

## CHO October 3 A Population Perspective on Chronic Disease

Presenters and their subjects:

“Trends in Asthma and Allergic Disease with Special Reference to the Australian Capital Territory”

Professor Anne-Louise Ponsonby, Murdoch Children’s Research Institute, Menzies Research Institute, Australian National University Medical School.

and

“Chronic Disease: Setting the Policy Context.”

Mr Ross O’Donoughue, Director, Health Improvement Branch, ACT Health.

### **Anne-Louise Ponsonby**

When I was speaking to Paul (Dr Paul Dugdale, ACT Chief Health Officer) about this session he thought that one of the more useful things I could talk about was how ACT Health routine surveillance data can be taken to the next step of knowledge generation with epidemiological research. I will therefore talk about trends in child asthma and allergic disease with special reference to the Australian Capital Territory.

I work for two research institutes, the Murdoch Children’s Research Institute and the Menzies Research Institute, and I have an honorary appointment at ANU. I am primarily based at ANU and therefore have interaction with ACT Health.

First, some definitions. When I use the word ‘atopy’ in this talk I am using it to refer to allergies; any positive response to an aeroallergen on skin prick testing. It could be pollen allergy, it could be dust mite allergy, it could be egg allergy. Atopic disease is the cluster of diseases that are linked to atopic allergies, such as hayfever and eczema. Finally, for asthma there are various population-based definitions, particularly ‘asthma ever asthma’ and ‘wheeze in past year’ including those from the international study of asthma and allergy in childhood.

We test for an allergic response with a skin prick test to various types of substances. We put a little drop punctured through the skin and after a period of time, usually fifteen minutes, we come back to see if a weal has developed. It looks like a little mosquito bite and indicates that that person or child has an allergic response to that substance.

There has been concern since the 1980s about how allergic diseases are increasing over time, but in 1998 the first suggestion was published by Erika von Mutius in the Lancet that the

temporal increase in hay fever may be uncoupled from asthma trends in school aged children. Erika von Mutius and colleagues conducted two cross-sectional surveys amongst German primary school children, one in 1991-92, and one in 1995-96. They found that hay fever had increased as expected over that time, but the proportion of children with recurrent wheeze had decreased from 25.9% in 1991-92 to 19.5% in 1995-96.

In the US there were similar suggestions, but unfortunately they had an increase in asthma, documented by the same routine surveillance system, right through the eighties and the nineties. They changed their surveillance system in 1996-97 and the prevalence of asthma rates started to drop. So they can't be sure with this US data, based on children aged from 0 – 17, whether there was a true decline in asthma prevalence or whether it was due to the change in the reporting system. It shows just how important reporting systems are.

Swiss data from two cross-sectional surveys, again on primary school children with under 2000 children per sample and published in 2004, showed that from 1992 to 2000, the proportion of children with current wheeze or with multi-test allergy stayed the same. This suggests there was a halt in the increase in the asthma and allergy in Switzerland over that time. And in Rome, Italy, between 1974 and 1992 cross-sectional surveys of children aged from six to fourteen showed a three-fold increase in asthma prevalence, but from 1992 to 1998 there was no further increase in asthma prevalence.

There have been two papers published from Australia on this issue, one by Toelle in the British Medical Journal in 2004 and one by Robertson in the Medical Journal of Australia, also in 2004. Both of them repeated two samples over two time periods. The one by Toelle in Belmont first looked at children born between 1987 and 1993. The second sample looked at children born between 1996 and 2002. They were all primary school-aged children at the time of testing, and the prevalence of recent wheeze declined from 27.2% in the earlier birth group to 20% in the later group, but uncoupled from that, hay fever increased from approximately 15% to 20%. Similar patterns were evident in Robertson's Melbourne study with the earlier study having wheeze of 28.6% dropping down to 23.7% in the later sample and the hay fever going in the other direction.

So we have a pattern where the asthma seems to be declining, but hay fever seems to be continuing to go up. Some of the Australian Institute of Health and Welfare data has been very informative on this issue. If we look at hospital separations for asthma per 100,000 people in Australia between 1993 and 2001, we can see that when we stratify by age of admission there has not been that much change in separations for the two groups aged 35 to 64 and 65 plus. The big decline has been in the group of 0 to 4 year olds.

