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Communicable Diseases Intelligence

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Contents:

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VIRUSES, CHLAMYDIAS, COXIELLAS, RICKETTSIAS AND MYCOPLASMAS REPORTING SCHEME: A total of 1,523 reports were processed during this period.

Six of the eight cases of measles reported during this period occurred in teenagers (5 males, 1 female, aged 14-15 years) from a boarding school in Victoria.

The seasonal increase in respiratory syncytial virus has commenced with 162 reports being received during this period.

OVERSEAS BRIEFS: DENGUE FEVER IN THE PACIFIC

Vanuatu: An epidemic of dengue fever started in April 1989. Type 1 was identified initially. In Vila, the epidemic peaked during the week ending 2 June 1989 with 499 cases being reported during the week. From 3-9 June 271 cases were reported bringing the total for Vila to approximately 3,300. However the epidemic is still increasing in other areas of Vanuatu. It has been estimated that there are 1,000 new cases each week throughout the country. In Vila, haemorrhagic symptoms have been reported in 54 cases, 15 of whom developed shock syndrome. To date, 8 deaths have been reported in Vanuatu.

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Wallis: A dengue 3 epidemic started in April 1989. As of late June, 1674 cases had been reported including 25 cases with haemorrhagic fever and one death.

Tuvalu: A dengue type 3 outbreak started in March 1989. One death has been reported.

Niue: Cases of dengue type 2 were reported in January and February 1989. No further details are available.

New Caledonia and French Polynesia: The epidemics of dengue fever in New Caledonia (type 3) and French Polynesia (type 1) reported earlier this year have waned. However the potential for another flare-up remains as only 20% of the susceptible population seroconverted and other serotypes are present in neighbouring countries.

TRAVEL RESTRICTIONS ON HIV-INFECTED PERSONS - 1989 REVISION

A number of countries have introduced entry restrictions for travellers, foreign workers or migrants. Below is an updated summary of AIDS testing requirements for various countries. In most cases, this information has been provided by diplomatic missions. Where the information is obtained from other sources this is indicated.

Country	Type of Visitor	Type of Restriction
Australia	Migrants with clinical AIDS	May be refused entry
Belgium	Foreign students applying for Belgian Government Scholarships	Compulsory testing in country of origin
Belize*	Foreign workers or migrants	Must have evidence of negative HIV test in past 3 months
Brazil	Persons holding temporary or permanent visas, including tourist visas	If there is a clear indication of HIV infection, entry will be refused.
Bulgaria*	Foreign nationals staying more than one month	Compulsory testing within 1-3 days of arrival
Chile	Applicants for permanent residence	Must be certified antibody negative
China	Foreign students & nationals staying for one year or more	Must be certified antibody negative
Colombia*	Visitors from USA, Haiti & Africa (under consideration)	Certified antibody negative
Costa Rica	Crews of all ships, foreigners applying for residence visa	Must be certified antibody negative
Cuba*	Foreigners, not tourists, & Cubans returning from endemic areas	Tested on arrival

Country	Type of Visitor	Type of Restriction
Cyprus	Foreign nationals working in nightclubs or cabaret, students from Africa	Tested on arrival
Czechoslovakia	Foreign students and resident workers	Compulsory testing on arrival. Antibody positive persons repatriated
Egypt*	Defence, Foreign Defence workers working at military establishments	Must be certified antibody negative
France	Applicants for resident status with clincial AIDS.	Application may be refused. A positive HIV test is not grounds for refusal of resident status, in the absence of clinical disease
Germany Democratic Republic	Foreign nationals staying more than 3 months (except diplomats)	Must be certified antibody negative in the past 3 months
Germany West (Bavaria only)	Foreign nationals applying for resident permits. Exemption EEC nationals, nationals of Andora, Finland, Iceland, Liechtenstein, Malta, Monaco, Norway, Austria, San-Marino, Sweden, Switzerland and Vatican City	Compulsory testing
Germany West	Students receiving scholarships from Ministry of Economic Co-Operation	Compulsory testing
Indonesia*	Visitors suspected of having AIDS or being antibody positive	Refused entry
India	Overseas students and foreigners staying more than a year, except diplomats	Compulsory testing on arrival
Iraq*	Overseas visitors and Iraqis returning, except diplomats and children less than 12 years of age	Compulsory testing within of 5 days arrival at specified clinics/hospitals
Japan**	Visitors displaying drug-related or homosexual behaviour	May be tested
Korea**	Applicants for longterm visas ie over 90 days (under consideration)	Certified antibody negative
Kuwait*	Foreign nationals applying for work permits	Must be certified antibody negative
Libya*	Foreign workers and visitors	Must be certified antibody negative

