

The lifetime occurrence of sexually transmitted diseases among a cohort aged 21

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Abstract

Aims. To determine the lifetime occurrence of sexually transmitted diseases (STDs) among a cohort aged 21.

Methods. Participants were interviewed at aged 21 as part of a multidisciplinary health and development study. Questions on STDs and sexual behaviour were presented by computer.

Results. Of the cohort members known to be alive, 92% responded. Among the sexually experienced 8.6% of the men and 17.3% of the women reported ever having had an STD. Genital warts and chlamydial infection were the commonest STDs among the men, and chlamydial infection, genital warts, and genital herpes among the women. General practice was the commonest place for treatment, and only a minority of people were treated at sexual health clinics. The risk of having an STD increased steeply with the lifetime number of sexual partners.

Conclusions. STDs are common problems among young New Zealanders, especially women. The rate was as high as the US. Prevention should be directed at increasing the use of condoms, but education aimed at reducing the number of sexual partners and delaying the onset of sexual involvement should be considered seriously. A more coordinated approach to treatment is required to take into account the diversity of settings where STDs are treated. Surveillance of STDs needs to be extended, as currently the only data are from sexual health clinics.

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The recent worldwide spread of the human immunodeficiency virus (HIV), the cause of AIDS, has highlighted the potential seriousness of sexually transmitted diseases (STDs). Other sexually transmitted viruses are also important. For example, herpes simplex virus can cause long term pain and distress, and infection with human papilloma virus (particularly subtypes 16 and 18) can result in cervical cancer.¹ Bacterial infections can cause both acute and chronic symptoms, and result in infertility and complications of pregnancy such as ectopic pregnancy.² Moreover it now appears that both ulcerative and nonulcerative STDs facilitate the transmission of HIV, and that STD control reduces the spread of HIV.³

The behaviours associated with the spread of STDs, unprotected sexual intercourse and multiple sexual partners, are common among New Zealanders, especially the young.^{4,5} However, data on the occurrence of STDs within populations are sparse and have been the subject of little systematic study. The only routinely collected information in New Zealand is from sexual health clinics (previously called STD clinics).⁶ These data underestimate the total occurrence of STDs as many affected people seek treatment elsewhere, such as from general practitioners and family planning clinics.

We present here the reported lifetime experience of diagnosed STDs among a cohort of 21 year olds. These data have been linked to demographic characteristics and past sexual behaviour. We also obtained information about where treatment was sought, and the circumstances of the diagnosis being made. Such information will aid in the development of appropriate policy for the control of STDs in New Zealand.

Sample and methods

The sample members were enrolled in the Dunedin Multidisciplinary Health and Development Study, a longitudinal study of a cohort born

in Dunedin between 1 April 1972 and 31 March 1973. The sample members were first followed up at 3 years of age when 1037 of 1139 eligible children were seen. Since then the sample was seen every 2 years until 15 years, then at 18 and 21 years. The full history of the sample has been described by Silva and Stanton.⁷

Information about sexual activity and STDs was sought at the assessment at age 21 years during 1993 and 1994. Wherever possible the sample members returned to Dunedin for the assessment, even if living elsewhere in New Zealand or overseas. The questions on sexual activity were based on those used in the 1990 British National Survey of Sexual Attitudes and Lifestyles, which had been developed after extensive piloting.^{8,9} Questions on STDs were developed from those asked during the 18 year old assessment three years previously.⁴ The questions were presented and the answers collected by computer. An interviewer was present who sat so that she could not see the participants' responses to the questions. She instructed the sample members in the use of the computer, and aided those with very low reading ability, if requested.

Information was sought on various aspects of recent and past sexual activity including age of first intercourse, and number of sexual partners since that time. Those who reported ever having had intercourse were introduced to questions on STDs with a statement "There are some diseases, or infections, that can be passed on during sex. These are called sexually transmitted diseases or STDs. Examples of sexually transmitted diseases are gonorrhoea, chlamydia, herpes, genital warts, urethritis, syphilis etc". The next question asked if they had ever had an STD. Those who responded positively were questioned on how often this had occurred (counting as one, recurrent episodes of the same infection). The condition was identified from a list of the common STDs. If the respondents did not recognise the disease on the list, they could type the name into the computer. The analysis reported here is restricted to bacterial or viral sexually transmitted infections, and the protozoal infection trichomoniasis. Although information on candidiasis (a fungal infection commonly affecting the genital tract which may or may not be sexually transmitted), scabies, and similar conditions, were in some cases provided by the sample members, they were not included in the analysis as they may not have been sexually transmitted. We also asked where treatment was sought, and the circumstances surrounding this (ie whether help was sought because of symptoms, because of contact with another person with an STD, or for another reason).

