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Laboratory Evidence of Human Viral and Selected Non-viral Infections in Canada

1989 to 1996

***Our mission is to help the people of Canada
maintain and improve their health.***

Health Canada

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LABORATORY EVIDENCE OF HUMAN VIRAL AND SELECTED NON-VIRAL INFECTIONS IN CANADA

1989-1996

**Laboratory Centre for Disease Control
Health Protection Branch
Health Canada**

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Introduction

In support of the virus surveillance program of the World Health Organization (WHO), the Laboratory Centre for Disease Control (LCDC), Health Canada, began a computer database in 1980 to collect data from contributing provincial laboratories on positive laboratory diagnoses of specific viral and selected non-viral agents⁽¹⁾. After cancellation of the WHO program in 1988, a simplified Canadian Virus Reporting System (CVR) was established at the beginning of 1989, and contributing laboratories were asked to submit only listings indicating the total number of specimens tested each month together with the total number of monthly positive findings for each agent, without clinical or patient information⁽²⁾.

Over 90 agents were reported in the CVR system. Positive findings included isolation of agents from specimens; detection of agents or their components, such as antigens, in specimens; and evidence of specific immune responses, either the increase (generally fourfold) of antibody level or the presence of

antibodies (usually specific IgM) indicative of current infections.

For each month and quarter, a national report was prepared based on data from each contributing laboratory; this was sent back to those laboratories and to interested epidemiologists. For each year, a summary of the findings from the laboratory surveillance system was reported in the Canada Diseases Weekly Report^(2,3) or the Canada Communicable Disease Report⁽⁴⁻⁷⁾.

The database management was set up and maintained with help from the Division of Biometrics, LCDC, Health Canada.

In 1989, 30 laboratories across Canada participated in the CVR system, and by 1996 the number had increased to 42. In total, 45 laboratories participated in the system during the 8 years. The cooperation of the directors and staff of the contributing laboratories (see Appendix) who collected and submitted data to the CVR database is greatly appreciated.

General Information

Over the 8 years from 1989 to 1996, an increasing number of positive findings of infection were reported, presumably due to a true increase in incidence, more participating laboratories, and probably also the increasing awareness of certain infections and greater availability of some laboratory assays. The total number of positive findings reported each year (1) is shown in Table 1.

Comparison of (1) with (5) showed that by 1990 over 85% of the positive reports were submitted with the number of specimens tested, and by 1993 approximately 95% were reported together with the number of specimens (8). The rates of positivity among specimens tested was about 5% (6).

Table 1. Annual Number of Positive Findings Reported Through CVR

Year	Total No. of Positives (1)	% (2)	No. of Labs Reporting (3)	Total No. of Specimens Tested (4)	No. of Positives from (4) (5)	(5)/(4) (6)	Increase in (4) (7)	(5)/(1) (8)
1989*	50,513	100	30	575,981	34,127	5.93%	1.00	67.56%
1990	61,468	122	30	838,399	53,610	6.39%	1.46	87.22%
1991	73,464	145	32	1,029,189	63,416	6.16%	1.79	86.32%
1992	68,354	135	33	1,058,862	62,491	5.90%	1.84	91.42%
1993	66,447	132	37	1,398,001	62,919	4.50%	2.43	94.69%
1994	65,925	131	37	1,307,141	62,521	4.78%	2.27	94.84%
1995	73,180	145	39	1,331,607	69,127	5.19%	2.31	94.46%
1996	83,105	165	42	1,544,047	79,021	5.12%	2.68	95.09%
TOTAL	542,456			9,083,227	487,232	5.36%		

* 1989 is the reference year for columns (2) and (7).

A 65% increase is noticed in 1996, as compared with 1989 (2), which may serve as a reference when temporal comparisons are made. Data on the total number of specimens tested were collected and intended for reference purpose, although some laboratories did not report these data, especially in the early years. Nevertheless, the total numbers of specimens tested (4) and the number of positive findings (5) submitted with these totals were extracted from the database.

Initially, reports were received from nine provinces, since those from Prince Edward Island (P.E.I.) were combined with the Nova Scotia reports. From 1993, positive diagnoses from P.E.I. laboratories were reported separately. The annual number of total positive reports from each province is shown in Table 2. These numbers may serve as references for comparison of infection levels of individual agents over different regions and time.

Table 2. Total Number and Proportion of Positive Reports From Each Province, 1989-1996

Year and % of total	BC	Alta.	Sask.	Man.	Ont.	PQ	NB	NS	PEI	Nfld.	Province	
											Total	
1989 (% of total)	8,469 (16.77)	5,964 (11.81)	6,461 (12.79)	224 (0.44)	19,755 (39.11)	3,788 (7.50)	1,100 (2.18)	2,800 (5.54)	0 (0.00)	1,952 (3.86)	50,513 (100.00)	
1990 (% of total)	8,986 (14.62)	6,518 (10.60)	5,823 (9.47)	7,815 (12.71)	25,422 (41.36)	3,379 (5.50)	878 (1.43)	1,932 (3.14)	0 (0.00)	715 (1.16)	61,468 (100.00)	
1991 (% of total)	10,226 (13.92)	5,058 (6.89)	6,962 (9.48)	8,862 (12.06)	32,657 (44.45)	5,574 (7.59)	1,128 (1.54)	1,984 (2.70)	0 (0.00)	1,013 (1.38)	73,464 (100.00)	
1992 (% of total)	12,379 (18.11)	4,997 (7.31)	6,454 (9.44)	7,507 (10.98)	28,372 (41.51)	4,336 (6.34)	1,352 (1.98)	2,153 (3.15)	0 (0.00)	804 (1.18)	68,354 (100.00)	
1993 (% of total)	11,882 (17.88)	7,054 (10.62)	5,697 (8.57)	7,943 (11.95)	24,879 (37.44)	3,809 (5.73)	1,854 (2.79)	2,136 (3.21)	308 (0.46)	885 (1.33)	66,447 (100.00)	
1994 (% of total)	13,682 (20.75)	2,889 (4.38)	6,320 (9.59)	7,083 (10.74)	25,969 (39.39)	5,105 (7.74)	1,776 (2.69)	1,843 (2.80)	555 (0.84)	703 (1.07)	65,925 (100.00)	
1995 (% of total)	14,860 (20.31)	4,824 (6.59)	6,121 (8.36)	7,756 (10.60)	29,580 (40.42)	4,425 (6.05)	1,672 (2.28)	2,356 (3.22)	813 (1.11)	773 (1.06)	73,180 (100.00)	
1996 (% of total)	16,804 (20.22)	8,551 (10.29)	6,231 (7.50)	6,979 (8.40)	33,461 (40.26)	4,785 (5.76)	2,220 (2.67)	2,738 (3.29)	703 (0.85)	633 (0.76)	83,105 (100.00)	

Temporal Patterns of Laboratory Reports of Viral and Selected Non-viral Infections in Canada

Tables 3 to 10 show the total number of reports of individual agents each month from 1989 to 1996. Herpesviruses as a group showed similar infection levels each year, whereas respiratory viral, *Mycoplasma pneumoniae* and enteroviral infections fluctuated annually. However, reported numbers of the sexually transmitted *Chlamydia trachomatis* have been decreasing since 1991, presumably reflecting the effect of the campaign against AIDS. Among respiratory infections, respiratory syncytial viral (RSV) infection occurred mostly between November and May, whereas parainfluenza viruses, adenoviruses and *Mycoplasma pneumoniae* showed fewer seasonal differences. The epidemic season of measles shifted from the spring in 1989 toward the summer in 1995 and 1996. Among enterovirus

infections, one or more of Coxsackie type A9, B1, B2, B4, B5, and enterovirus type 4, 6, 9, 11, and 30 predominated in the epidemic season of different years.

The five most frequently diagnosed agents each year are shown in Table 11. Noteworthy are the decreasing reports of *C. trachomatis* and HIV. Another significant shift is the increase in reports of hepatitis C virus (HCV), to 19,518 in 1996. This may reflect a rise in the frequency of HCV infections, greater awareness of the infection, increasing effort in its detection as well as the availability of testing methods. Laboratory-diagnosed RSV infection also increased, from 2,808 in 1989 to 4,919 in 1996, accounting for 5.92% of total infections in that year.

