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Surveillance of respiratory viruses

A 10-year laboratory-based study

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Respiratory virus isolates made at the National Institute for Virology from 1982 to 1991 were studied. An active virus surveillance programme, 'viral watch', which recruits throat swab specimens from a network of monitoring centres — mainly in the Witwatersrand and Vereeniging area with one centre in Middelburg — that represent a cross-section of the population, provided 68% of the specimens and 74% of the isolates, with an isolation rate of 25,5%. This was significantly higher than that of routine specimens (17,7%). Of the 966 isolates, influenza viruses accounted for 527 (54,7%), para-influenza for 122 (12,6%), respiratory syncytial virus for 34 (3,4%) and adenovirus for 106 (11,0%). Influenza viruses showed a definite seasonal peak between June and August whereas the other viruses, although they showed a winter predominance, were isolated throughout the year. An active virus surveillance programme is particularly valuable in monitoring respiratory virus epidemiology in the population.

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Various methods have been used for disease surveillance, including the reporting of notifiable diseases as well as laboratory-based, hospital-based and population-based surveillance.[1] Monitoring of respiratory tract infections has been carried out by means of some of these same methods,[2,3] as well as general practitioner networks,[4] morbidity reports and reports of school and work absenteeism.[5] A combination of two or more of these methods has been found to be more precise than any single method alone.[5-8] For detecting outbreaks of disease and characterising the aetiological agent, laboratory-based surveillance has been shown to be a useful tool.[1]

In order to improve the monitoring of respiratory disease, especially influenza, a 'viral watch' surveillance programme was started at the National Institute for Virology (NIV) to recruit suitable specimens for isolation of respiratory viruses from patients with respiratory tract infection. Similar programmes have been used in Belgium[7] and France.[8]

This paper describes 10 years of continuous monitoring of respiratory virus isolates from actively recruited specimens from the viral watch programme as well as from respiratory specimens routinely sent in to the NIV for virus isolation.

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Materials and methods

Respiratory specimens received at NIV for isolation of viruses between 1 January 1982 and 31 December 1991 were reviewed. Specimens submitted with a diagnosis other than respiratory infection, e.g. meningitis, were excluded from the study. Respiratory specimens consisted of throat swabs, tracheal aspirates, bronchial lavages, lung biopsies and sputa. Throat swab specimens were specifically recruited from 16 viral watch centres which represent a cross-section of the population including all race, age and socio-economic groups. Fifteen of these centres are situated in the Witwatersrand and Vereeniging area and one in Middelburg, Transvaal, and comprised general practitioners, paediatric outpatients, a mine hospital, factory workers, university students, and staff at a hospital as well as at the NIV. A maximum of two specimens per week was accepted from each centre. A specifically designed specimen label was provided to accompany the specimen.

All specimens were inoculated into both embryonated chicken eggs and cell cultures. Positive influenza isolates were typed by haemagglutination inhibition and sent for confirmatory typing to the World Influenza Centre, National Institute for Medical Research, Mill Hill, London.

Results

In this study 4 133 specimens received between 1982 and 1991 were reviewed; the number per year ranged from 218 to 525 (median 456). Three thousand five hundred and seventy (86,4%) were throat swabs, 261 (6,3%) tracheal aspirates, 104 (2,5%) lung biopsy specimens, 100 (2,4%) bronchial lavage specimens and 98 (2,4%) sputum specimens. Viral watch specimens accounted for 2 811 (68%) of the specimens (Fig. 1).

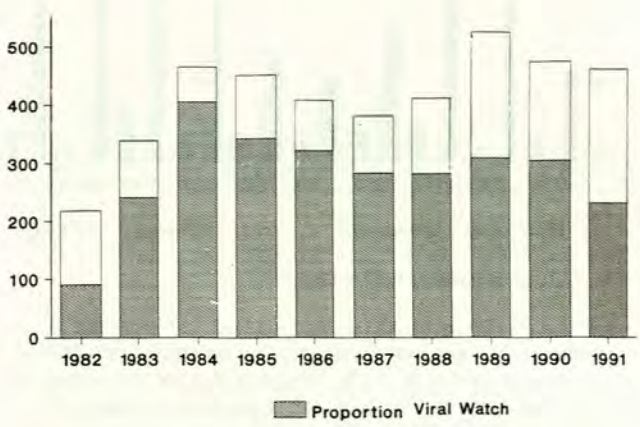

Fig. 1. Proportion of viral watch specimens.