The 1991 New Zealand Census of Populations and Dwellings was used to assess the representativeness of our sample. Data on questions asked in the census which were also used in our study were obtained for each month of age of the sample. The census data were weighted by the number of the sample at each month of age living in New Zealand at the time of the assessment at aged 21 years to obtain the profile expected for those young people in New Zealand as a whole with the same age distribution as our sample.

The socioeconomic status of the sample member's family was derived from the reported occupation of their parents at the 15 year assessment (for those who attended at that time) using the Elley Irving socioeconomic index for New Zealand occupations.¹⁰ An indication of educational level was determined from the reported highest school attainment at the 21 year assessment. Data have not been reported by ethnicity as the numbers reporting Maori ethnic group or any Maori ancestry were small, and we cannot be sure that this group would reflect Maori in the population as a whole.

Differences in proportions were tested using the chi squared tests of association, and trends using chi squared tests of trend. Comparisons with the census population were by the chi squared goodness of fit test.

Results

Sample. Of the 1037 members of the cohort formed at aged three, 1020 were believed to be alive at the 21 year old

assessment in 1993 and 1994. Of these, nine could not be contacted, 19 refused participation in the study, 42 completed a telephone or shortened assessment that did not include questions on sexual behaviour or STDs, 14 declined to answer the questions on sexual behaviour, and for one person the computer failed to save the responses. Thus 935 (91.7% of survivors) completed the questions on their sexual experiences.

Of the 477 men, 89% were seen within 6 months of their twenty first birthday, as were 93% of the 458 women.

A few differences were found compared to the New Zealand population at the same age as determined from the 1991 census. Our sample members were more likely to have gained a school qualification (for males 82.6% versus 75.1%, $p < 0.001$, and for females 89.0% versus 79.7%, $p < 0.001$). The men were equally likely as those of the same age in the whole population to be living with their parents, a partner (or spouse), their children or siblings, but more likely to be flatting (41.9% versus 35.2%, $p = 0.002$). The women were more likely to be living with a partner (or spouse) (28.7% versus 23.0%, $p = 0.004$), but less likely to be living with their children (9.2% versus 15.9%, $p < 0.001$). No significant differences were found with other living arrangements. Our respondents were less likely to report having any Maori ancestry (males 12.0% versus 19.4%, $p < 0.001$, females 13.0% versus 20.8%, $p < 0.001$).

Sexually transmitted diseases. Of the 477 men, 421 reported ever having had intercourse, and 36 of these stated that they had had an STD. The cumulative incidence of having an STD was 8.6% among the sexually experienced, and 7.5% among all the men. The cumulative incidence is a measure of the lifetime occurrence of any STD. The 36 men reported 38 infections, with two men each reporting two infections. Of the 458 women, 421 reported ever having had intercourse, and 73 of these said they had had an STD. The cumulative incidence of STDs was therefore 17.3% among the sexually experienced, and 15.9% among all the women. The 73 women reported 89 infections, with 10 women reporting two, and two reporting four STDs. Thus STDs were reported significantly more often by the women than by the men ($p = 0.0001$).

Among the sexually experienced men, no significant associations were found between reporting ever having had an STD and either the socioeconomic status of the sample member's family (at the 15 year old assessment), or the individual's school attainment (Table 1). However, among the women, there was a significant trend for women with lower school qualifications to more commonly report STDs, but there was no significant association with their parents' socioeconomic status. Those 280 men living in Dunedin at the time of the 21 year old assessment had a similar rate of STDs to those living elsewhere in New Zealand, but the rate among the 25 men living overseas at the time of the 21

year old assessment was significantly higher than the rest. For the women the rates did not differ significantly by place of residence.

The commonest reported STDs among the men were genital warts and chlamydial infection (Table 2), with cumulative incidences of 4.7% and 2.4% respectively among the sexually experienced. For the women, chlamydial infection was the commonest disease, with a cumulative incidence of 9.0% among the sexually experienced. The next commonest were genital warts and genital herpes infection with incidences of 6.9% and 3.1% respectively.