Table 11. The Five Most Frequently Diagnosed Agents, 1989-1996

Rank	1	2	3	4	5	Others	Total
1989 Agent	CT	HSV	RSV	HBV	EBV		
No. of Positives	13,327 26.38	11,190 22.15	2,808 5.56	2,627 5.20	2,436 4.82	18,125 35.88	50,513 100.00
1990 Agent	CT	HSV	HIV-1	HBV	RSV		
No. of Positives	15,489 25.20	12,256 19.94	4,490 7.30	3,578 5.82	3,518 5.72	22,137 36.01	61,468 100.00
1991 Agent	CT	HSV	HIV-1	HBV	HCV		
No. of Positives	14,475 19.70	13,524 18.41	5,269 7.17	4,252 5.79	4,039 5.50	31,905 43.43	73,464 100.00
1992 Agent	HSV	CT	HCV	HIV-1	HBV		
No. of Positives	14,890 21.78	10,258 15.01	5,255 7.69	5,148 7.53	4,646 6.80	28,157 41.19	68,354 100.00
1993 Agent	HSV	CT	HCV	HBV	EBV		
No. of Positives	15,738 23.69	10,817 16.28	7,705 11.60	3,970 5.97	3,346 5.04	24,871 37.43	66,447 100.00
1994 Agent	HSV	HCV	CT	HBV	EBV		
No. of Positives	14,448 21.92	11,702 17.75	9,491 14.40	3,684 5.59	3,246 4.92	23,354 35.43	65,925 100.00
1995 Agent	HCV	HSV	CT	HBV	EBV		
No. of Positives	16,031 21.91	14,718 20.11	8,777 11.99	4,084 5.58	3,594 4.91	25,976 35.50	73,180 100.00
1996 Agent	HCV	HSV	CT	HBV	RSV		
No. of Positives	19,518 23.49	16,289 19.60	9,745 11.73	5,070 6.10	4,919 5.92	27,564 33.17	83,105 100.00

CT = *C. trachomatis*; HSV = herpes simple virus; RSV = respiratory syncytial virus; HBV = hepatitis B virus;
 EBV = Epstein-Barr virus; HCV = hepatitis C virus; HIV = human immunodeficiency virus

Table 12 summarizes the data on those agents that can cause infections in the respiratory tract, including adenoviruses, influenza viruses, parainfluenza viruses, RSV, rhinoviruses, *Mycoplasma pneumoniae*, *Chlamydiae psittaci*, and *Chlamydiae pneumoniae*. Laboratory-confirmed infections caused by these agents accounted for 12.6% of all laboratory-diagnosed infections. A large

proportion of patients infected with respiratory agents usually do not see a physician, and for a proportion of the patients who do, specimens will not be sent to the laboratory for viral examination. Nevertheless, the burden of respiratory infections caused by these viral, mycoplasma and chlamydiae agents is significant.

Table 12. Laboratory Evidence of Infections Caused by Respiratory Viral and Selected Non-viral Agents*

Year	Total No. of Positive Findings	No. of Positive Findings of Respiratory Agents	%
1989	50,513	6,873	13.61
1990	61,468	8,433	13.72
1991	73,464	9,559	13.01
1992	68,354	7,271	10.64
1993	66,447	8,128	12.23
1994	65,925	7,835	11.88
1995	73,180	9,474	12.95
1996	83,105	10,766	12.95
Total	542,456	68,339	12.60

* Includes adenoviruses, influenza viruses, parainfluenza viruses, RSV, rhinoviruses, *Mycoplasma pneumoniae*, *Chlamydiae psittaci* and *Chlamydiae pneumoniae*.

Laboratory Reports From Each Province Between 1989 and 1996

Laboratory evidence of infections with different agents varied among provinces (Tables 13 to 20). The proportion of reports of respiratory agents was higher in Alberta and Quebec but lower in the other provinces than the average proportion for all provinces. The number of positive reports of bloodborne or sexually transmitted pathogens, specifically HCV, HIV-1, parvovirus B19 and hepatitis B virus, was higher in British Columbia. Several

factors could have been affecting the regional differences, such as incidence, diagnostic capability or emphasis of individual laboratories, and use of different methods with variable sensitivities. It would be of interest to identify the differences in real incidence and to investigate the contributing or limiting factors if there are indeed differences in incidence rates among different provinces.

Temporal Trends of Selected Agents in Different Regions of Canada

Respiratory viruses and enteroviruses showed seasonal variations, the former peaking in the winter and the latter in the summer/fall. It was noticed that influenza epidemic seasons appeared earlier in the west and then moved to the east⁽⁸⁾. It was also demonstrated that infections of rotavirus showed similar shifting patterns in North America⁽⁹⁾.

To determine whether laboratory reports of these and other agents that cause infections in the respiratory tract or the gastrointestinal tract shared this characteristic during the whole 8-year period, the monthly number of reports from British Columbia, the prairie provinces (Alberta, Saskatchewan, Manitoba), Ontario, Quebec and the Atlantic provinces (New Brunswick, Nova Scotia, Prince Edward Island and Newfoundland) were plotted against the totals for Canada (Figures 1-12).

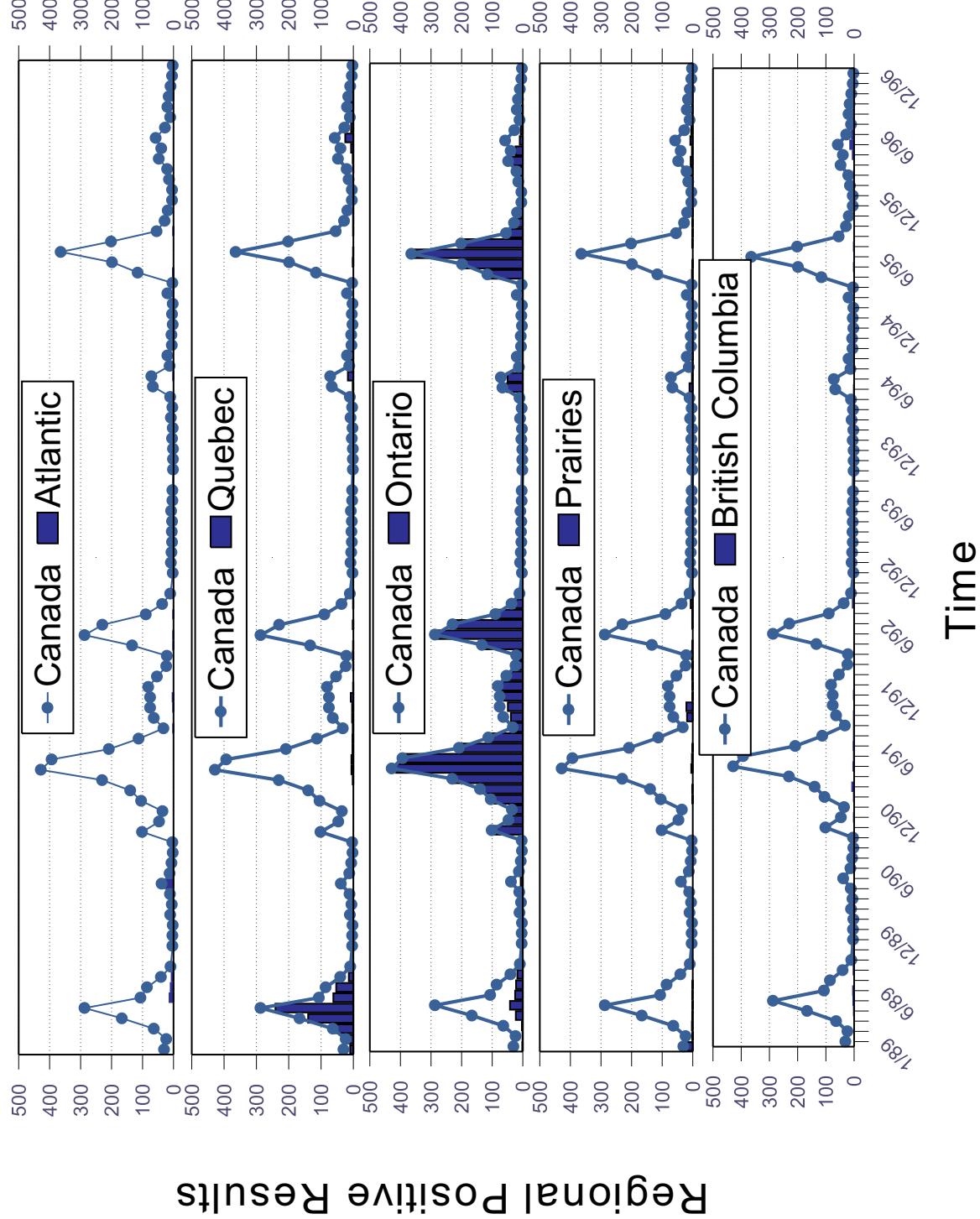
The national pattern for laboratory diagnosis of measles was largely determined by outbreaks in one province in any 1 year (Figure 1). For adenoviruses, laboratory diagnoses suggested a year-round pattern of infection (Figure 2). The start of laboratory diagnosis of influenza A virus in British Columbia and the prairie provinces may have given rise to relatively more laboratory diagnoses earlier in some seasons. This may partly reflect the enthusiasm of some western laboratories for diagnosing influenza earlier in the season or the relative success of influenza surveillance programs in these same regions (Figure 3). It appears that influenza B arose later in the Atlantic provinces than nationally, whereas in the prairies and to some extent in British Columbia, influenza B diagnosis appeared to peak earlier than the national

average (Figure 4). However, no regional trends were seen for parainfluenza laboratory diagnoses (Figure 5). RSV laboratory diagnosis peaked earlier in Quebec but later in Atlantic Canada than the national average (Figure 6). Overall, the peak of respiratory virus diagnosis may have been earlier in Quebec than nationally (Figure 7).