If we consider another trend graph, this time from the Beach Survey of General Practice, which is a very important Australian resource for showing us morbidity patterns in general practice, again we find a similar picture to what we found with the hospital admission data. It shows there is a decline over time and it is particularly evident for the 0 to 4 year olds. Episodes of asthma in UK general practice show a similar pattern. A graph of the mean weekly incidence of asthma attendances by year shows there was an increase during the 1980s and then a peak around 1991 to 92 followed by a decline thereafter. There was a steeper rise for the 0 to 4 year olds than for 5 to 14 year olds with the former reaching a higher peak and then a steeper decline. What's interesting about that peak is that it occurred around 1991 and 1992. That is of interest for those of us who worked in the field of Sudden Infant Death Syndrome because a graph showing how rates per 100,000 live births of Sudden

Infant Death Syndrome have changed in the UK over time reaches a peak about 1988 – four years prior to the weekly asthma peak for the 0 to 4 year olds. Considering SIDS is a disorder occurring primarily in the first six months of life it is of some interest that we are having this shift in disease rate with SIDS occurring four years before we have a parallel change in child asthma in the UK. In an attempt to understand this connection further we have done some work with the Tasmanian cohort, where quite a lot of SIDS research was conducted, to try and link it to hospital asthma databases. However, we haven't got much to show you with that yet.

So now we come to the ACT's specific work. Firstly though, a greater understanding of the marked international and temporal variation in the prevalence of child atopic diseases is required to improve the understanding of the aetiology of these disorders. In 2006 the findings of the international study of asthma and allergies in childhood was reported in *The Lancet* and it was based on two cross-sectional surveys, one that was mostly conducted in 2002 and 2003 and an earlier one that was conducted mainly in the mid nineties.

For children of 6-7 years the prevalence of asthma increased only in some centres while decreasing in others. It particularly decreased in prevalence in the centres that had had higher asthma prevalence in the mid-nineties to start with. In contrast, for both eczema and hay fever the prevalence increased in the majority of centres and this was irrespective of the results from the results in the mid-90s. We are seeing a lot of international variation. There does seem to be decline in asthma occurring in many different countries, particularly those that had higher asthma rates in the 1980s. However, those data were only available at two points in time and data have not been readily available from serial annual surveys to examine these trends beyond assessments at two time points.

I'm also going to talk a little about migrant history and asthma risk because the ACT School Health data illuminates some issues pertaining to it. Several studies have previously looked at country of birth and atopic disease and in both Australia and the UK, Asian born immigrants tend to have lower asthma prevalence. This is particularly marked in those who migrate before the age of five. The advantages of comparing country of birth effects within a region such as the ACT are that it does not have the problem of the comparison across countries and time periods which can be limited by study participation rates, the questionnaire might be interpreted differently in the different languages - even though there are now video supplements to try and help standardise things across countries, and differences in disease diagnostics of health care. If you are looking at differences in asthma rate by country of birth and each country has its own system for classifying asthma it is going to be very difficult to truly understand what is happening biologically. Although the international study for asthma and allergy in childhood has been a very useful large study, there is concern that both the prevalence of symptoms and diagnoses of asthma are heavily dependent on the awareness of asthma in the populations studied.

The aim of this study was to look at how asthma, eczema, allergic rhinal conjunctivitis (otherwise known as hay fever) and respiratory symptoms in the ACT school-entry survey differ by country of birth. Further, as the annual school entry surveys were available we looked at temporal trends in these conditions and we examined whether these temporal trends differed by country of birth.

The methods in this study are that the school health nurses offer a health assessment to new entrants to kindergarten classes in all primary schools in the ACT. Before the health

assessment a child health screening questionnaire is sent home to parents who have to complete it before the assessment.

From 1999, this questionnaire has included questions on respiratory history, including parent-reported asthma, respiratory symptoms, eczema and hay fever. Also, the survey includes some core questions from the international study of asthma and allergy in childhood. (As an aside, some past work that ACT CHO Paul Dugdale, myself and others have been involved with has validated some of those questions against position diagnosis in the ACT and found it was a fairly valid report of asthma). Because this survey is required from all new school entrants, we rapidly accumulate very large samples. The results I am going to show you are based on 22,882 children aged between 4 and 6 years, who began school in the ACT and had parent completed questionnaire data available. The proportion of children with completed questionnaire data by school entry year was very good. With many modern studies we suffer very badly from people being too busy to participate in surveys so to get the response rate of over 80% that we did with the schools is thought to be excellent in modern first world countries. This survey not only started off with a response rate of over 80% but by 2005 it was up to 89%, which is a really fantastic achievement for the ACT School system and ACT Health.