A total of 966 viruses was isolated during the 10-year period, the number per year varying from 46 to 147 with a mean isolation rate of 23,4%. Table I shows the isolation rate for each kind of specimen. The isolation rate for viral watch specimens was significantly higher ($P < 0,0001$) than that for throat swabs received from other sources (Table II).

Diagnoses provided for 852 (82,2%) of the patients with positive isolates were influenza, upper respiratory tract infection, pneumonia, bronchiolitis, croup and tonsillitis/pharyngitis. The viruses isolated were identified as influenza (527; 54,6%), paramyxoviruses (169; 17,5%), adenovirus (106; 11,0%), herpesviruses (91; 9,4%), enteroviruses (70; 7,2%) and reoviruses (3; 0,3%) (Fig. 2).

Table I. Isolation rate (%) per type of specimen

Specimen	Isolation rate
Throat swabs	23,9
Tracheal aspirate	21,5
Lung biopsy	24,0
Bronchial lavage	18,4
Sputum	15,3

Table II. Isolation rates from throat swabs (%)

Year	Viral watch	Other
1982	18,9	18,0
1983	27,8	25,0
1984	21,0	17,3
1985	22,7	20,8
1986	18,3	12,9
1987	23,0	16,4
1988	25,2	4,8
1989	35,0	14,0
1990	30,5	24,0
1991	32,5	20,8
Total	25,5	17,7

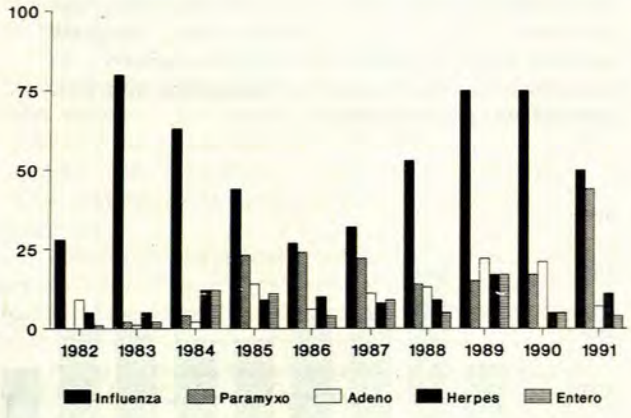

Fig. 2. Type of isolate, 1982 - 1991.

Influenza viruses were further typed as influenza A H_1N_1 (193), influenza A H_3N_2 (198), influenza B (120) and influenza C (16). Influenza A H_1N_1 and H_3N_2, as well as influenza C, were detected in 7 of the 10 years studied and influenza B in 8. Only 1 subtype of influenza (A H_1N_1) was detected in 1987 and all 3 subtypes were detected in 1984, 1985 and 1989. The serotypes and strains are shown in Table III and Fig. 3. Although influenza viruses were isolated sporadically throughout the year, influenza showed a distinct seasonal pattern, with the first isolates usually appearing by mid-June. The mean duration of the 'season' of influenza isolation was 12 weeks. Only in 1 of the 10 years studied did the 'influenza season' start before the middle of May and last for more than 14 weeks, i.e. in 1989 the first and last isolates were made on 10 April and 16 October respectively. In 1983 a substantial number of isolates were made between the middle of September and the end of November, some 6 weeks after the cessation of normal winter activity. This was followed in 1984 by a severe outbreak of influenza (Fig. 4).[9]

Table III. Influenza strains identified

Year	Influenza subtype	Strains
1982	A H_1N_1	A/Belgium/2/81
	B	B/Singapore/222/79
1983	A H_1N_1	A/Hong Kong/2/82
	A H_3N_2	A/Philippines/2/82
1984	A H_1N_1	A/Chile/1/83
	A H_3N_2	A/Philippines/2/82; A/Belgium/2/81
	B	B/USSR/100/83
1985	A H_1N_1	A/Switzerland/79/85; A/Chile/1/83
	A H_3N_2	A/Christchurch/4/85; A/Wellington/4/85
	B	B/USSR/100/83
1986	A H_1N_1	A/Singapore/6/86
	B	B/Victoria/102/83; B/USSR/100/83
1987	A H_1N_1	A/Taiwan/1/86
1988	A H_3N_2	A/Sichuan/2/87
	B	B/Victoria/2/87
1989	A H_1N_1	A/Victoria/36/88
	A H_3N_2	A/Shanghai/11/87; A/OMS/5389/88
1990	A H_3N_2	A/Beijing/352/89; A/Hong Kong/25/90; A/Shanghai/11/87
	B	B/Victoria/2/87
1991	A H_1N_1	A/Taiwan/6/86
	B	B/Panama/45/90