No predictable pattern could be identified for hepatitis A virus (HAV), except for the decline in the number of reports in Quebec after 1992 and the variability of HAV diagnosis by region over time (Figure 8). There were no reports of Coxsackie A and B viruses from the coastal provinces, and the number of reports from Ontario was disproportionately low relative to the population. Peak occurrences of Coxsackie viruses are sometimes the result of outbreaks in only one region (Figure 9). It is interesting to note the very limited echovirus reporting from coastal provinces and the predominance of reporting from the prairies and Quebec (Figure 10). For rotavirus, the prairies appeared to lead seasonal diagnoses, peaking earlier than the national average. The Quebec results seemed to be average in most years, but in the 1991-1992 and 1993-1994 seasons the Quebec rotavirus peaks built up earlier than average (Figure 11). For enteroviruses as a whole, a seasonal pattern was nevertheless noticeable, although increasing numbers of interseasonal diagnoses have been reported from Ontario and the prairies. In contrast to Coxsackie A and B viruses and echoviruses, enteroviruses were reported from the Atlantic and B.C. provinces (Figure 12).

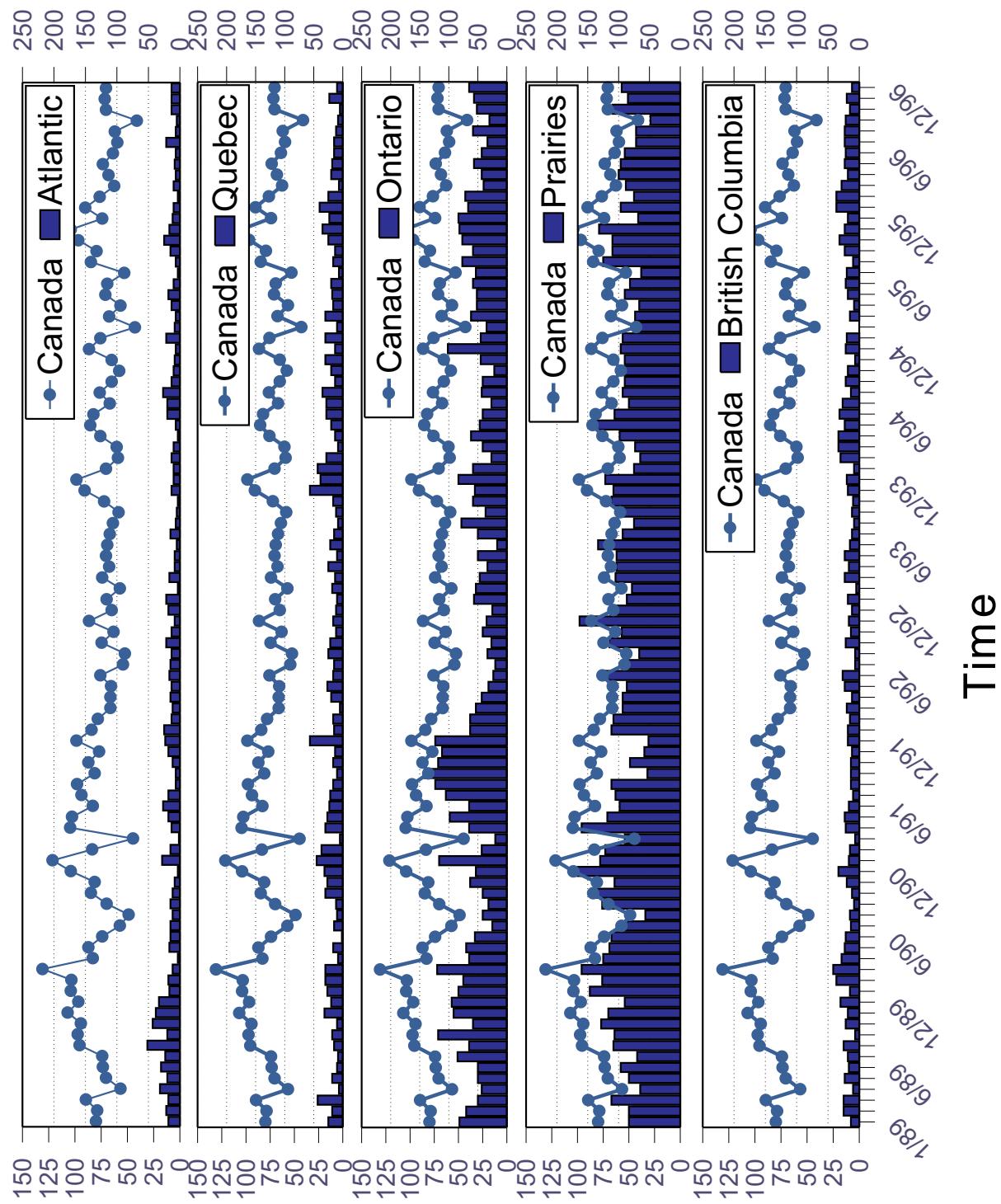
Figure 1

Measles Virus in Canada by Region by Month



National Positive Results

Figure 2
Adenoviruses in Canada by Region by Month



Regional Positive Results

Figure 3

Influenza A Virus in Canada by Region by Month

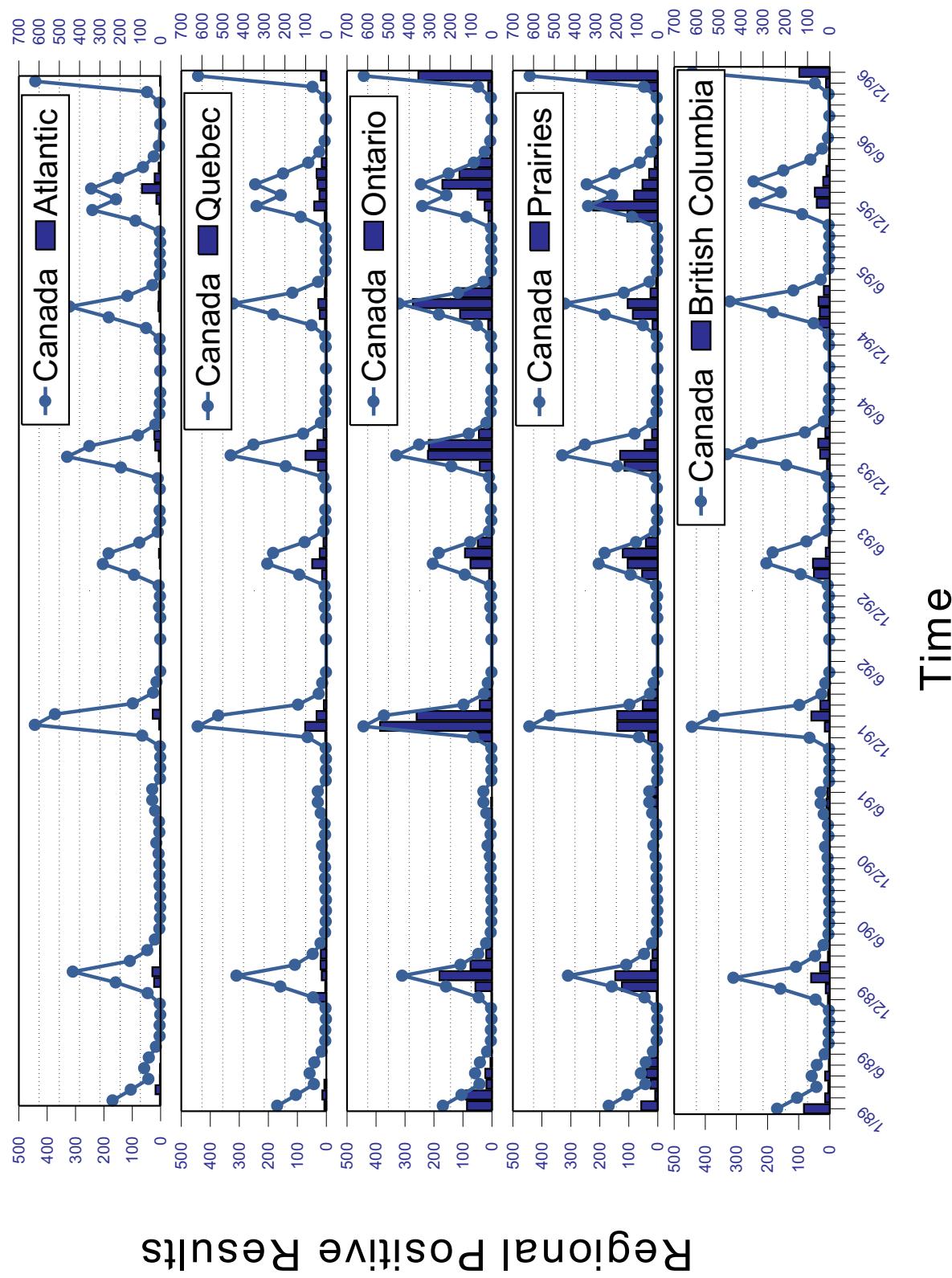


Figure 4

Influenza B Virus in Canada by Region by Month

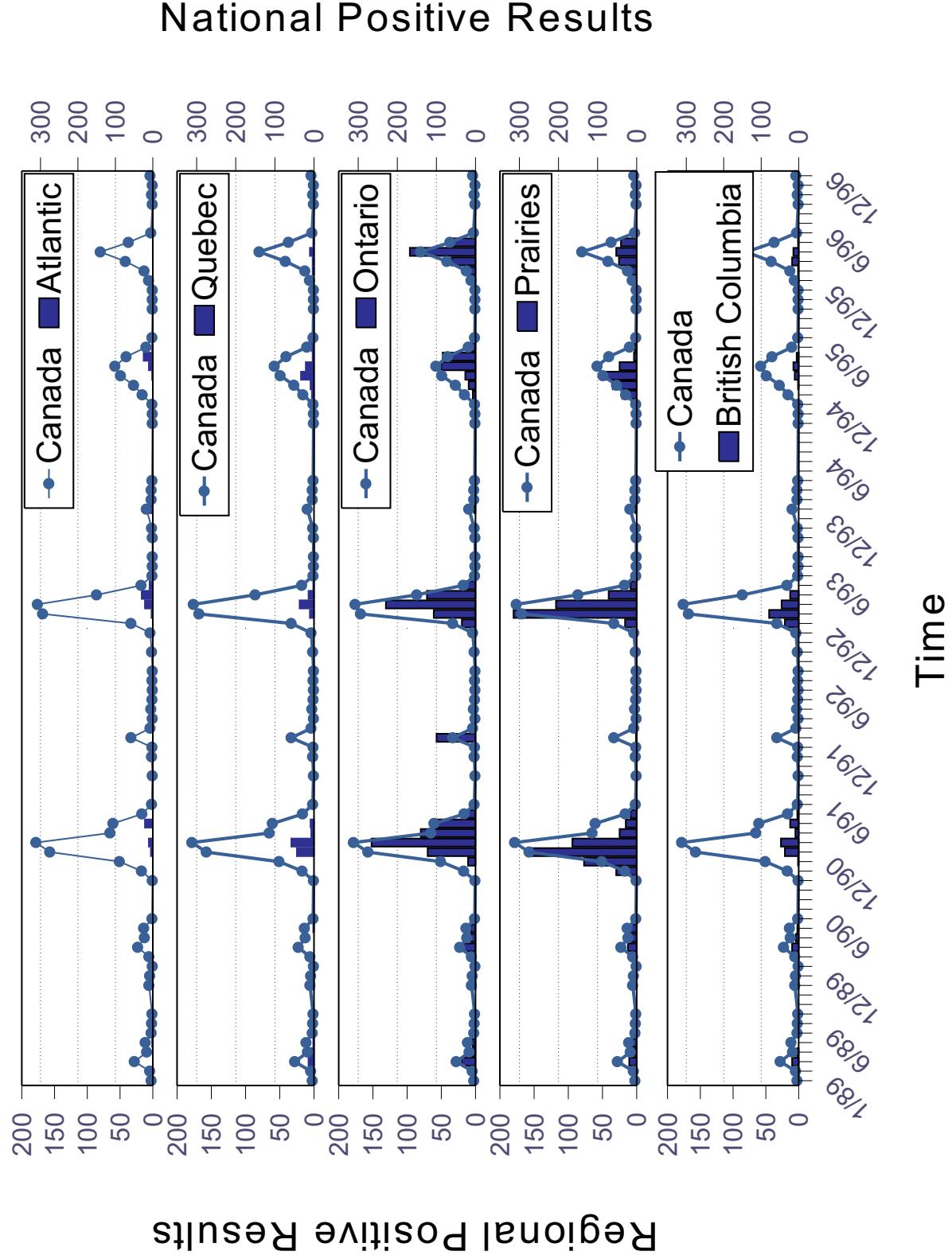
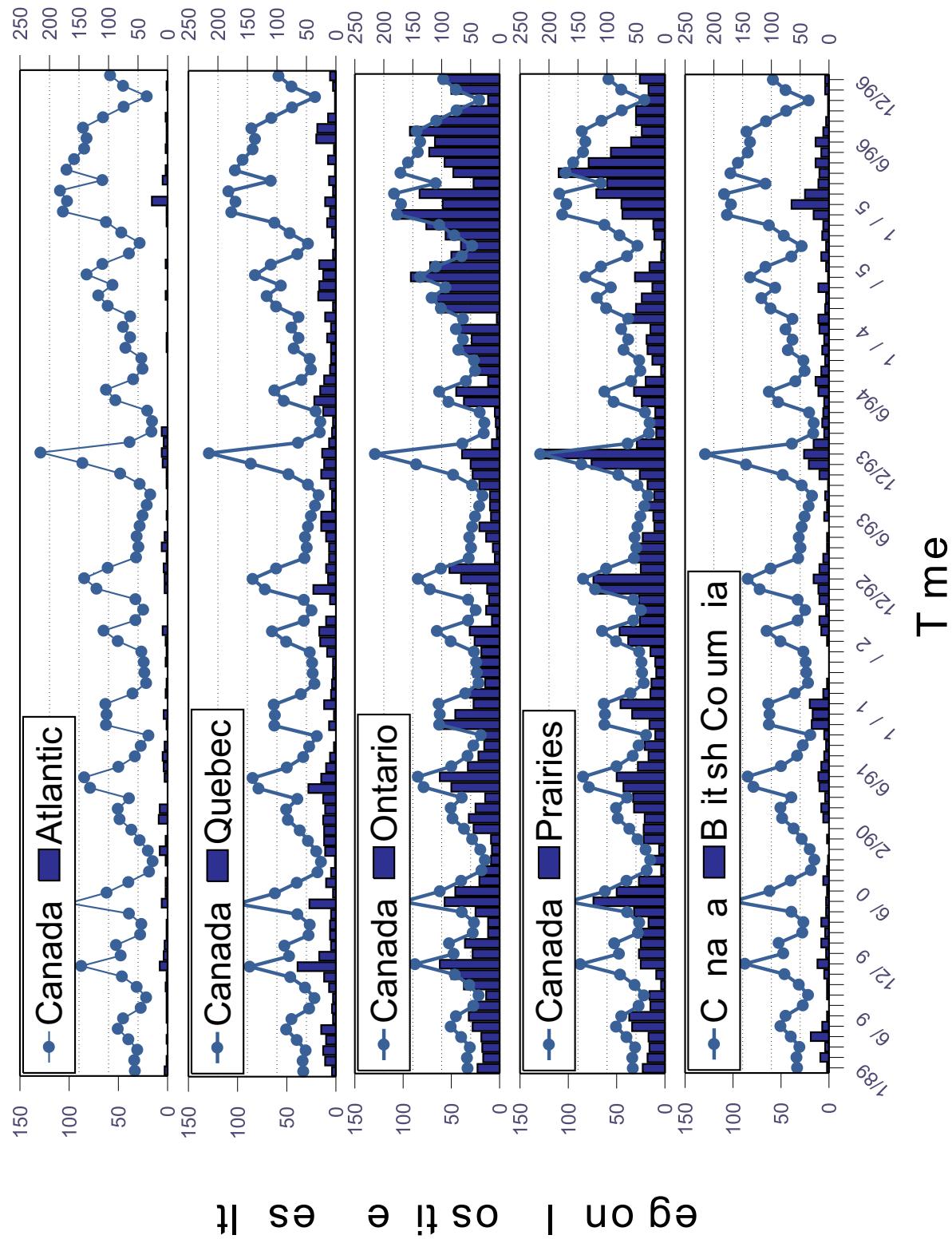