The survey had roughly 50% males and 50% females. The mean age did not change much. It was 4.9 in 2000 and 5.1 in 2005. The proportion of children born outside Australia was 5.4% in 2000 and 6.1% in 2005, so that did not vary much either. There was some variation in the type of emigrants with an increase in children born in Asia and also an increase in children born in Africa.

The proportion of these children who reported eczema, hay fever or asthma was 31.5% in 2000. By 2005 it was 37.5%. For hay fever, it was 20.4% in 2000, which significantly decreased to 17.5% in 2005. Asthma was 24.7% in 2000, but for the school entrance in 2005 it declined to 19.6%. Now most other surveys have only two points in time, like 2000 or 2005, but because we had points on every year we could try and fit curves to see what sort of pattern this change made. Did it have an unusual U-shaped pattern or an S-shape pattern? Actually it didn't, seeming instead to have quite linear trends. So we fitted what is called a fractional polynomial plot which allowed the data to shape the curve rather than artificially putting in a line of best fit. It confirmed that the change was mainly linear over time. Now we have this interesting uncoupling with the eczema rates going up, the hay fever going down slightly, which is unusual compared with many other communities, and the asthma ever declining as has been reported from other countries. The results were also reflected in respiratory symptoms and asthma medication.

So we looked at the percentages, then we looked for a line of best fit. Now we are going to look at odds ratios with their 95% confidence intervals for atopic disease of respiratory symptoms per increase in the air from 2000 to 2005. What that odds ratio tells you is the multiplicative increase in risk as one moves from year to year. If there was an adjusted odds ratio of 2 that would mean that for that disease it was doubling in prevalence every year, or if it is 0.5, that means it is halving.

Further, the 95% confidence intervals, if that excludes one, the range from the lower to the higher value, that means it is significant at P less than 0.05. And what we can see here is that the year by year trend for eczema is significantly increasing but asthma was decreasing over the same period.

There are interesting figures for children according to where they are born with the diseases eczema, hay fever and asthma. The figures show considerable variation in the percentage of children with eczema, also for hay fever and asthma. Now, which are the countries with the highest disorder rates? For asthma, Australia has 35%, New Zealand 37%. Which ones have the lowest? Asian born children have lower rates of eczema reported by parents at school entry. And there is a similar pattern with asthma. Children born in New Zealand have slightly higher rates than children born in Australia, but children born in Asia or Africa have a lower prevalence of asthma by school entry.

If you are born in Asia rather than Australia the adjusted odds ratio for eczema ever by school entry is 0.32 and significant. For hay fever it's 0.37 and for asthma ever 0.50. That helps to back up what has been found in international surveys. It would be simplistic to suggest that they are just under reporting asthma in Asia, but they have similar diagnostic systems – and we have done a lot of supplementary analyses on how often these children went to the doctor as well as how often they use medication – and we still find that they seem to have lower rates of these disorders.

We have noted declining rates of these diseases for both the Australian and overseas born. The fact that there was a decline in both groups suggests that whatever is driving the decline appears to operate in early life, but not in the pre-natal period alone because otherwise you would expect the children who came from the different countries, of country of birth, not to have had the same type of rate drop as the Australian children.

I would like to look at what could be some of the reasons for the uncoupling of asthma and eczema trends. National survey data from AIHW indicates there has been improvement in the exposure to passive smoking. In 1995, 31% of children were exposed to tobacco smoking in the home. By 2001 it was down to 20%. If we are trying to look at factors that might be affecting the decline of asthma, but not eczema, then passive smoking is one to be considered as a candidate because it has a lung-specific effect.

In contrast, if we are trying to think about what is driving up eczema and not asthma then dietary factors are of interest. A/Prof Ray Mullins has a very interesting paper about his specialist allergy practice in the Medical Journal of Australia this year. He reported that there was a 12-fold increase in the proportion of children with food allergy in his practice. Now, when you are coming from a practice base, rather than a population base, all sorts of selection forces can come in – perhaps he actually developed a reputation because he is a very fine allergist and perhaps there was a shift in the type of patients. But he included in his article a population-based assessment which was tying in with his local ACT practice-based results. The assessment is from the Australian national morbidity database for hospitals and looks not just at children but all Australians. For food anaphylaxis there were increased hospital admission rates from 1993-94 up to 2004-05. There are increases in other related things like angioedema, and so on.

So, the use of surveillance data has shown us that child asthma rates do not appear to be increasing in the ACT among school entrants over recent but eczema rates continue to increase. That is there has been an uncoupling in the time trends for these two disorders over time. The challenge now is to better understand the reasons that underlie these very interesting population-based trends.