Table 2. - Number and cumulative incidence (per 100) of STDs by type of infection

Type of infection	Males (n=421)		Females (n=421)	
	No	percent*	No	percent*
Chlamydial infection	10	2.4	38	9.0
Genital warts	20	4.7	29	6.9
Genital herpes	4	1.0	13	3.1
Gonorrhoea	1	0.2	5	1.2
Nonspecific urethritis	1	0.2	0	0
Trichomoniasis	0	0	3	0.7
Syphilis	0	0	1	0.2
Other	2	0.5	0	0

* Restricted to sexually experienced responders

General practice was the commonest place where treatment was sought, and was reported to have been where about half of both men and women affected attended (Table 3). The respondents were able to indicate more than one site of treatment, but none reported attending a sexual health clinic and elsewhere. Thus only 29% (11/38) of the infections among the men, and 20% (18/89) among the women were treated at a sexual health clinic.

Table 3. - Reported place of treatment for men and women reporting STD. Number and proportion attending each place.

Place of treatment	Males (n=38)		Females (n=89)	
	No	percent	No	percent
General practice	18	47.4	45	50.6
Sexual health clinic	11	28.9	18	20.2
Family planning clinic	1	2.6	32	36.0
Student health clinic	4	10.5	3	3.4
Other or not answered	3	7.9	2	2.2
No treatment sought	3	7.9	2	2.2

Numbers add to more than the number of STDs, and percentages add to greater than 100%, as in some cases treatment was sought from more than one site

The reasons for the diagnoses being made were different for the men and women (Table 4). For the men overall the condition was reported to have been diagnosed because of symptoms for 79% (30/38), because of contact with a person

Table 1. - Number and cumulative incidence (per 100) of STDs among sexually experienced men and women according to socioeconomic status of parents, educational attainment and place of residence

Social and demographic characteristic	Males		p value	Females		p value
	No	percent		No	percent	
Socioeconomic status of parents*						
Class 1-2	13/131	9.9		24/136	17.6	
Class 3-4	16/197	8.1		30/182	16.3	
Class 5-6	3/33	9.1	$p = 0.84$	12/39	30.8	$p = 0.10 \ddagger$
Highest school qualification†						
University bursary or scholarship	11/102	10.8		13/112	11.6	
Higher school certificate or 6th form cert	8/153	5.2		30/172	17.4	
School certificate or no qualification	17/152	11.2	$p = 0.13$	29/128	22.6	$p = 0.08 \S$
Place of residence at aged 21						
Dunedin	22/280	7.9		43/266	16.2	
Elsewhere in New Zealand	7/108	6.5		26/120	21.7	
Overseas	6/25	24.0	$p = 0.02$	4/31	12.9	$p = 0.34$

* Excluding 42 men and 43 women whose parents could not be classified on this scale at 15 year assessment

† Excluding 8 males and 5 females with overseas or other qualifications

‡ Chi squared for linear trend, $p = 0.22$

§ Chi squared for linear trend, $p = 0.03$

with an STD for 13% (5/38), and for the remaining episodes for other or unspecified reasons. In contrast, for the women, only 49% (44/89) were detected because of symptoms, 16% (14/89) were diagnosed because of contact with an infected person, and for the remaining 35% (31/89) the diagnosis was made when visiting a health professional for another reason. The overall cumulative incidence for symptomatic conditions only remained higher for the sexually experienced women (10.5%) than for the sexually experienced men (7.1%), although this was no longer statistically significant ($p=0.11$).

Table 4. - Reason for attendance for people with STDs

Reason for attendance	Males (n=38)		Females (n=89)		p value
	No	percent	No	percent	
Symptomatic	30	78.9	44	49.4	
Contact with a person with an STD	5	13.2	14	15.7	
Attending health professional for another reason	1	2.6	31	34.8	$p=0.0005$

No reason stated by 2 men

Among the women the circumstances of the diagnosis also depended on the condition. Only 26% (10/38) of cases of chlamydial infection and 40% (2/5) of cases of gonorrhoea were diagnosed because the women presented with symptoms. In contrast 69% (20/29) of cases of genital warts, and 85% (11/13) of cases of genital herpes were symptomatic.

It is important to know if those who attended a sexual health clinic were representative of all the people reporting an STD by this age, as currently such clinics are the only source of information on affected people in New Zealand. Because of small numbers, differences in the source of care were assessed for the men and women combined. As shown in Table 5, we found that those who attended a sexual health clinic with their problem were more likely to have first experienced an STD at age 19 or older; younger people were comparatively under represented. There was no significant difference with respect to place of residence at age 21.