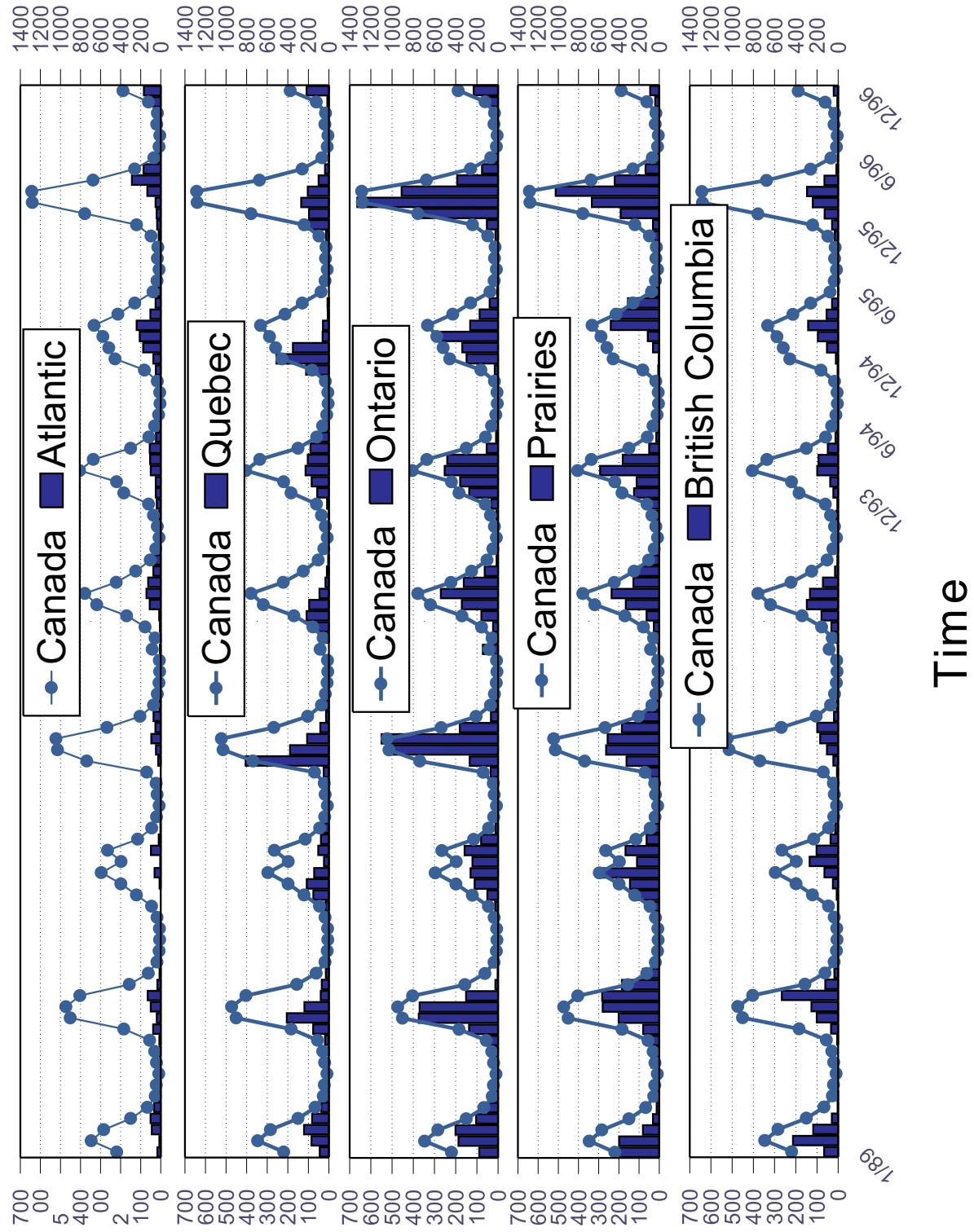
Figure 5

Parainfluenza Viruses in Canada by Month



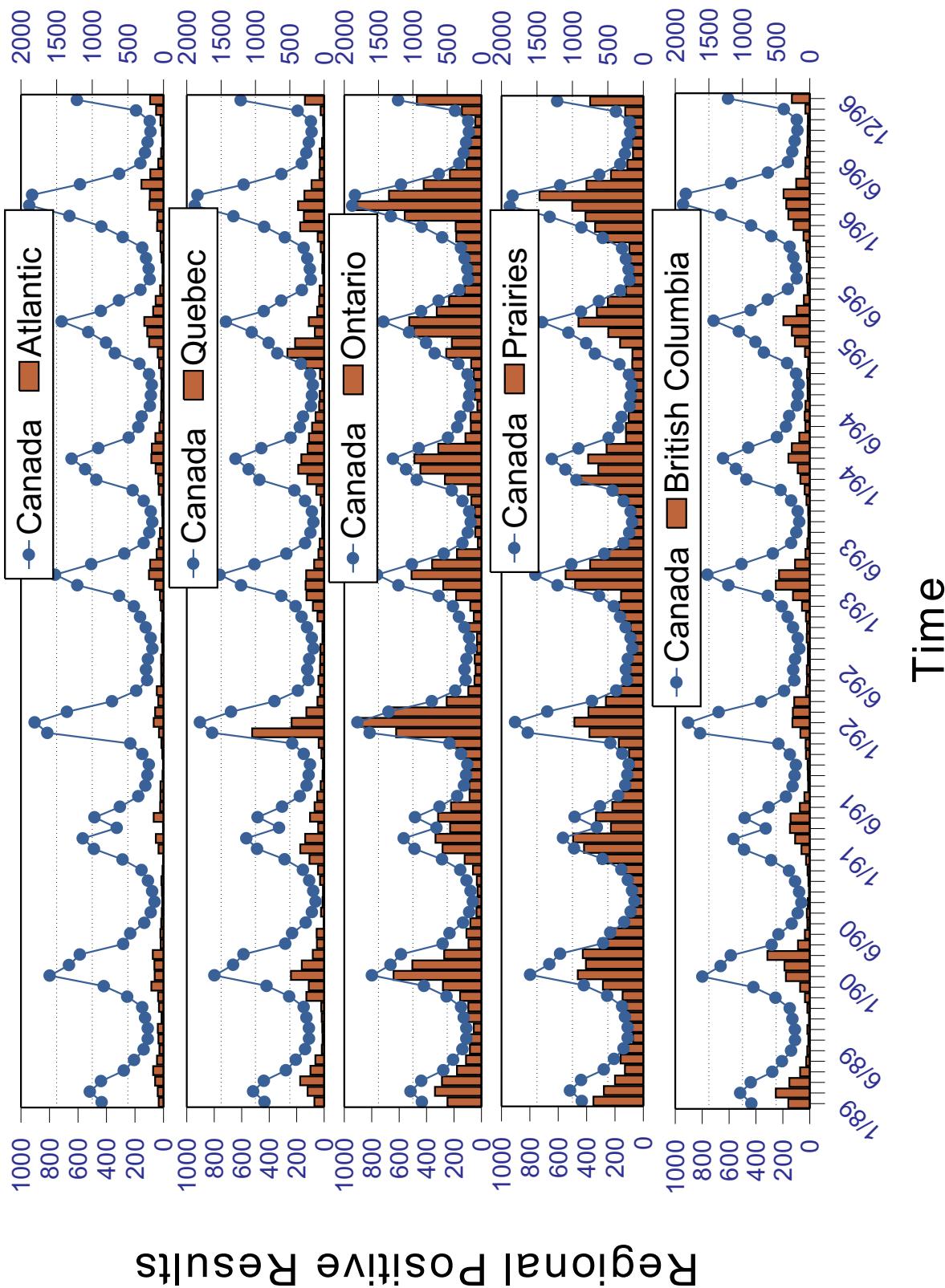
National Positive Results

Figure 6
Respiratory Syncytial Virus in Canada by Region by Month