Country	Type of Visitor	Type of Restriction
Mexico	Foreigners applying for permanent residence	Must be certified antibody negative
Mongolia*	Foreign students	Must be certified antibody negative
Pakistan**	Foreigners planning an 'extended stay'	Must be certified antibody negative
Papua New Guinea	Foreign workers	Introduction of antibody screening under consideration No current restriction.
Philippines	All immigrants, refugees (except those who have been admitted only for processing, are confined to a Refugee Processing Center, and who are to proceed later to a recipient country), illegal residents found to be residing permanently in the Philippines, visitors for longer than 6 months, and aliens seeking a change in status from temporary visitor to permanent resident	Must be certified antibody negative
Poland	Foreign students	Must be certified antibody negative
Qatar*	Foreign nationals applying for work permits, except diplomats	Compulsory testing, or have an AIDS certificate issued in the past 6 months
Saudi Arabia*	Applicants for work or resident permits	Must be certified antibody negative
South Africa	No restrictions at present - under consideration.	
Spain	Applicants for work permits and resident permits	Must be certified antibody negative
Syria*	Foreign nationals applying for work permits, foreign students	Compulsory testing on arrival at specified centres
Thailand	Foreign nationals who suffer from AIDS	Refused entry
United Arab Emirats (UAE)*	Foreign nationals applying for work or resident permits, except diplomats	Compulsory testing in UAE
United Kingdom	Visitors who are subject to immigration control and who are either entering the UK for medical treatment or who may require medical treatment during their stay. HIV positivity and/or the fact that a visitor is an AIDS sufferer are not in themselves grounds for refusing entry.	HIV antibody positive persons may be excluded if they cannot satisfy the immigration officer that they have sufficient funds to pay for treatment

Country	Type of Visitor	Type of Restriction
Union of Soviet Socialist Republics**	Foreigners intending to stay more than 3 months, except diplomats	Must be certified HIV antibody negative within the month prior to arrival or be tested on arrival. Certificates must be issued by institutions recognised by the Soviet authorities.
United States of America	All aliens seeking residence	Tested for HIV antibody. HIV infection is listed as a 'dangerous, contagious disease' There have been cases where travellers holding US visas have been denied entry because they are HIV positive. It is suggested that affected persons should seek guidance from the US mission issuing the visa before travel plans are finalised.

* This advice has not been updated since last published

** Obtained from the AIDS Newsletter (published by the Bureau of Hygiene and Tropical Diseases, London, UK.)

ZIDOVUDINE: POTENTIAL TOXICITY TO BE MONITORED

In correspondence to the British Medical Journal [1] in late 1987, it was reported that the increase in number of HIV-positive patients being transfused (with a doubling of blood consumption for 1986) in St Stephen's Hospital, London, was attributed to the introduction of zidovudine. It was indicated that the strain on the local blood transfusion centre would lead to the curtailment of the drug's use. Such a drastic measure evidenced the serious need for blood transfusion in a number of HIV-infected persons treated with zidovudine.

The widespread availability of this drug has recently led to a growing tendency to prescribe zidovudine for asymptomatic HIV-infected patients even though the U.S. Food and Drug Administration's licence is only for treatment of certain AIDS patients. Dissent exists between clinicians who see this as a compassionate response and those who are sympathetic to the plight of patients but nevertheless concerned about the widespread use of such a toxic drug, especially as there is little evidence that the benefits will outweigh the risks. The Pasteur Institute in Paris was quoted as saying that French specialists are increasingly inclined to prescribe zidovudine as soon as the number of CD4+ (helper) T-cells in an HIV-infected person falls [2].

In preclinical studies the toxicological potential of zidovudine has been investigated in several species [3]:

- In rats and mice the median lethal dose (LD_{50}) was
  > 750 mg/kg intravenously, and
  > 3,000 mg/kg orally.
- In rats and dogs, no significant toxicological alterations were obvious in subacute intravenous toxicity studies.
- In cynomolgous monkeys, which (like humans) rapidly and extensively glucuronidate zidovudine, a reversible, dose-related, macrocytic anaemia was evident in animals given 35, 100 or 300 mg/kg per day for three or six months.
- In three-month and six-month oral toxicity studies in rats, treatment-related alterations consisted of a mild increase in blood glucose level in female rats in both studies and a reversible slight-to-mild macrocytic anaemia in the six-month study.
- There was no evidence of teratogenicity in rats or rabbits given the drug during gestation.
- Results for zidovudine were negative in a bacterial mutagenic assay, but the drug was weakly mutagenic at concentration of 1,000 to 5,000 ug/ml in mammalian cells.
- Zidovudine caused chromosomal aberrations in cultured human lymphocytes at concentrations of 3 ug/ml and higher, and had positive results in a cell transformation assay at concentration of 0.5 ug/ml and higher.
- No bone marrow chromosomal alterations were noted in a cytogenetics study in rats given zidovudine at several intravenous dose levels up to 300 mg/kg.

The above initial findings appeared to provide support for the safety of the drug. However, subsequent long-term administration of zidovudine has elicited serious adverse effects in a number of HIV-infected patients:

- Myopathy was observed in a number of cases:

  - Two AIDS and 2 AIDS-related complex (ARC) patients were reported [4] to have developed a polymyositis-like syndrome during long-term treatment with zidovudine. Symptoms included muscle pains, tenderness, weakness and severe muscle atrophy; one patient lost 18 kg owing to muscle wasting. There was symptomatic improvement in 3 patients on discontinuation of treatment.
  - One case of necrotising myopathy was reported [5]; 7 days after cessation of zidovudine the patient's proximal weakness and muscle tenderness improved considerably and muscle force returned to normal 2 months later.
  - Eight (7 AIDS, 1 ARC) out of 113 zidovudine-treated patients (80 with AIDS, 33 with ARC) had clinical and biochemical evidence of myopathy after 240-386 (mean 329) days on treatment [6]. Five were on full-dose treatment (1200 mg daily) and 3 were on reduced doses of 600 or 800 mg daily (for a mean of 81 days) because of bone marrow toxicity. A severe proximal myopathy, predominantly affecting the legs, seemed to be a significant complication on long-term zidovudine therapy, even at reduced doses; in this group it affected 18% of the patients who had received treatment for more than 200 days. Other drugs could not be implicated. The pathogenicity is obscure; the myopathy resolves on cessation of zidovudine, but not on dose-reduction, though there is then a risk of rebound encephalitis [7]. This disorder is distinct

from HIV-associated myopathy [5], in which pain and tenderness are usually absent and muscle enzyme levels are normal. In the report the authors proposed that:

- clinical and biochemical features, together with a cautious dose cessation of zidovudine would seem to be a useful means of distinguishing between the two; and
- the need for vigilance in monitoring the use of zidovudine in severely ill patients and some caution in its use in the early stages of HIV infection ought to be highlighted.