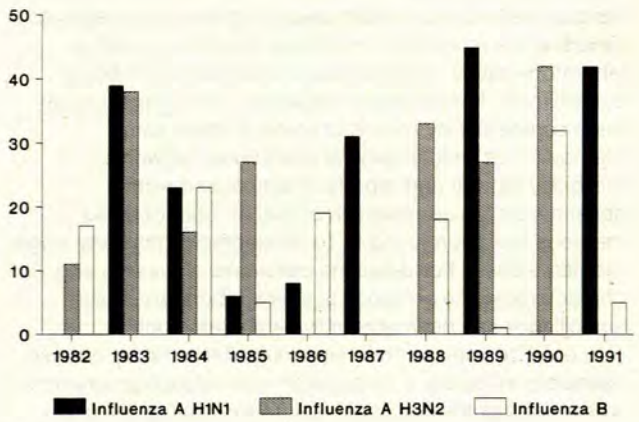

Fig. 3. Influenza serotypes, 1982 - 1991.

Ages were known for 458 (89,6%) of the 511 patients from whom influenza A or B was isolated. The age distribution for all 3 subtypes was similar with ranges of 1 month to 67 years (median 18 years) for influenza A H_1N_1, 1 month to 79 years (median 13 years) for A H_3N_2 and 4 months to 57 years (median 16 years) for influenza B. The vast majority of influenza isolates (510/527; 96,8%) were made from throat swabs. Diagnoses were known for 513 (97,3%) patients. The most common diagnosis was influenza (47,2%) followed by upper respiratory tract infection (URTI) (34,5%).

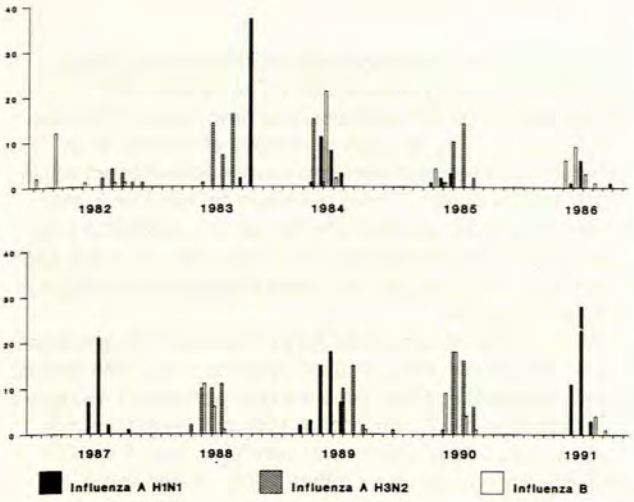

Fig. 4. Seasonal distribution of influenza viruses.

Of the 122 parainfluenza viruses isolated type 3 was the most common, i.e. 101 (82,8%). Isolates were made throughout the year but the majority (62,3%) were isolated during the months April to September. Respiratory syncytial virus (RSV) was only isolated occasionally between January and March, with 29/34 (85,3%) being isolated between April and August (Fig. 5). Although for both parainfluenza and RSV the majority of patients were aged under 5 years, the proportion was significantly higher for RSV (87,1%) than parainfluenza (60,9%) ($P = 0,0123$) (Fig. 6). The majority (124/156; 79,5%) of parainfluenza and RSV isolates were made from throat swabs, with 25 (15%) from tracheal aspirate and bronchial lavage specimens and 2 isolates from post-mortem lung biopsy and 5 from sputum specimens. Two of the 5 measles virus isolates were made from tracheal aspirates, 1 from a post-mortem lung biopsy and the remaining 2 from throat swabs. The 8 mumps virus isolates were all made from throat swabs. The diagnosis was given for 83% of patients with parainfluenza and 74% of those with RSV isolates. The spectrum of diagnoses for parainfluenza and RSV was similar, with URTI responsible for the largest group (25,4%), followed by pneumonia (23,0%).