Table 5. - Proportion of people with STDs attending a sexual health clinic by demographic characteristics. Men and women combined

Characteristic	No	percent	p value
Place of residence (at age 21)			
Dunedin	13/65	20.0	
Elsewhere in New Zealand	12/33	36.3	
Overseas	4/10	40.0	$p=0.16$
Age at time of first STD			
18 years or less	7/45	15.6	
19 years or more	22/63	34.9	$p=0.04$

Risk behaviour. The risk of having had an STD increased steeply with the number of sexual partners for both men and women (Figure 1). The lifetime incidence was 1.5% and 2.6% for men and women respectively who reported only one sexual partner, compared to 14.4% and 39.3% for men and women who reported having had 10 or more sexual partners. Both of the men who reported having had two episodes of an STD, and nine of the 12 women who reported multiple infections had had 10 or more partners.

Reported condom use in the last 12 months according to number of sexual partners in the last 12 months is shown in Table 6. Overall 20.9% of men and 35.3% of women reported never using a condom, and only 15.2% of men and 11.8% of women reported that condoms were always used. Reporting of some condom use did increase with increasing number of sexual partners for both men and women, but there was no increase in the proportion that reported always using a condom.

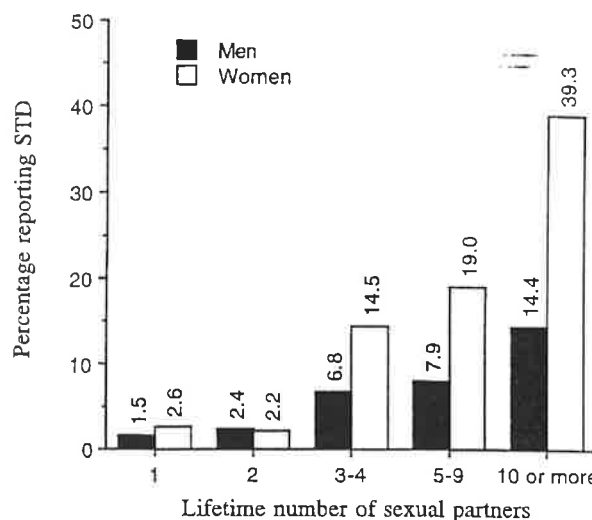


Figure 1. - Proportion of sexually experienced men and women who reported ever having had an STD and lifetime number of sexual partners.

Table 6. - Reported condom use in the past 12 months among sexually active males and females according to number of sexual partners in the last 12 months

Number of sexual partners in last 12 months	No	Use of condoms (percent)		
		Never	Some*	Always
Males				
1	160	32.5	50.6	16.9
2	72	16.7	70.8	12.5
3-4	88	10.2	71.6	18.2
5 or more	67	11.9	77.6	10.4
Total	387	20.9	63.8	15.2
Females				
1	245	41.6	45.7	12.7
2	61	24.6	60.7	14.8
3-4	60	33.3	60.0	6.7
5 or more	33	12.1	78.8	9.1
Total	399	35.3	52.9	11.8

* Reported as "sometimes" or "usually"

Discussion

Several features of this study make it likely that the results truly reflect the experience of the cohort. Firstly, the response rate of 92% of the surviving cohort, and 98.5% of those attending a day of assessments, is considerably higher than that usually achieved in random sample surveys of sexual behaviour, where a 60-70% response is common. This suggests a high level of willingness to provide information, and may reflect the fact that through many years the confidence of the sample members has been maintained. In addition, the questions were presented by computer, a method that had been used successfully during the previous assessment at 18 years, and has also been found, at least among adolescent girls, to be more acceptable than either face to face or written questionnaires.¹²

Compared to their age group in the country as a whole our sample members were similar, but they had a slightly higher level of educational achievement. For the women we found that lower educational achievement was significantly associated with reporting an STD, therefore we are likely to have underestimated the national occurrence of STDs, at least among females.

The results confirm the importance of STDs amongst adolescents and young adults, with 7.5% of all men, and 15.9% of all women reporting an STD by age 21 years. Moreover 16% of women who reported an STD reported more than one episode. The occurrence of STDs may be higher than reported here, especially among men, as a proportion of affected people are either completely

asymptomatic (and have not been screened) or have symptoms they do not recognise as requiring treatment. Asymptomatic chlamydial and herpes simplex infections are common in both men and women.¹³

Few other comparable studies of the cumulative incidence of STDs are available. The US national survey of sexual practices conducted in 1993 found that 9.8% of men and 16.5% of women aged 18 to 24 who were sexually active reported a sexually transmitted infection.¹⁴ This is very similar to the 8.6% of sexually active men and 17.3% of sexually active women aged 21 in our survey. A similar recent study in England and Wales asked about attendance at a sexual health clinic and found that 5.0% of men and 5.2% of women aged 16 to 24 reported attending such a clinic.⁸ Clinic attendance has been regarded as a proxy for STD occurrence in England and Wales because up to 90% of STDs were thought to be treated in such settings.^{3,15} Nevertheless these lower rates recorded in England and Wales and the lack of female preponderance at this age may reflect attendance at other sites for treatment of STDs, particularly by women.