- Haemarthroses: A striking increase in bleeding frequency was observed in a patient with AIDS and haemophilia A who was taking ibuprofen when he began zidovudine treatment [8].

- Neutropenia: Neutropenia developed in an HIV-infected renal transplant recipient when zidovudine (200 mg/4 hour) was added to his immunosuppressive and prophylactic (sulphamethoxazole-trimethoprim) regimen. Institution of lower dosage (100 mg/6 hour) and cessation of other medication lead to the resolution of neutropenia.

In a study conducted by Roberts et al [9] where five AIDS patients had required discontinuation of zidovudine therapy due to profound neutropenia, the institution of lithium therapy was reported to increase thrombopoiesis and a simultaneous increase in platelet counts. In each of the cases, initial response in neutrophil counts allowed reinstitution of zidovudine therapy. Three of five patients were able to tolerate at least 1,000 mg/day of zidovudine while receiving lithium. One of the remaining two patients showed an initial response; however, 10 weeks after therapy with lithium neutropenia recurred. His bone marrow biopsy demonstrated no infectious or infiltrating process. The major adverse side effect noted was tremulousness.

- Anaemia: Development of anaemia has been evaluated as part of a trial of zidovudine therapy where patients with AIDS and Kaposi sarcoma were randomised to one of three treatment groups or a placebo group [10]. Transfusion-requiring anaemia (haemoglobin < 100 g/L) developed in 6 of 15 patients on zidovudine therapy at a mean of 6 weeks after starting treatment:

  - a fall in the reticulocyte count was the earliest peripheral blood indicator of toxicity;
  - mean corpuscular volume increased markedly in patients on zidovudine therapy not developing anaemia yet remained stable or only slightly increased in those who become anaemic;
  - bone marrow examination showed pure red cell aplasia in 2 patients, erythroid maturation arrest in 1, and erythroid hypoplasia in 3;
  - megaloblastic erythropoiesis was present in 2 of the 6 anaemic patients; and
  - erythropoietin levels measured at the time of first transfusion were increased.

Thus it was concluded that the anaemia associated with zidovudine therapy is due to red cell hypoplasia or aplasia.

. Bone marrow failure was observed in 4 patients with AIDS and a history of *Pneumocystis carinii* pneumonia, who developed severe pancytopenia 12 to 17 weeks after the initiation of zidovudine therapy [11]:

  - haemoglobin < 85g/L;
  - granulocytes < 0.5 x 10^9/L;
  - platelets < 30 x 10^9/L.

  The bone marrow was markedly hypocellular in three patients and moderately hypocellular in the fourth. Partial bone marrow recovery was documented within 4 to 5 weeks in three patients, but no marrow recovery has yet occurred in one patient during the more than 6 months since zidovudine treatment was discontinued. The authors warned that zidovudine should be used cautiously, with close monitoring of blood values.

However in a separate report on the effect of zidovudine on HIV-related thrombocytopaenia [12], platelet counts rose in 6 of 7 AIDS patients with *Pneumocystis carinii* pneumonia and thrombocytopenia within 2 weeks after zidovudine treatment while the haematocrit decreased exponentially with 3 requiring transfusions by week 4. It was also noted that no haematological toxicity was observed in a man who overdosed with 10-20 gm of zidovudine in a suicide attempt [13]. Acute ataxia and nystagmus developed and the patient was admitted with headache and nausea. The patient suffered transient neurological symptoms but no long-term effects or toxicity from the drug and there were no long-term sequalae.

The transient toxic effects of overdose with zidovudine have been confirmed in two other reports [14,15] and one group in St Stephen's Hospital, London, suggested that the absence of toxicity to the marrow in these patients warrants investigation of intermittent high-dose zidovudine.

The overall toxicity of zidovudine treatment has been evaluated in a double-blind, placebo-controlled trial of oral zidovudine involving 282 patients with AIDS or ARC. Although it was recognised that significant clinical benefit had been documented [16], the study outlined serious adverse reactions [17], in particular bone marrow suppression:

. nausea, myalgia, insomnia, and severe headaches were reported more frequently by recipients of zidovudine;
. anaemia with haemoglobin levels 75g/L developed in 24% of zidovudine recipients and 4% of placebo recipients ($p<0.001$); and
. neutropenia (<500 cells/mm^3) occurred in 16% of zidovudine recipients, compared with 2% of placebo recipients ($p<0.001$).

Subjects who entered the study with low CD4+ lymphocyte counts, low serum vitamin B12 levels, anaemia, or low neutrophil counts were more likely to have haematological toxic effects. The study indicated that concurrent use of paracetamol was also associated with a higher frequency of haematological toxicity. The authors warned that, although a subset of patients tolerated zidovudine for an extended period of time with few toxic effects, the drug should be administered with caution because of its toxicity and the limited experience with it to date.

