20	320	40	03/22/02	N2
5 A/PERU/3135/03	160	80	10	20	840	40	160	04/09/03	N1
6 A/NEWMENGLAND/62/02	40	640	80	80	40	320	80	01/25/02	N1
7 A/HAWAII/15/01	40	40	20	20	320	<10	160	02/17/01	N1
TEST ANTIGENS									
8 A/VIRGINIA/20/2003	160	640	640	320	80	320	40	11/05/03	N2
9 A/BELM/84038/2003	640	1280	320	640	80	640	80	05/08/03	n d
10 A/DAKAR/85/2003	320	1280	320	320	320	1280	160	10/09/03	n d
11 A/NAGANO/1328/2003	160	1280	160	160	160	640	80	UNKN	n d
12 A/CANADA/657/03	320	1280	160	160	640	1280	160	10/24/03	n d
13 A/SINGAPORE/66/2003	320	640	160	160	160	1280	80	09/02/03	n d
14 A/ICELAND/122/2003	320	640	320	320	40	320	80	12/06/03	n d



Influenza A(H1) Isolates Characterized by CDC

	U S A	North America	Europe	Asia	Cent/So America	Africa, Australia, New Zealand	Total (%)	
October 2002 - March 2003								
A/N Caledonia/20/99like	281	34	9	8	17	1	350 (98%)	
A/N Caledonia/20/99-like (low)	4	1				2	7 (2%)	
						Total	357	
April 2003 - September 2003								
A/N Caledonia/20/99like	10	4	3		105	2	124 (95%)	
A/N Caledonia/20/99like (low)						6	6 (5%)	
						Total	130	
October 2003 - February 2004								
A/N Caledonia/20/99like	2	2		1	2	1	9 (90%)	
A/N Caledonia/20/99like (low)			1				1 (10%)	
						Total	10	
	Total	293	41	13	9	124	12	497

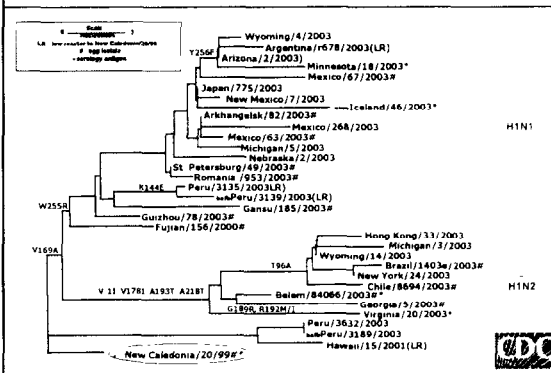


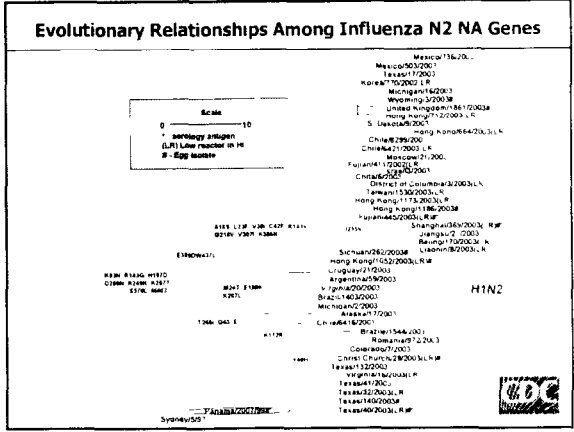
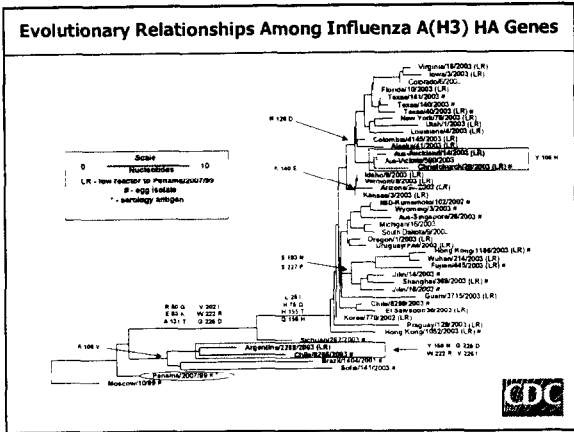
Influenza A(H1N1) & A(H1N2) Isolates Identified by CDC

	U S A	North America	Europe	Asia	Cent/So America	Africa, Australia, New Zealand	Total (%)	
October 2002 - March 2003								
H1N1	209	24	9	7	3	1	253 (71%)	
H1N2	76	11		1	16		104 (29%)	
						Total	357	
April 2003 - September 2003								
H1N1	8	4	3		43	1	59 (47%)	
H1N2	2	64				1	67 (53%)	
						Total	126	
October 2003 - February 2004								
H1N1	1					1	2 (40%)	
H1N2	1	2					3 (60%)	
	Total	297	105	12	8	62	4	488