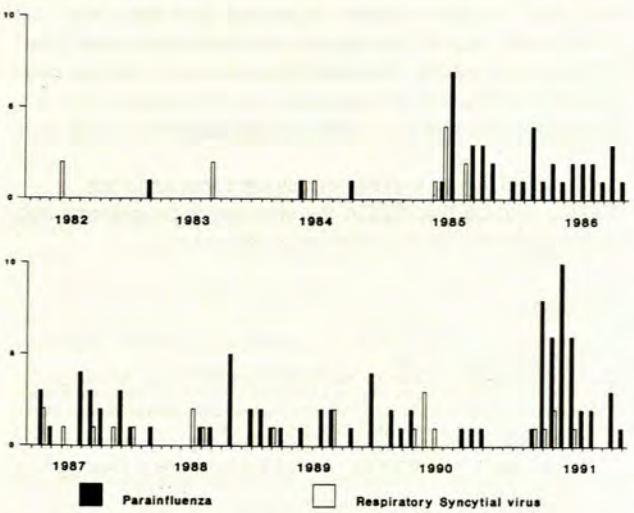

Fig. 5. Seasonal distribution of paramyxoviruses.

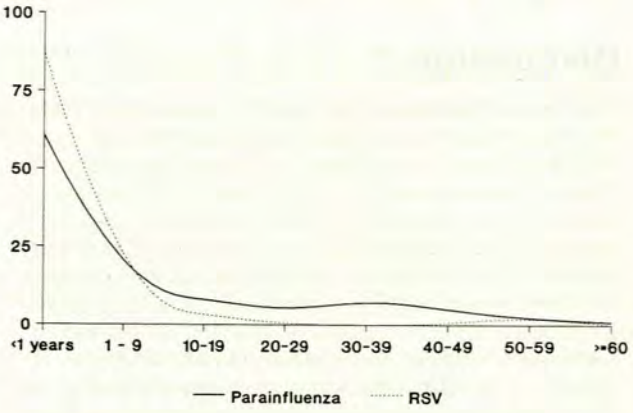

Fig. 6. Age distribution of paramyxoviruses.

Adenoviruses were isolated throughout the year and no seasonal pattern was observed (Fig. 7). Ages were known for 91 patients and ranged from 1 month to 60 years (median 18 months), with the largest group (35; 38,5%) under 1 year of age. The majority (75; 70,8%) of isolates were made from throat swabs, 17 (16,0%) from tracheal aspirates, 10 (9,4%) from post-mortem lung biopsies and 4 (3,8%) from sputum specimens. Diagnoses were known for 74 (70%) patients of which the largest group (26; 35,1%) had URTI, followed by 21 (28,4%) with tonsillitis/pharyngitis.

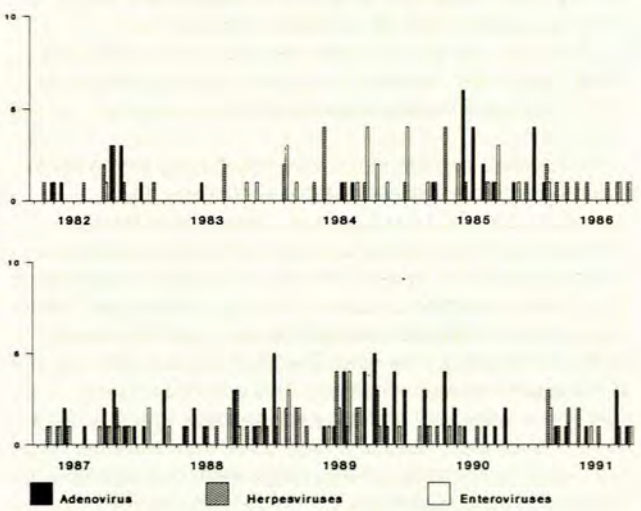

Fig. 7. Seasonal distribution of adenoviruses, herpesviruses and enteroviruses.

Twelve herpesviruses were identified as cytomegalovirus and 79 as herpes simplex virus (HSV) (50 HSV type 1, 6 HSV type 2 and 23 not typed). Isolates were made throughout the year and no seasonal pattern was detected (Fig. 7).

Of the enteroviruses, 9 were identified as Coxsackie A, 24 as Coxsackie B, 13 as echovirus and 13 as poliovirus; 11 were not identified further. Although there was no clear seasonal pattern few isolates (17/70; 24%) were made during the winter months (Fig. 7).