Neurological toxicity elicited by zidovudine treatment is yet to be determined. Preliminary reports have indicated:

. that twice after administration of zidovudine, a seropositive subject had grand mal epileptic seizures for which no other cause could be identified [18].
. that manic syndrome associated with zidovudine treatment was observed in two cases. Symptoms disappeared on discontinuation of the drug. One patient had been taking zidovudine for 14 months before hospital admission [19].

Hepatic toxicity in the form of cholestasis and hepatitis has also been reported [20] in a 39 year old man with *Pneumocystis carinii* pneumonia and cytomegalovirus infection who received cotrimoxazole (trimethoprim and sulfamethoxazole) therapy for 3 weeks followed by zidovudine 200 mg every 4 hours. Seven days after zidovudine therapy began the patient presented with a 2 day history of abdominal discomfort and intermittent fever. Zidovudine therapy was withdrawn and the patient received dicycloverine hydrochloride. After 6 days the patient was rehospitalised with a temperature of 38.9°C, jaundice, right upper quadrant pain and hepatomegaly, diagnosed as clinical hepatitis. These symptoms resolved and the patient was discharged after 8 days. Zidovudine therapy, 100 mg every 4 hours was continued 16 days after discharge; symptoms returned after 7 days. Zidovudine was again discontinued, but symptoms worsened. The patient was rehospitalised with clinical hepatitis 4 days after zidovudine withdrawal. Liver function tests returned to within normal levels after 1 month. Granulomotosis of the liver was ultimately found. This case report indicated that clinicians initiating zidovudine therapy should monitor this potential adverse effect.

Although the proponents supporting the widespread use of zidovudine may argue that the reported toxic effects were mainly observed in AIDS or ARC patients with either a diminished immunocompetence or a predisposition to succumb to adverse biochemical changes, the potential toxicity of this drug cannot be ignored when prescribed for asymptomatic HIV infected patients or for the prophylaxis of healthy persons exposed to HIV through injury or accidental contamination. Such concern does not seem to affect the criteria used in conducting the following studies:

. In May last year, Burroughs Wellcome announced a new study to test zidovudine in health care workers exposed to HIV in accidents on the job. The program is unusual because it tests zidovudine in people recently exposed to the virus who show no signs of infection. The levels of viral proteins and antibodies in the workers would be monitored for a year. The trial is a controlled, double-blind study.
. As an adjunct to the Burroughs Wellcome study, the U.S. National Institute of Allergy and Infectious Disease (NIAID) has applied to the Food and Drug Administration for permission to give zidovudine to all health care or laboratory workers who have had massive exposure to HIV.

The latter study assumes that people exposed to large quantities of the virus may be more likely to become infected and for that reason should receive zidovudine as a matter of course. Other workers exposed to smaller amounts of HIV are regarded as more appropriate for the Burroughs Wellcome study.

Both studies have yet to determine what constitutes a massive exposure versus a small one.

In any case there would be logistical problems with the Burroughs Wellcome study [21]:

- It will take at least several thousand participants to be able to determine whether zidovudine prevents infection since the actual infection rate is so low - currently estimated at an average of 0.4 to 0.5% among health care workers with needlestick injuries.
- Zidovudine kills bone marrow cells in many AIDS patients - the risk of toxicity is unknown in healthy people exposed to HIV, but could be greater than the risk of becoming infected.
- It may become increasingly difficult to justify why only health care workers; and not people who fear exposure to HIV because of sexual contact or other means, should be allowed to participate in the study.
- Workers who suspect they are getting placebo instead of zidovudine may not comply with the terms of the study and obtain the drug by some other means.

Zidovudine is now used widely for patients with symptomatic HIV disease in all subgroups of group IV of the CDC classification of HIV infection, assuming that all such patients will benefit from therapy. Experience of nearly two years of uncontrolled use of zidovudine suggests potentially serious side-effects. Despite existing concerns about the potential haematological toxicity of zidovudine, clinicians are often tempted to use it early in the course of HIV infection ie. in symptomless patients - in the hope that such treatment will delay or even prevent the progression to symptomatic disease and death.

To answer this question of whether early treatment with zidovudine in symptomless seropositive patients (CDC group II or III) delays progression to symptomatic disease and whether it reduces case fatality, two placebo-controlled trials have started, one in the USA - a 3-year randomised trial of two doses of zidovudine *vs* placebo which began in October 1987 - and one in the UK and France - the joint MRC/INSERM trial (Concorde 1). Although supporting the necessity to establish the value of zidovudine in asymptomatic HIV infected persons through large-scale placebo-controlled trials before the drug is given indiscriminately, a recent editorial in the *Lancet* [22] indicated that trials such as Concorde 1 would face enormous difficulties because:

- Blinding is hard to achieve, but physicians and patients in the MRC/INSERM trial will be blinded to the result of mean corpuscular volume, red cell count, packed cell volume, and p24 data.
- Viral resistance is emerging; Wellcome has sent letters alerting physicians in 26 countries [23] to this potential problem, and laboratory findings have been published [24]. Further *in vitro* and clinical studies are continuing. During the past year, several groups have reported studies showing that the beneficial effects of zidovudine are reduced with time. This effect is brought about by development of resistance, the drug being only partially effective, and toxicity limiting its effectiveness.