There was a striking sex difference in the reported rates of STDs. Although much of this difference was associated with more screen-detected cases amongst the women, the cumulative occurrence of symptomatic disease was also higher among the women. This sex difference in STD occurrence among young people is consistent with findings from the Christchurch sexual health clinic in 1993, when more than half of new attenders under age 20 were female, while there was a male preponderance among older attenders.⁶ There are both behavioural and biological reasons why STDs could occur more among young women than men. Firstly, young women have been shown to have more sexual partners older and more sexually experienced than themselves, therefore the rate of STDs in women would be expected to be related to that of relatively older men, rather than to men of the same age.⁹ Secondly, we found in an earlier study on this cohort that young men with multiple sexual partners were more likely to report protection with condoms than were the young women.⁴ Thirdly, it has also been found that transmission of most sexually transmitted agents is more efficient from a man to a woman than vice versa during sexual intercourse, hence following an equal number of contacts with infected partners, more women would become infected.¹⁶

The occurrence of STDs was also strikingly associated with the reported number of sexual partners for both men and women, as might be expected and has been found in other studies. Condom use in the last year was reported more frequently by those with more sexual partners in the last year, but a substantial proportion of men and women reported inconsistent or no use of them. Even if condom use were more widespread it is unlikely to eliminate the risk of sexual transmission for diseases of very high infectivity such as gonorrhoea and chlamydial infection. Laumann and colleagues have calculated the probability of transmission of gonorrhoea to a woman from 10 sexual encounters with an infected male partner as 40%.¹⁴ This assumes that the partner always uses a condom, and a condom failure rate of 10%.

STD occurrence was less strongly related to other social and demographic factors. For women, but not for men, the reported rates were higher in those with lower school achievement. The socioeconomic status of the parents was not significantly related to the occurrence of STDs for either sex. Men living overseas reported significantly higher rates of STDs than those resident in New Zealand, which may reflect differential emigration according to sexual lifestyle. A lack of association of health status among adolescents with parental social class has been observed for a number of measures of health status and social class in the UK.¹⁷ Instead measures of adolescent social position based on occupation and educational attainment do show an association with health status,¹⁸ which is in accord with our finding for educational attainment for women.

Only a minority of people with an STD reported attending a sexual health clinic (29% of men and 20% of

women). Instead most attended either a general practitioner or a family planning clinic. We have confirmed that the low proportion of STDs treated at sexual health clinics is not peculiar to Dunedin residents, as only 31% of people with STDs who resided elsewhere in New Zealand reported attending a sexual health clinic. Young people, aged 18 or less, were less likely to be treated at such clinics, as were females. These findings suggest that using sexual health clinic data for surveillance will give a biased picture of STD patterns as well as underestimate the occurrence of STDs in New Zealand, at least among young people. We are not in a position to say whether this pattern would be seen in older people with STDs, however in 1968 in Auckland it was estimated that twice as many cases of STDs were seen in general practice as attended hospital clinics,¹⁹ and in 1977 that an equal number on gonorrhoea cases were diagnosed in STD clinics and privately.²⁰

The implications of these findings for the control of STDs in New Zealand relate to the prevention, treatment and surveillance of STDs. The prevention of STDs should be directed at increasing the use of condoms, but education aimed at reducing the number of sexual partners⁵ and delaying the onset of sexual involvement²¹ should be considered seriously.

Skilful diagnosis, treatment and contact tracing for bacterial STDs is effective in reducing the incidence of these diseases.²² To do this requires either specialised services such as are available at sexual health clinics, or practitioners skilled in STD management in family planning clinics and general practice. In the UK, where there has been debate about the wisdom of splitting the roles of contraceptive provision and STD treatment, a call has been made for a coordinated sexual health service in both family planning and genitourinary medicine.²³ We have no evidence from our study that there are deficiencies in the service provided in New Zealand. But some diagnostic and contact tracing facilities are available only in sexual health clinics where only a minority of cases among young people are treated. This suggests that there is a need for a more coordinated approach in New Zealand too.