National Positive Results

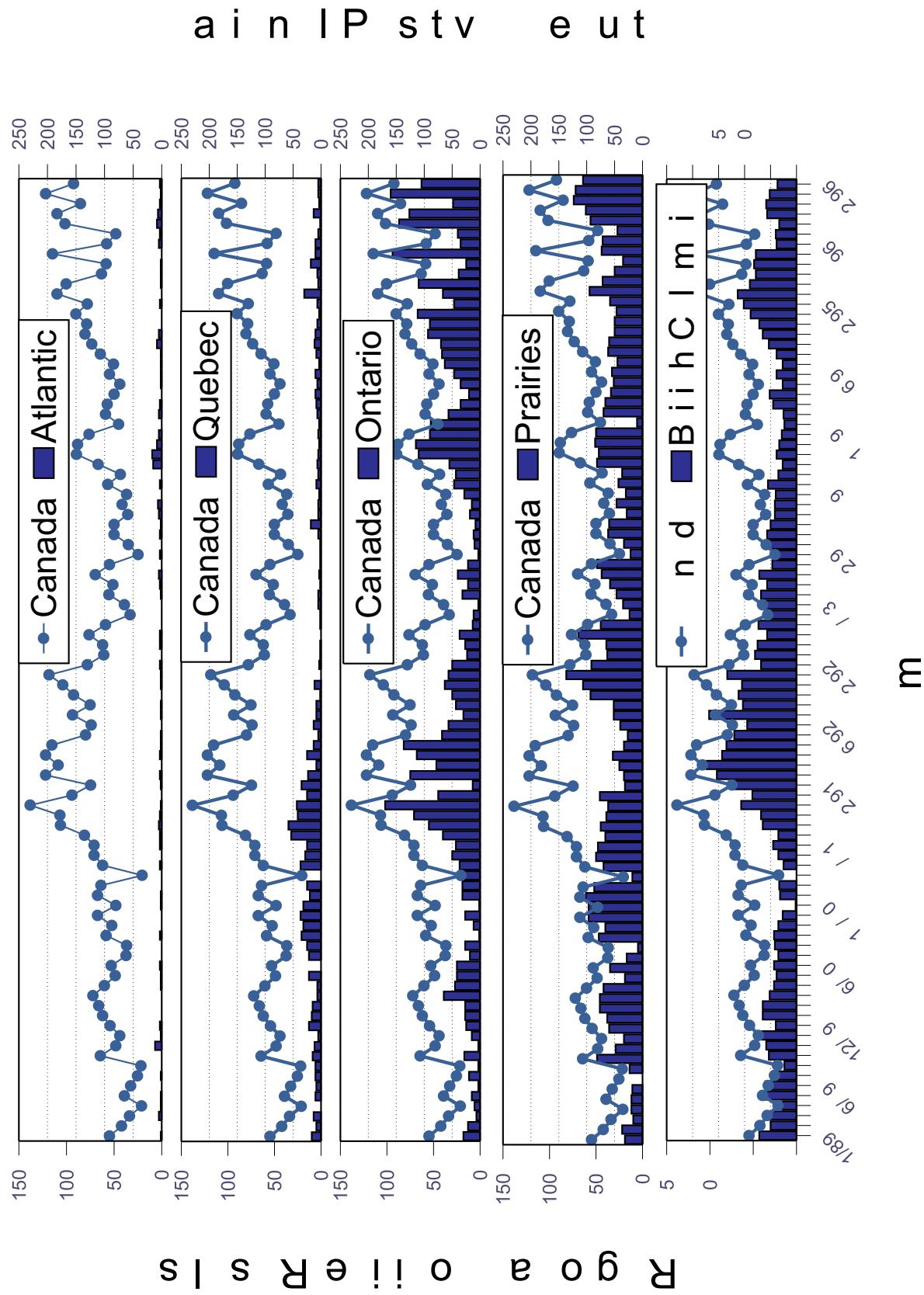
Figure 7
Respiratory Viruses in Canada by Region by Month



Regional Positive Results

Figure 8

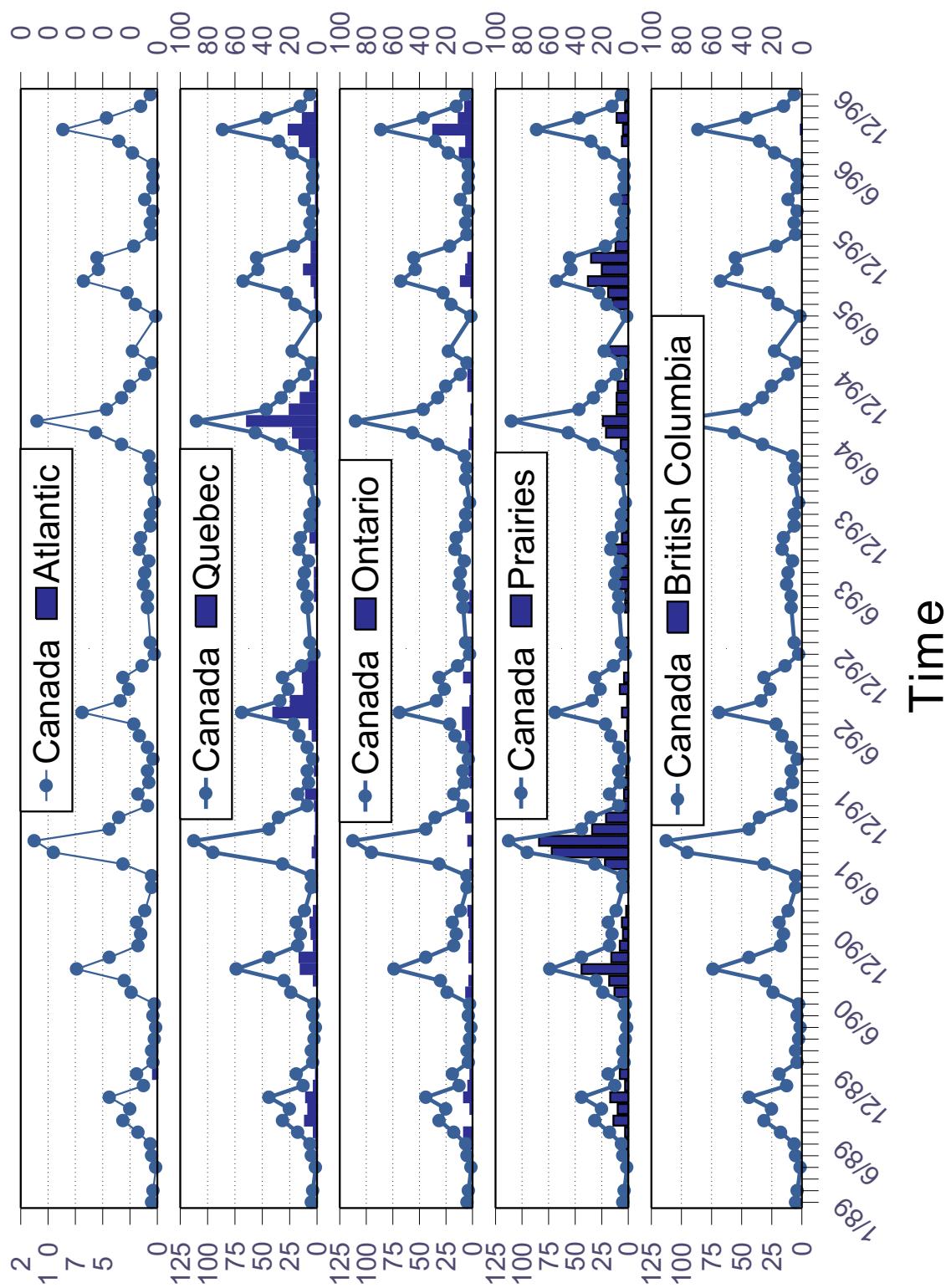
Hepatitis A Virus in Canada by Region by Month