. The move towards antiviral therapy in symptom free patients puts considerable psychological pressure on seropositive individuals, who are constantly reminded about the risk of progression at follow-up visits.

The long term value of zidovudine is still being debated since the results obtained from various studies conflict [25,26]. Despite this, it appeared that many clinicians are convinced that the use of zidovudine would be beneficial in asymptomatic HIV infection. Furthermore, patients are demanding therapeutic agents to delay HIV infection from progressing to AIDS for as long as possible. However, extrapolating the potential efficacy of this drug in asymptomatic HIV-infected persons to advocate the use of zidovudine as a prophylactic agent in persons potentially exposed to HIV should be justified on the basis of scientific evidence.

REFERENCES

1. Costello C, Mir N, Luckit J. The blood transfusion service and zidovudine treatment for AIDS. Br Med J Clin Res 1987;295:1486.
2. International Herald Tribune 22/12/87:p2.
3. Ayers KM. Preclinical toxicology of zidovudine. An overview. Am J Med 1988;85:186-8.
4. Bessen LJ, Greene JB, Louie E, et al. Severe polymyositis-like syndrome associated with zidovudine therapy of AIDS and ARC. N Engl J Med 1988;318:708.
5. Necrotising myopathy and zidovudine. Lancet 1988;1:1050-1.
6. Helbert M, Fletcher T, Peddle B et al. Zidovudine-associated myopathy. Lancet 1988;2:689-90.
7. Helbert M, Robinson D, Peddle B, et al. Acute meningo-encephalitis in dose reduction of zidovudine. Lancet 1988;1:1249-52.
8. Ragni MV, Tama G, Lewis JH, Ho M. Increased frequency of haemarthroses in haemophilic patient treated with zidovudine. Lancet 1988;1:1454-5.
9. Roberts DE, Berman SM, Nakasato S, et al. Effects of lithium carbonate on zidovudine associated neutropenia in the Acquired Immunodeficiency Syndrome. Am J Med 1988;85:428-31.
10. Walker RE, Parker RI, Kovacs JA, et al. Anemia and erythropoiesis in patients with the acquired immunodeficiency syndrome (AIDS) and Kaposi sarcoma treated with zidovudine. Ann Intern Med 1988;108:372-6.
11. Gill PS, Rarick M, Byrnes RK. et al. Azidothymidine associated with bone marrow failure in the acquired immunodeficiency syndrome (AIDS). Ann Intern Med 1987;107:502-5.
12. Hymes KB, Greene JB, Karpatkin S. The effect of azidothymidine on HIV-related thrombocytopenia. N Engl J Med 1988;318:516-7.
13. Spear JB, Kessler HA, Lehrman SN, de Miranda P. Zidovudine overdosage. Ann Intern Med 1988;109:76-7.
14. Hargreaves M, Fuller G, Costello C, Gazzard B. Zidovudine overdose. Lancet 1988;2:509.
15. N Engl J Med 1988;318:518.
16. Fischl MA, Richman DD, Grieco MH, et al. The efficacy of azidothymidine (AZT) in the treatment of patients with AIDS and AIDS-related complex. A double-blind, placebo-controlled trial. N Engl J Med 1987;317:185-91.
17. Richman DD, Fischl MA, Grieco MH, et al. The toxicity of azidothymidine (AZT) in the treatment of patients with AIDS and AIDS-related complex. A double-blind, placebo-controlled trial. N Engl J Med 1987;317:192-7.
18. Azidothymidine in the treatment of AIDS. N Engl J Med 1988;318:250-1.
19. Maxwell S, Scheftner WA, Kessler HA, Busch K. Manic syndrome associated with zidovudine treatment. JAMA 1988;259:3406-7.
20. Dubin G and Braffman MN. Zidovudine induced hepatoxicity. Ann Intern Med 1989;110:85-6.
21. Barnes DM. Health workers and AIDS: questions persist. Science 1988;241:161-2.
22. Zidovudine in symptomless HIV infection. Lancet 1989;1:415-6.
23. Zidovudine-resistant HIV isolated. Scrip 1989;1396:38.
24. Lader BA, Darby G, Richman DD. HIV with reduced sensitivity to zidovudine (AZT) isolated during prolonged therapy. Science 1989;243:1731-4.
25. Creagh-Kirk T, Doi P, Andrews E, et al. Survival experience among patients with AIDS receiving zidovudine. Follow-up of patients in a compassionate plea program. JAMA 1988;260:3009-15.
26. Dournon E, Matheron S, Rozenbaum W, et al. Effects of zidovudine in 365 consecutive patients with AIDS or AIDS-related complex. Lancet 1988;2:1297-302.

AUSTRALIA - COMMUNICABLE DISEASES INTELLIGENCE

VIRAL IDENTIFICATIONS FROM CONTRIBUTING LABORATORIES
BASED ON DATE OF REPORTING

PERIOD 25/5/89 TO 7/6/89

1. CODE 019 - FAIRFIELD(VIC)
2. CODE 065 - STATE LAB(WA) PMH(WA)
3. CODE 110 - IMVS(SA)
4. CODE 111 - RCH(VIC)
5. CODE 112 - ICPMR(NSW) WVH(ACT)
6. CODE 113 - PHH POW(NSW)
7. CODE 114 - RAHC(NSW)
8. CODE 115 - STATE LAB(QLD)