Finally surveillance of STDs needs to be enhanced, as to rely on sexual health clinic data is misleading. Even trends over time are likely to be of little value as the clientele of sexual health clinics change.⁶ Reporting of all laboratory diagnosed STDs would be a major improvement. In addition making some STDs notifiable should be considered.

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IN PRACTICE

DNA-based diagnostics for adrenoleukodystrophy in a large New Zealand family

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Abstract

Aim. To develop a DNA-based diagnostic test for adrenoleukodystrophy (ALD) in a large New Zealand family.

Methods. Mutation screening of the X chromosome-linked ALD gene was undertaken by direct sequencing of PCR amplified products encompassing defined exons of the ALD gene. The identification of a mutation led to the development of a simple restriction enzyme digestion protocol of a PCR amplified product to identify those individuals with the mutation.

Results. A nonsense mutation, resulting in deduced premature termination of translation of the ALD gene product, was detected in exon 4 of the ALD gene in an affected male. This mutation was found in three obligate gene carriers in the same ALD family. A DNA-based test was established to identify this mutation by Bgl II digestion of a PCR amplified product encompassing exons 3 and 4 of the ALD gene. The DNA-based test was applied to a chorionic villus sampling for prenatal diagnosis.

Conclusions. A simple DNA-based test has been developed for ALD in a large New Zealand family. This test provides a rapid means of determining carrier status and for undertaking prenatal diagnosis for ALD in this family.

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Adrenoleukodystrophy (ALD) is an X chromosome-linked inherited disease characterised in most affected males (hemizygotes) by progressive multifocal demyelination of the nervous system and adrenal cortical insufficiency.¹ The most common onset of ALD is in childhood, with neurological symptoms beginning between 4 and 8 years of age, rapidly progressing to death within a few years of the first symptom. More than 90% of affected children have evidence of adrenal disease. A milder form, termed adrenomyeloneuropathy (AMN), has later onset and predominant spinal cord involvement initially. AMN is thought to be allelic with ALD and these and other forms may coexist in the same family. Less common presentations in male hemizygotes include adrenal insufficiency without nervous system involvement, progressive cerebral dysfunction in adults or biochemical manifestations without symptoms. Ten to fifteen percent of female carriers (heterozygotes) develop comparatively mild neurological

symptoms.

ALD is associated with the accumulation of very long chain fatty acids (VLCFA) in neural white matter, adrenal glands, cultured fibroblasts and plasma.¹ This accumulation is due to an impairment of beta oxidation of fatty acids in peroxisomes. Serum VLCFA levels can be normalised by a diet low in VLCFA supplemented with Lorenzo's oil, a combination of lipids believed to inhibit competitively the endogenous synthesis of VLCFA. Clinical trials suggest that this regimen may have little effect on established neurological disease, but presymptomatic treatment is still under trial; thrombocytopenia is a common side effect.^{2,3} Bone marrow transplantation is also under trial.⁴

A recent study described the isolation of a candidate gene for ALD, which comprises 10 exons and encodes a 3.7 kb transcript.⁵ To date, several intragenic deletions of the gene ranging in size from 0.5-19.2 kb have been identified by southern blot analysis of genomic DNA,⁶⁻⁹ which accounts for ~4.2% of the total number of patients analysed. Point mutations and/or microdeletion/insertion events in the ALD gene are thought to account for the manifestation of the disorder in the remaining patients and a variety of such mutations have been described.⁸⁻¹⁵ These mutations are distributed throughout the ALD gene with a high proportion clustered within the central exons.

We have analysed the ALD gene transcript for mutations in a large New Zealand-based ALD pedigree in order to provide supporting evidence that this gene is implicated in the disorder. We have detected a nonsense mutation that causes premature termination of translation of the ALD gene product in an affected male. This mutation segregates with the disease in the family reported here. The development of a DNA-based assay to detect this mutation has also allowed prenatal diagnosis to be undertaken.

Materials and methods

The affected family. We studied members of a large kindred affected by ALD; partial pedigree shown in Figure 1. We know of at least 389 descendants, in five generations, of the Maori woman who is the earliest known obligate heterozygote. Some males in early generations died in childhood with illnesses suggestive of a neurodegenerative disease, but the first with detailed medical records were four brothers who presented in the 1950s and '60s. Subsequently, other affected males were identified in a pattern suggesting X-linked inheritance. A pathological diagnosis of leukodystrophy (sudanophilic) was first made in 1972. The changes in the nervous system were consistent with ALD, but there had been no overt adrenal insufficiency and the specific diagnosis was