National Positive Results

Figure 9

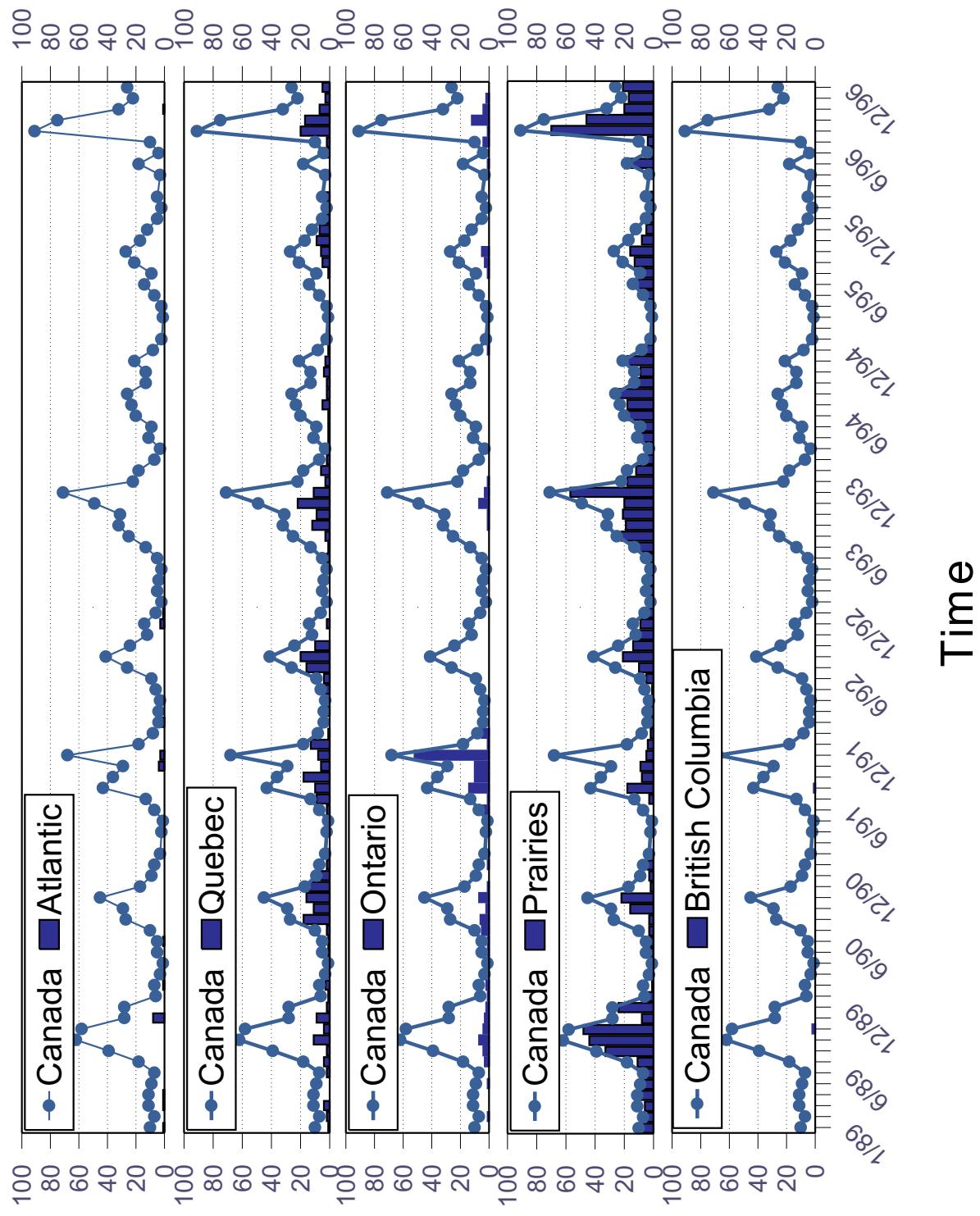
Coxsackie A and B Viruses in Canada by Region by Month



Regional Positive Results

National Positive Results

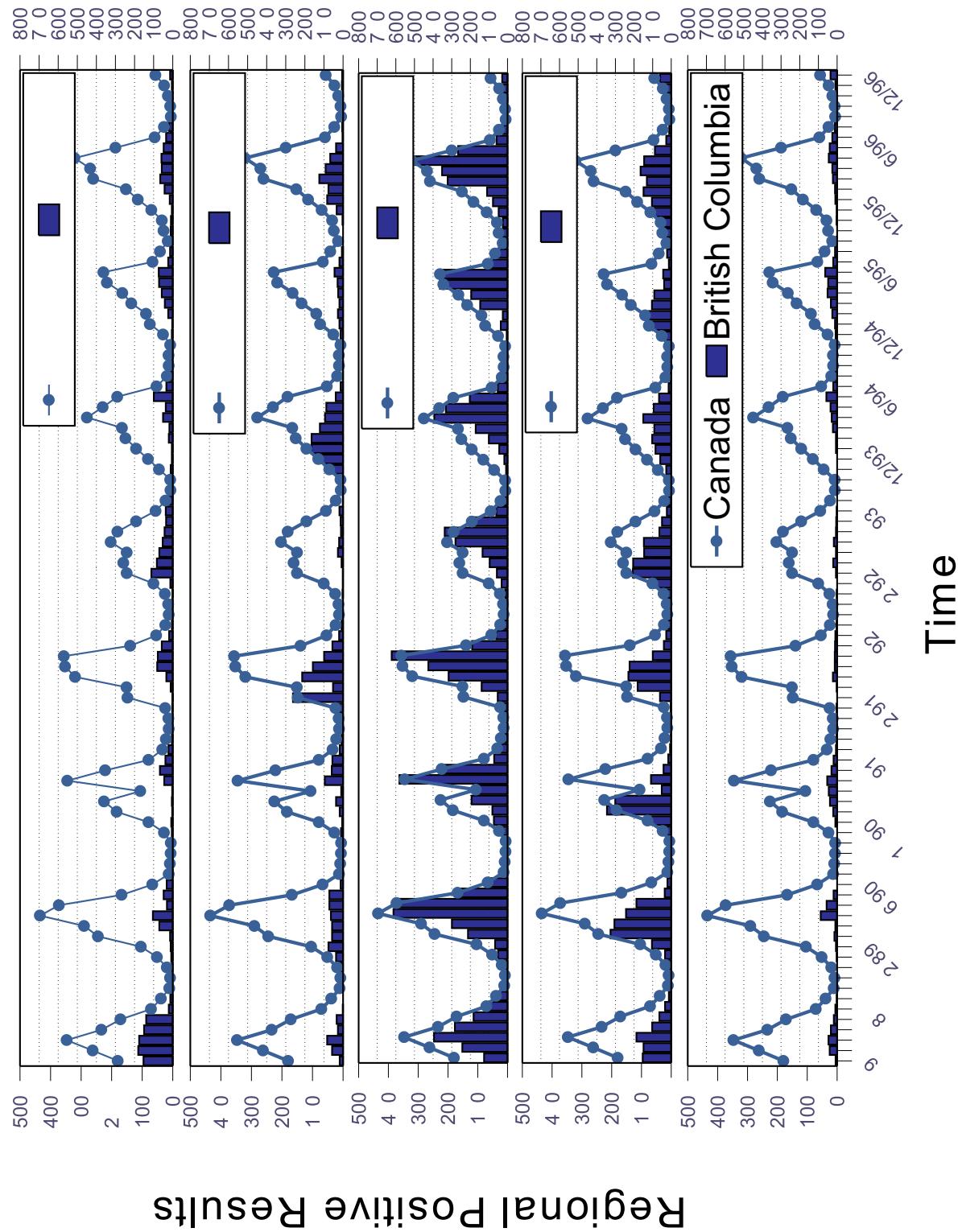
Figure 10
Echoviruses in Canada by Region by Month