		019	065	110	111	112	113	114	115	TOTAL
0100	ADENOVIRUS NOT TYPED	2	6	0	0	1	1	1	10	21
0101	ADENOVIRUS TYPE 1	1	0	0	0	0	0	0	0	1
0102	ADENOVIRUS TYPE 2	2	0	2	2	0	0	0	0	6
0103	ADENOVIRUS TYPE 3	2	0	3	0	3	0	0	0	8
0104	ADENOVIRUS TYPE 4	5	0	0	0	0	0	0	0	5
0107	ADENOVIRUS TYPE 7	0	0	0	5	0	0	0	0	5
0108	ADENOVIRUS TYPE 8	1	1	0	0	0	0	0	0	2
0111	ADENOVIRUS TYPE 11	0	0	0	0	1	0	0	0	1
0119	ADENOVIRUS TYPE 19	1	0	0	0	1	0	0	0	2
0130	ADENOVIRUS TYPE 30	1	0	0	0	0	0	0	0	1
0199	ADENOVIRUS TYPING PENDING	1	0	0	5	0	2	0	0	8
0201	INFLUENZA A VIRUS	0	1	0	0	0	0	0	0	1
0203	INFLUENZA B VIRUS	0	1	0	0	0	0	0	0	1
0301	PARAINFLUENZA VIRUS TYPE 1	0	0	0	1	0	0	0	0	1
0302	PARAINFLUENZA VIRUS TYPE 2	2	0	2	12	0	1	0	5	22
0303	PARAINFLUENZA VIRUS TYPE 3	6	0	0	20	0	1	0	1	28
0400	RESPIRATORY SYNCYTIAL VIRUS (R	11	25	18	36	2	2	12	56	162
0500	RHINOVIRUS (ALL TYPES)	11	2	11	11	4	0	0	0	39
0600	MYCOPLASMA PNEUMONIAE	4	1	0	11	0	1	0	0	17
0700	ORNITHOSIS-PSITTACOSIS	1	0	0	0	0	0	0	0	1
0809	COXSACKIEVIRUS A9	0	0	0	1	0	0	0	0	1
0900	COXSACKIEVIRUS GROUP B - NOT T	0	0	1	0	0	0	0	0	1
0904	COXSACKIEVIRUS B4	0	1	0	0	0	0	0	0	1
1000	ECHOVIRUS NOT TYPED	0	1	0	0	0	0	0	0	1
1004	ECHOVIRUS TYPE 4	1	0	0	1	0	0	0	0	2
1009	ECHOVIRUS TYPE 9	10	1	0	1	1	0	0	0	13
1013	ECHOVIRUS TYPE 13	0	0	0	0	1	0	0	0	1
1030	ECHOVIRUS TYPE 30	4	4	0	0	0	1	1	0	10
1100	POLIOVIRUS NOT TYPED	0	0	0	4	0	2	0	0	6
1101	POLIOVIRUS TYPE 1	0	0	0	5	0	0	0	0	5
1102	POLIOVIRUS TYPE 2	0	0	1	0	0	0	0	0	1
1103	POLIOVIRUS TYPE 3	1	0	0	0	0	0	0	0	1
1104	POLIOVIRUS - MIXED VACCINAL ST	0	1	0	0	0	0	0	0	1
1200	MUMPS VIRUS	1	0	0	1	0	0	0	0	2
1300	HERPES VIRUS GROUP - NOT TYPED	1	0	0	0	3	1	0	8	13
1301	HERPES SIMPLEX VIRUS - NOT TYP	1	5	0	0	71	0	1	0	78
1302	EPSTEIN-BARR VIRUS (EB VIRUS)	8	11	14	4	1	2	2	0	42
1303	VARICELLA-ZOSTER VIRUS	7	3	2	1	0	3	0	2	18
1306	HERPES SIMPLEX TYPE 1	76	14	19	0	3	0	0	26	138
1307	HERPES SIMPLEX TYPE 2	143	60	22	0	18	0	0	24	267
1399	HERPES VIRUS TYPING PENDING	3	1	0	7	0	0	0	2	13
1502	PICORNIA VIRUS - NOT TYPED = E	0	1	0	0	0	4	0	22	27
1521	MEASLES VIRUS	7	0	0	0	0	1	0	0	8
1522	RUBELLA VIRUS	6	3	2	0	0	0	0	0	11
1532	HEPATITIS B ANTIGEN	66	14	16	1	62	8	2	22	191
1535	HEPATITIS A ANTIBODY	2	2	0	0	0	0	1	0	5
1541	CHLAMYDIA A - C. TRACHOMATIS	0	46	29	0	24	3	0	23	125
1556	CMV - CYTOMEGALOVIRUS	75	5	4	10	2	2	2	19	119
1564	ROTAVIRUS	1	8	1	0	1	2	1	0	14
1571	ENTEROVIRUS TYPE 71 (BCR)	0	0	0	0	1	0	0	0	1
1599	ENTEROVIRUS TYPING PENDING	0	0	0	11	0	14	3	0	28
9992	ROSS RIVER VIRUS	17	18	9	0	1	0	0	0	45
9994	SMALL VIRUS (LIKE) PARTICLE	0	1	0	0	1	0	0	0	2
TOTAL		481	237	156	150	202	51	26	220	1523

Correction - Viral identifications, CDI 89/5:
Please delete the report of rabies virus (code 1552)
and add one to hepatitis B antigen (code 1532)