Evolutionary Relationships Among Influenza A(H1) HA1 Genes





HI Antibody Response to 2003-2004 Vaccine (children 6-23 months of age)

Population N	Antigen	% Rise	% with HI titer >= 40			
			Pre	Post	Pre	Post
			GMT	GMT	Vaccine	Vaccine
USA	A/Panama/2007/99	63	5	50	0	64
	A/Texas/40/2003	44	5	33	0	48
	A/Fujian/445/2003	44	5	31	0	48
	A/Chile/82660/2003	41	5	13	0	24
	A/Nagasaki/52/2003	44	5	29	0	48

Microneutralization Antibody Responses to the H3* Component Among Students Vaccinated with 2003-2004 Inactivated Vaccine

N	Antigen	% Fold Rise	n, with MN titer >= 160			
			Pre	Post	Pre	Post
			GMT	GMT	Vacc	Vacc
49	A/Panama/2007/99	71	22	195	7	71
	A/Fujian/411/2002	49	20	68	7	35
	A/Fujian/445/2003	49	15	49	7	22
	A/Christchurch/28/2003	14	17	24	0	7

Microneutralization Titers of Influenza H3N2 viruses

Strain designation	Reference Ferret Antisera							
	PN/2007	FJ/411	KO/170	WY/02	KUM/102	SH/69	HK/118	CC/28/03
A/Panama/2007/99	320	40	36	80	80	70	40	28
A/Brazil/1404/02	80	60	250	90	40	180	260	160
A/Fujian/411/2002	40	380	380	420	80	180	180	640
A/Korea/770/2002	30	320	360	360	100	160	710	320
A/Wyoming/03/2002	40	280	290	380	180	840	180	120
A/Kumamoto/102/2002	60	170	210	250	175	320	90	80
A/HK/118/2003	20	80	240	130	90	270	130	180
A/Christchurch/28/03	20	60	80	85	80	245	40	100
A/Fujian/466/03	20	200	80	225	30	830	100	450

Summary for H3N2 Viruses

- H3N2 viruses have circulated widely and have been responsible for most reported outbreaks of influenza in Europe and North America during the 2003-04 influenza season
- A/Fujian/411/2002-like viruses have predominated; viruses that are well inhibited by post infection antiserum to the A/Panama/2007/99 vaccine strain continue to circulate
- Genetic heterogeneity among current H3N2 viruses has been observed but without an antigenic correlate
- Reassortment has occurred among H3N2 viruses such that some viruses with a Fujian-lineage HA have a Chile-lineage NA

Influenza B

HEMAGGLUTINATION INHIBITION REACTIONS OF INFLUENZA B VIRUSES

640	320							
640	640							
		640	1280	320	1280	320	320	
		640	640	280	320	320		
		320	640	640	1280	160	160	
		320	640	160	640	160	160	
		160	80	80	320	320	160	
		80	160	80	320	320	640	
		320	640	320	640	160	160	
160	160							
160	160							
80	160							
80	80							
80	160							
80	160							
160	160							
		80	80	80	160	320	160	
		40	40	40	80	160	80	
		80	40	80	160	320	160	



HEMAGGLUTINATION INHIBITION REACTIONS OF INFLUENZA B VIRUSES

640	640	320	80	160				
640	640	320	160	320				
1280	640	160	80	160				
320	320	160	80	160				
160	160	80	40	160				
					320	1280		
640	640	320	160	80				
640	640	320	160	320				
160	320	160	160	160				
160	160	160	80	160				
160	160	160	80	80				
80	80	80	80	80				
80	160	160	80	80				
160	160	160	80	80				
320	320	160	160	160				
160	320	160	160	160				
160	160	160	80	160				
80	160	160	80	80				
160	160	160	80	80				
160	160	80	80	80				
80	80	80	80	80				