Discussion

Respiratory infections are an important cause of morbidity and mortality in the developing world. Monitoring of respiratory disease is important in the early recognition of influenza outbreaks and the determination of circulating strains. The cornerstone of influenza surveillance has been the monitoring of deaths due to pneumonia and influenza. However, with this method, an outbreak may be in progress for several weeks before it is identified.[5] Laboratory-based surveillance has proved useful in detecting widespread outbreaks of disease[1] and in obtaining early isolates of influenza virus.[6] Surveillance only of routine specimens sent to the laboratory would be of less value as shown in our study where 68% of the specimens and 74% of the isolates originated from the viral watch programme. Laboratory-based data are not really representative and are more qualitative than quantitative in nature; this precludes estimation of the rate of attack in the general population. However, even sporadic reporting of individual cases can uncover unusual disease activity.[1] When very few specimens are received, the chances of detecting an outbreak of a respiratory illness decrease as the respiratory viruses are in permanent circulation and a single isolate would not indicate an outbreak.

The NIV forms part of the global network of WHO National Institutes of Influenza established to collect and analyse influenza data and strains throughout the world[9] in order to identify and characterise strains in circulation and detect antigenic variants in order to design the vaccine composition.[8] For this purpose the viral watch system has proved extremely valuable. During the 10-year period only 11% of annual influenza isolates came from routine specimens.

Participating doctors in the viral watch programme are in a good position to collect suitable specimens; this maximises the virus isolation rate. From time to time changes have been made to include different geographical areas and different types of centres. Although the number of specimens submitted by each viral watch centre was limited so as not to overburden the laboratory, specimens were received throughout the year. Continual contact with doctors at these centres was necessary. This ensured that the specimens were sent and allowed feedback to the doctors about the isolates. Ages and diagnoses were available for all viral watch specimens, whereas ages were only available for 132 (53,2%) and diagnoses for 134 (54,0%) routine specimens. The data, however, remain skewed as only patients attending doctors were included and were thus not representative of the general population. However, the presence of viruses in the community and the period of circulation of these viruses can be determined.[8]

The pattern of respiratory virus isolation was similar for all 10 years, with influenza starting on average by mid-June and lasting a mean of 12 weeks. The same subtypes had usually been isolated in the northern hemisphere during the preceding winter season, although the strains often differed. In the 1989/90 season influenza A/Shanghai/11/87 (H_3N_2) caused the most severe influenza season of the past decade in Europe[10] whereas only mild to moderate influenza activity was experienced in the Witwatersrand, with the majority of the influenza A H_3N_2 isolates being typed as A/Beijing/352/89. Only one major outbreak of influenza[9] occurred during the 10-year period studied. The herald wave phenomenon, i.e. the detection of a new strain of influenza which causes a minor wave of disease at the end of an epidemic and is then followed by major epidemic activity in the following season,[11] does not seem to hold true in this study. Only in 3 years were the last strains isolated in one season and the first strains isolated the next, i.e. 1982, 1986 and 1989, and these did not cause major epidemic activity the following year.

Of the three influenza subtypes circulating throughout the world, influenza A H_1N_1 circulated prior to 1957, with the last major epidemic in 1953; the subtype disappeared and only reappeared in 1977.[2] Influenza A H_1N_1 has been shown to have a specific age attack rate, with fewer than 5% of patients having been born before 1950.[2] In this study, however, where ages were known for 166/193 patients with influenza A H_1N_1, 23 (13,9%) were born before 1950.

Previous studies have shown that influenza A was only isolated from children over 6 months of age[3] whereas we found that 13 (3,7%) of the patients with influenza A isolates were aged less than 6 months. Influenza A H_1N_1 has also been shown to occur less frequently than A H_3N_2 in children younger than 6 years, especially in those less than 2 years of age.[12] However, during the 10-year period, similar proportions for both A H_1N_1 and A H_3N_2 were found in the less than 6 (25,3% and 24,4%) and less than 2 (8,4% and 10,9%) year age groups.

Unlike in other studies[3,5,13] RSV was not the most frequent isolate from the specimens of children; however, the majority of the children in this study presented with URTIs. Of the 328 children younger than 5 years, 31,7% presented with lower respiratory tract infections and of these only 12 (11,5%) had positive RSV isolates. (The low isolation rate for RSV in this study may be partly due to the fact that although all specimens were taken early in the illness and placed in viral transport medium, in many instances the specimens were in transit for up to 48 hours.) With only sporadic isolates of RSV in the late summer/autumn months, the characteristic winter distribution[14] was also evident in this study, with a slightly more variable seasonality for parainfluenza, although the majority of isolates were also made during the winter months. During the 10 years, RSV was never isolated between September and December.

Laboratory-based surveillance provides data on the type of viruses circulating. However, the viral watch programme augmented this surveillance, provided more specimens, a higher isolation rate and more detailed epidemiological data.

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