Regional Positive Results

National Positive Results

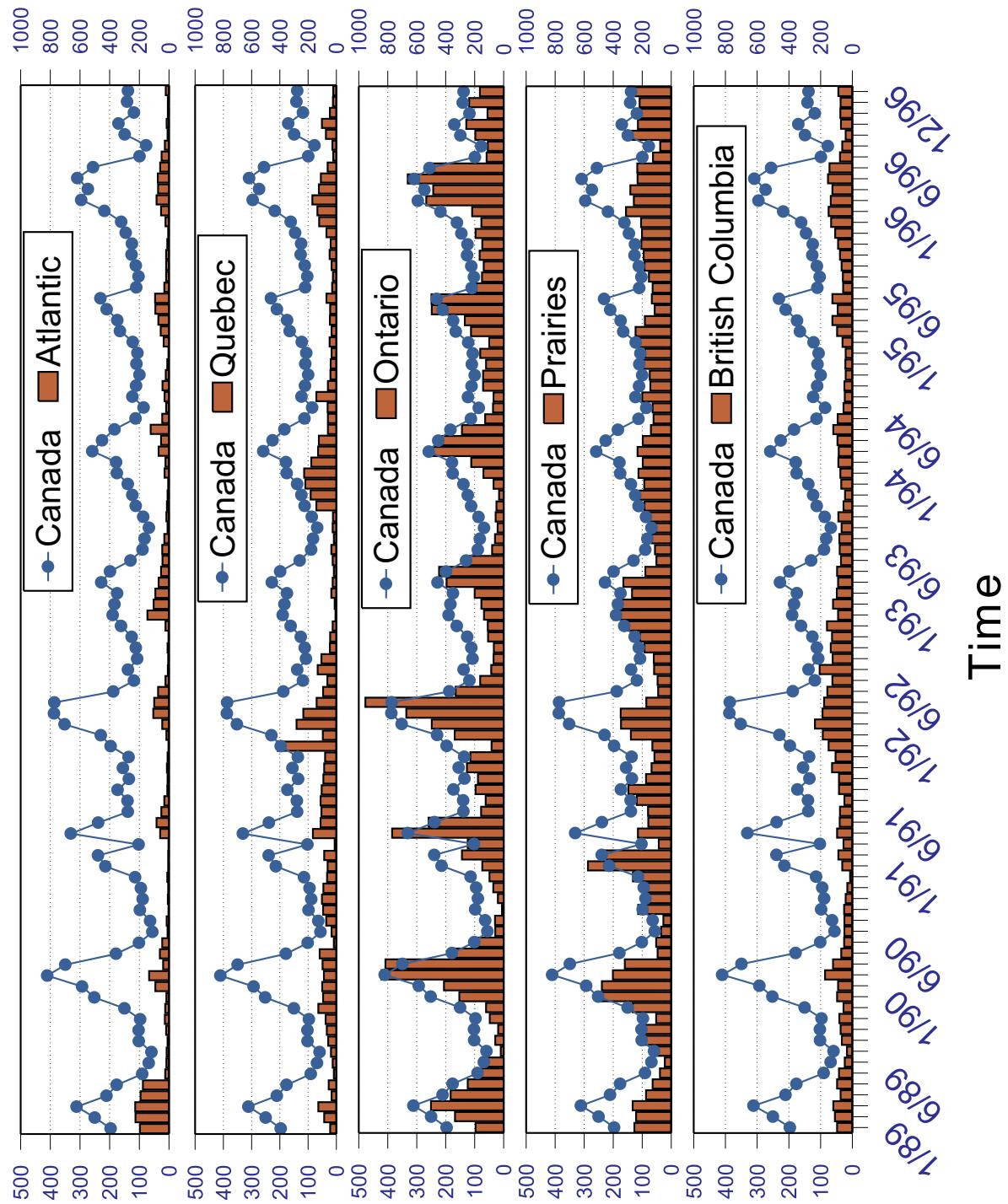
Figure 11
Rotavirus in Canada by Region by Month



National Positive Results

Figure 12

Enteroviruses in Canada by Region by Month



Regional Positive Results

Discussion

The CVR is a laboratory-based surveillance system for infections caused by viruses and selected *Mycoplasma* and *Chlamydiae* agents of public health importance. Over 90 species, types and subtypes are reported each month by over 40 laboratories from all 10 provinces across Canada. Therefore, the system provides national data on trends of laboratory diagnosis of these infectious agents in different regions of the country over time. For many agents, this system is probably the only source of national data. Furthermore, since the reporting format is relatively straightforward and based on the records of participating laboratories, the data collected through the system should be fairly reliable.

However, it should be pointed out that trends demonstrated by the system may not always accurately reflect regional differences in incidence rates, since the effort that goes into laboratory disease diagnosis in response to new infections may vary on a per capita basis by region, time and agent. Analysis of reporting patterns for various agents over a number of years has indicated that new diagnostic techniques, availability of diagnostic services, awareness of the role an agent plays in disease, and real changes in the occurrence of a disease may influence the number of positive laboratory reports for a particular agent⁽¹⁾. Recent availability and awareness of laboratory diagnostic technology for HCV, and diagnostic capability and special interest in rhinoviruses have likely been significant contributors to the increasing numbers of these agents being reported⁽⁴⁾. Nevertheless, the data from this system should provide relatively reliable estimates or indicators of year-to-year trends of the agents reported, especially if the number of reporting laboratories and the total number of

specimens tested are also considered. For example, trends in infections with influenza virus revealed through the system were consistent with those derived from another surveillance system for respiratory viruses^(8,10). Certainly, data from both surveillance systems reflect only a proportion of the real incidence, as already stated, but a true reflection of the real incidence trends is often what can be expected.

Another example is measles virus infections. In 1986, the largest number of cases of laboratory-diagnosed measles since 1979 was reported and corresponded to a widespread resurgence of measles infection in Canada^(1,11). Moreover, the increased prominence of HIV-1 reports among positive laboratory diagnoses reported to LCDC in 1987 and 1988 corresponded to a similar increase in disease surveillance reports collected by the Canadian Federal Centre for AIDS^(1,12).

Weber and Parker compared the number of laboratory reports and the number of cases reported for some viruses causing notifiable diseases⁽⁵⁾. For AIDS/HIV-1, hepatitis B and hepatitis C, there were many more positive laboratory tests for evidence of infection each year than there were notifiable cases. Presumably, this reflects repeated monitoring of patients by laboratory testing, duplicate reporting of positive findings for different detection methods (for example, Western blot and p24 antigen testing for the same HIV-1-infected patient) or delayed reporting of AIDS/HIV-1 infections. For other notifiable diseases, such as chickenpox/varicella-zoster, mumps, and measles, clinical diagnosis is generally reliable, and relatively fewer laboratory tests are performed for each case. Yet for other agents, such as hepatitis A and

rubella, the ratio of notified cases to laboratory reports is much lower, reflecting a strong reliance on laboratory confirmation for these agents. Last, laboratory detection of polioviruses is presumed to result largely from postvaccination investigations in which the virus is detected after vaccination with live oral polio vaccine, and does not necessarily imply notifiable cases of poliomyelitis.

Certain circumstances are more likely to make positive laboratory diagnoses a useful proxy for actual changes in the incidence of a

disease agent. These conditions include the following: (a) significant illness exists such that medical help is sought by the patient, (b) the condition presents nonspecific symptoms such that the physician seeks laboratory diagnosis, (c) reliable laboratory technology exists and is available to diagnose the suspected agent and (d) specific treatment of the disease condition or control of the disease agent is warranted and dependent upon the identification or characteristics of the suspected agent⁽¹⁾

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APPENDIX:

List of Laboratories Participating in the Canadian Virus Reporting System, 1989 to 1996

Public Health Laboratory (B.C. Centre for Disease Control) - Vancouver, BC
Diagnostic Virology and Reference Laboratory, UBC - Vancouver, BC
British Columbia Children's Hospital - Vancouver, BC
Public Health Laboratory - Edmonton (Northern AB)
Public Health Laboratory - Calgary (Southern AB)
Royal University Hospital - Saskatoon, SK
Public Health Laboratory - Regina, SK
Cadham Provincial Laboratory - Winnipeg, MB
Regional Public Health Laboratory - Thunder Bay, ON
Public Health Laboratory - Sault Ste. Marie, ON
Regional Public Health Laboratory - Timmins, ON
Regional Public Health Laboratory - Windsor, ON
Public Health Laboratory - London, ON
St. Joseph's Health Centre - London, ON
Public Health Laboratory - Hamilton, ON
St. Joseph's Hospital - Hamilton, ON
Public Health Laboratory - Orillia, ON
Regional Public Health Laboratory - Palmerston, ON
Hospital for Sick Children - Toronto, ON
Public Health Laboratory - Toronto, ON
Toronto Medical Laboratories (The Toronto Hospital) - Toronto, ON
University of Toronto - Toronto, ON
Wellesley Hospital - Toronto, ON
Women's College Hospital - Toronto, ON
Public Health Laboratory - Peterborough, ON
Regional Public Health Laboratory - Kingston, ON
Children's Hospital for Eastern Ontario - Ottawa, ON
Regional Public Health Laboratory - Ottawa, ON
Hôpital général de Montréal - Montréal, PQ
Hôpital Ste-Justine - Montréal, PQ
Montreal Children's Hospital - Montréal, PQ
Royal Victoria Hospital - Montréal, PQ
Centre hospitalier universitaire - Sherbrooke, PQ
Laboratoire régional de virologie de l'Université Laval - Ste-Foy, PQ
Centre hospitalier St-Joseph - Trois-Rivières, PQ
Chaleur Regional Hospital - Bathurst, NB
Hôpital régional de Campbellton - Campbellton, NB
Hôpital régional d'Edmunston - Edmunston, NB
Dr. Everett Chalmers Hospital - Fredericton, NB
Hôpital Georges L. Dumont - Moncton, NB
The Moncton Hospital - Moncton, NB
St. John's Regional Hospital - Saint John, NB
Queen Elizabeth Hospital - Charlottetown, PEI
Queen Elizabeth II Health Sciences Centre - Halifax, NS
Public Health Laboratory - St. John's, NF

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