AUSTRALIA - COMMUNICABLE DISEASES INTELLIGENCE

VIRAL IDENTIFICATIONS BY CLINICAL INFORMATION TABLE 1

PERIOD 25/5/89 TO 7/6/89

1. CODE 00, 99 ..... - NO ILL OR DATA
2. CODE 01, 02, 11, 12 - RESPIRATORY
3. CODE E3 ..... - ENCEPHALITIS
4. CODE M3 ..... - MENINGITIS
5. CODE 04 ..... - PARALYSIS
6. CODE 05, 13 ..... - CNS OTHER UNSPEC
7. CODE 07, 49 - GASTRO INTESTINAL
8. CODE 17, 47 - HEPATIC
9. CODE 19 ... - CVS
10. CODE 89 ... - URINARY TRACCT
11. CODE 06 ... - SKIN MUCOUS

		1	2	3	4	6	7	8	9	10	11	TOTAL
0100	ADENOVIRUS NOT TYPED	2	8	0	0	0	7	0	0	1	0	18
0101	ADENOVIRUS TYPE 1	0	1	0	0	0	0	0	0	0	0	1
0102	ADENOVIRUS TYPE 2	0	5	0	0	0	0	0	0	0	0	5
0103	ADENOVIRUS TYPE 3	2	3	0	0	0	0	0	0	0	0	5
0107	ADENOVIRUS TYPE 7	0	5	0	0	0	0	0	0	0	0	5
0108	ADENOVIRUS TYPE 8	1	0	0	0	0	0	0	0	0	0	1
0111	ADENOVIRUS TYPE 11	1	0	0	0	0	0	0	0	0	0	1
0119	ADENOVIRUS TYPE 19	1	0	0	0	0	0	0	0	0	0	1
0130	ADENOVIRUS TYPE 30	0	0	0	0	0	1	0	0	0	0	1
0199	ADENOVIRUS TYPING PENDING	0	4	0	0	0	1	0	0	0	0	5
0201	INFLUENZA A VIRUS	0	1	0	0	0	0	0	0	0	0	1
0301	PARAINFLUENZA VIRUS TYPE 1	0	1	0	0	0	0	0	0	0	0	1
0302	PARAINFLUENZA VIRUS TYPE 2	0	21	0	0	0	0	0	0	0	0	21
0303	PARAINFLUENZA VIRUS TYPE 3	0	28	0	0	0	0	0	0	0	0	28
0400	RESPIRATORY SYNCYTIAL VIRUS (R	1	160	0	0	0	0	0	0	0	0	161
0500	RHINOVIRUS (ALL TYPES)	0	37	0	0	0	0	0	0	0	0	37
0600	MYCOPLASMA PNEUMONIAE	3	12	0	0	1	0	0	0	0	0	16
0700	ORNITHOSIS-PSITTACOSIS	0	1	0	0	0	0	0	0	0	0	1
0809	COXSACKIEVIRUS A9	0	1	0	0	0	0	0	0	0	0	1
0900	COXSACKIEVIRUS GROUP B - NOT T	0	1	0	0	0	0	0	0	0	0	1
1000	ECHOVIRUS NOT TYPED	1	0	0	0	0	0	0	0	0	0	1
1004	ECHOVIRUS TYPE 4	0	0	0	2	0	0	0	0	0	0	2
1009	ECHOVIRUS TYPE 9	1	1	1	9	0	0	0	0	0	0	12
1013	ECHOVIRUS TYPE 13	1	0	0	0	0	0	0	0	0	0	1
1030	ECHOVIRUS TYPE 30	1	2	0	4	0	1	0	0	0	0	8
1100	POLIOVIRUS NOT TYPED	0	2	0	0	0	2	0	0	0	0	4
1101	POLIOVIRUS TYPE 1	0	3	0	0	0	0	0	0	0	0	3
1102	POLIOVIRUS TYPE 2	0	1	0	0	0	0	0	0	0	0	1
1104	POLIOVIRUS - MIXED VACCINAL ST	0	0	0	0	0	0	0	0	0	1	1
1200	MUMPS VIRUS	1	0	0	0	0	0	0	0	0	0	1
1300	HERPES VIRUS GROUP - NOT TYPED	0	1	0	0	0	0	0	0	1	3	5
1301	HERPES SIMPLEX VIRUS - NOT TYP	18	0	0	0	0	0	0	0	0	16	34
1302	EPSTEIN-BARR VIRUS (EB VIRUS)	14	3	0	0	0	0	0	1	0	1	19
1303	VARICELLA-ZOSTER VIRUS	1	0	0	0	0	0	0	0	0	15	16
1306	HERPES SIMPLEX TYPE 1	9	4	0	0	0	0	0	0	0	61	74
1307	HERPES SIMPLEX TYPE 2	11	1	0	0	0	0	0	0	0	89	101
1399	HERPES VIRUS TYPING PENDING	0	1	0	0	0	0	1	0	0	6	8
1502	PICORNIA VIRUS - NOT TYPED = E	1	10	0	0	2	13	0	0	0	0	26
1521	MEASLES VIRUS	4	0	0	0	0	1	0	0	0	2	7
1522	RUBELLA VIRUS	2	0	0	0	0	0	0	0	0	7	9
1532	HEPATITIS B ANTIGEN	116	0	0	0	0	0	54	0	0	0	170
1535	HEPATITIS A ANTIBODY	2	0	0	0	0	0	2	0	0	0	4
1541	CHLAMYDIA A - C. TRACHOMATIS	3	0	0	0	0	2	0	0	0	0	5
1556	CMV - CYTOMEGALOVIRUS	4	24	0	1	0	2	1	2	8	0	42
1564	ROTAVIRUS	0	0	0	0	0	13	0	0	0	0	13
1571	ENTEROVIRUS TYPE 71 (BCR)	1	0	0	0	0	0	0	0	0	0	1
1599	ENTEROVIRUS TYPING PENDING	0	3	0	5	0	15	0	0	0	1	24
9992	ROSS RIVER VIRUS	6	0	0	0	0	0	0	0	0	2	8
9994	SMALL VIRUS (LIKE) PARTICLE	1	0	0	0	0	1	0	0	0	0	2
TOTAL		209	345	1	21	3	59	58	3	10	204	913