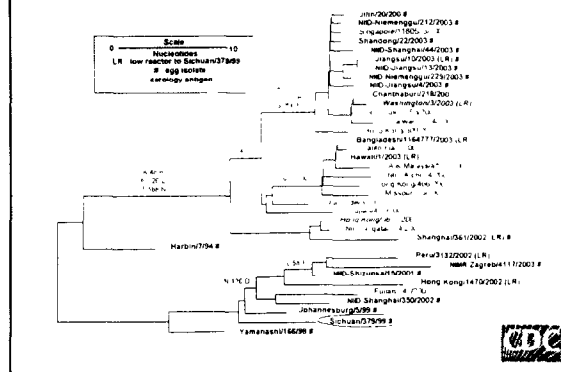


Influenza B Isolates Characterized by CDC

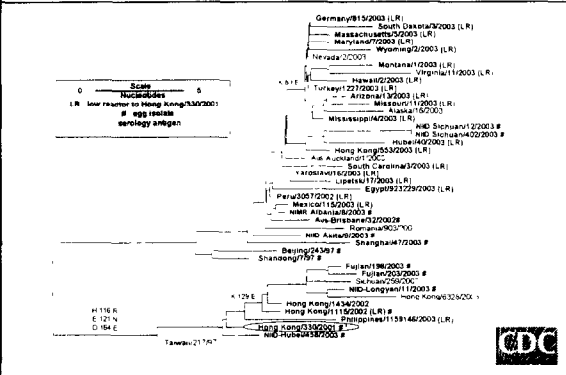
	U.S.A.	North America	Europe	Asia	Central America	Africa	Australia	New Zealand	Total (%)
April 2002 - September 2002									
B/Hong Kong/330/2004 like	56			22	59	17			154 (43%)
B/HA/33/2003 like (low)	41			68	49	16			174 (48%)
B/Sichuan/7/99 like	2			10	2				14 (4%)
B/Sichuan/7/99 (low)	1			6	8				15 (4%)
Total									357
October 2002 - March 2003									
B/Hong Kong/330/2004 like	130		12	96	6	1			245 (62%)
B/HA/33/2003 like (low)	136	2		82	6				226 (58%)
B/Sichuan/7/99 like				10					10 (1%)
B/Sichuan/7/99 (low)	1		1	7					9 (2%)
Total									470
April 2003 - September 2003									
B/Hong Kong/330/2004 like	5	3		4		1			13 (30%)
B/HA/33/2003 like (low)	11				2				15 (35%)
B/Sichuan/7/99 like				1					1 (2%)
B/Sichuan/7/99 (low)	1			10		1			12 (27%)
Total									41
October 2003 - February 2004									
B/Hong Kong/330/2004 like	1								1 (8%)
B/HA/33/2003 like (low)					1				1 (8%)
B/Sichuan/7/99 like	2								2 (17%)
B/Sichuan/7/99 (low)	8				4	1			13 (79%)
Total									17
Total	394	5	21	289	132	47			888



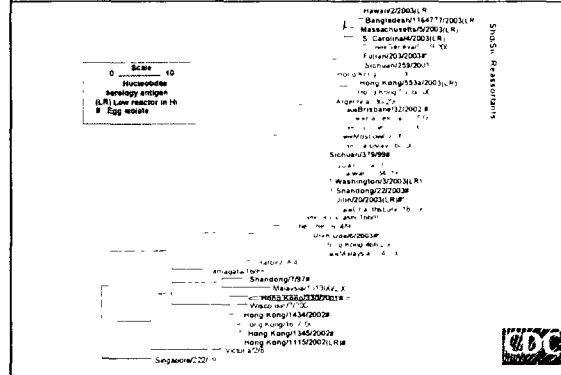
Evolutionary Relationships Among Influenza B/Yamagata HA Genes



Evolutionary Relationships Among Influenza B/Victoria HA Genes



Evolutionary Relationships Among Influenza B NA Genes



Summary for Influenza B Viruses

- Viruses from both the B/Yamagata and B/Victoria lineages have continued to circulate, however, B/Yamagata viruses have predominated overall
- Relatively little influenza activity has been attributed to influenza B viruses
- Most recent influenza B viruses from the U.S., Europe and Asia are most closely related antigenically to B/Shanghai/361/2002 and B/Jilin/20/3002
- Influenza B neuraminidase gene sequences also form 2 separate lineages, the majority of recent viruses have NA genes from the Yamagata lineage



HI Antibody Responses to the H3* Component Among Students Vaccinated with Flumist or Inactivated Vaccine

Vaccine	N	Antigen	% Rise	Pre		Post		% with HI titer > 40	
				GMT	GMT	Pre Vacc	Post Vacc		
Flumist1	100	A/Panama/2007/99 Resvir -17*	6	17	22	33	44		
		A/Wyoming/3/2003	12	14	18	26	33		
		A/Christchurch/28/2003	2	6	6	2	4		
		A/Fujian/445/2003	8	10	11	15	20		
Inactivated Vaccine1	49	A/Panama/2007/99 Resvir -17*	68	13	98	24	86		
		A/Wyomin p/3/2003	64	10	61	36	76		
		A/Christchurch/28/2003	36	6	14	4	31		
		A/Fujian/445/2003	64	8	42	10	63		