AUSTRALIA - COMMUNICABLE DISEASES INTELLIGENCE

VIRAL IDENTIFICATIONS BY CLINICAL INFORMATION TABLE 2

PERIOD 25/5/89 TO 7/6/89

12. CODE 10 - EYE
13. CODE 59 - GENITAL
14. CODE 39 - ENDOCRINE/SALIVARY GL.
15. CODE 38 - RETICULO-ENDOTHELIAL
16. CODE 29 - MUSCLE/JOINT
17. CODE 69 - CONGENTIAL
18. CODE P8 - PUO
19. CODE G8 - FEVER/MALAISE
20. CODE 09 - OTHER
21. CODE A1 - SIDS

		12	13	14	15	16	17	18	19	20	21	TOTAL
0100	ADENOVIRUS NOT TYPED	2	0	0	0	0	0	0	0	1	0	3
0102	ADENOVIRUS TYPE 2	0	0	0	0	0	0	0	0	0	1	1
0103	ADENOVIRUS TYPE 3	0	1	0	0	0	0	0	2	0	0	3
0104	ADENOVIRUS TYPE 4	5	0	0	0	0	0	0	0	0	0	5
0108	ADENOVIRUS TYPE 8	1	0	0	0	0	0	0	0	0	0	1
0119	ADENOVIRUS TYPE 19	0	1	0	0	0	0	0	0	0	0	1
0199	ADENOVIRUS TYPING PENDING	0	1	0	0	0	0	0	2	0	0	3
0203	INFLUENZA B VIRUS	0	0	0	0	0	0	0	1	0	0	1
0302	PARAINFLUENZA VIRUS TYPE 2	0	0	0	0	0	0	0	1	0	0	1
0400	RESPIRATORY SYNCYTIAL VIRUS (R	0	0	0	0	0	0	0	1	0	0	1
0500	RHINOVIRUS (ALL TYPES)	0	0	0	0	0	0	0	0	2	0	2
0600	MYCOPLASMA PNEUMONIAE	0	0	0	0	0	0	0	1	0	0	1
0904	COXSACKIEVIRUS B4	0	0	0	0	0	0	0	0	1	0	1
1009	ECHOVIRUS TYPE 9	0	0	0	0	0	0	0	1	0	0	1
1030	ECHOVIRUS TYPE 30	0	0	0	0	0	0	0	1	1	0	2
1100	POLIOVIRUS NOT TYPED	0	0	0	0	0	0	1	0	0	1	2
1101	POLIOVIRUS TYPE 1	0	0	0	0	0	0	0	0	0	2	2
1103	POLIOVIRUS TYPE 3	0	0	0	0	0	0	0	0	0	1	1
1200	MUMPS VIRUS	0	0	1	0	0	0	0	0	0	0	1
1300	HERPES VIRUS GROUP - NOT TYPED	0	8	0	0	0	0	0	0	0	0	8
1301	HERPES SIMPLEX VIRUS - NOT TYP	0	43	0	0	0	0	0	0	1	0	44
1302	EPSTEIN-BARR VIRUS (EB VIRUS)	0	0	17	0	1	0	0	3	2	0	23
1303	VARICELLA-ZOSTER VIRUS	1	0	0	0	1	0	0	0	0	0	2
1306	HERPES SIMPLEX TYPE 1	5	49	0	0	0	0	0	2	8	0	64
1307	HERPES SIMPLEX TYPE 2	0	159	0	0	0	0	0	0	7	0	166
1399	HERPES VIRUS TYPING PENDING	0	4	0	0	0	0	0	0	1	0	5
1502	PICORNIA VIRUS - NOT TYPED = E	0	0	0	0	0	0	0	1	0	0	1
1521	MEASLES VIRUS	0	0	0	0	0	0	0	1	0	0	1
1522	RUBELLA VIRUS	0	0	0	0	1	0	0	0	1	0	2
1532	HEPATITIS B ANTIGEN	0	1	0	0	0	0	0	1	19	0	21
1535	HEPATITIS A ANTIBODY	0	0	0	0	0	0	0	0	1	0	1
1541	CHLAMYDIA A - C. TRACHOMATIS	4	116	0	0	0	0	0	0	0	0	120
1556	CMV - CYTOMEGALOVIRUS	0	1	0	3	0	3	0	6	64	0	77
1564	ROTAVIRUS	0	0	0	0	0	0	0	1	0	0	1
1599	ENTEROVIRUS TYPING PENDING	0	0	0	0	0	0	0	2	0	2	4
9992	ROSS RIVER VIRUS	0	0	0	0	36	0	0	0	1	0	37
TOTAL		18	384	18	3	39	3	1	27	110	7	610