

INTERNATIONAL STUDY OF ASTHMA AND ALLERGIES IN CHILDHOOD

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(Attention Innes Asher)

ISAAC WEB SITE

<http://isaac.auckland.ac.nz> ←

A recent exciting addition to the ISAAC web site is a discussion forum (see Feedback page). Visitors to the web site can view existing messages, respond to comments made by other visitors, or post messages on new topics. We hope that the forum will be a useful, lively discussion area where ISAAC collaborators can ask questions, offer advice or just reflect on their experiences of ISAAC. We urge all collaborators with access to the world wide web to visit and contribute to the forum regularly at:

<http://isaac.auckland.ac.nz/Feedback/FeedFrame.html>

We are keen to keep the 'Publications' section of the web site as up to date and comprehensive as possible. If you have any recent publications that you believe should be listed in this section please email details (including an accurate reference in the Vancouver style) to me at the IIDC.

We are open to any suggestions for new features for the ISAAC web site - we promise to do our best to action them (as long as they are feasible and legal of course!). Happy browsing!

* Tadd Clayton
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NEWSLETTER – July 1999

Welcome to this ISAAC Newsletter. We aim to produce a Newsletter twice a year and welcome contributions, however small, from any ISAAC collaborators. "Bits and pieces" on your own area of interest, or from your local centre, and items of fun would be welcomed. We would also like to hear about any ISAAC publications we have missed.

The ISAAC programme is in good heart and as active as ever. The Phase Two Modules Manual, was published last year, by the University of Münster and prepared by Stephan Weiland, David Strachan and Erika von Mutius, with contributions from other members of the ISAAC Steering Committee. Over the page you will read Stephan's update on ISAAC Phase Two, which is going very well.

Plans for ISAAC Phase Three are developed and coordinated by Richard Beasley and myself, along with the ISAAC Steering Committee and ISAAC International Data Centre. A Phase Three Manual is being developed, and more than 80 centres have expressed an interest in participating. You will read more information about Phase Three in this Newsletter.

Major funding is being sought for these phases, including the running of the International Data Centres for Phase Two in Münster and Phase Three in Auckland, and coordination of these Phases.

The European Respiratory Society meeting is being held in Madrid from 9-13 October 1999. The Annual Meeting of the ISAAC Steering Committee will be held in Madrid on October 8 & 9. We are very pleased to invite you to a social function on Saturday night at 2000hrs (see enclosed invitation). Everyone who has been involved in ISAAC, or who plans to be involved in ISAAC, is warmly invited to attend. This includes everyone who receives this Newsletter, field workers, research workers, as well as principal investigators. We are aware that there is an overlap with the opening ceremony of the ERS, which starts at 1800hrs but AstraZeneca have arranged transport to and from the ERS Congress Centre to help. Come for just part of the time if you can't come for all - we'd love to see you.

ISAAC Phase One Principal Investigators will find enclosed a reprint of the latest worldwide publication, **Worldwide variations in the prevalence of symptoms of atopic eczema in the international study of asthma and allergies in childhood**. We have also included a complimentary copy of 7 slides of ISAAC Phase One worldwide maps, which we hope you will find useful.

On behalf of the ISAAC Steering Committee and the International Data Centre, I thank you once again for your splendid work and friendly communications.

Innes Asher
Chairperson, ISAAC Steering Committee
July 1999

"Sarah, woman of faith of the Hebrew scriptures, knew about hope. After she said yes to uprooting, leaving behind her security, trekking into the vast unknown, she gives birth to Isaac, a name meaning 'laughter' (Gn 21:1-7). Isaac was the new beginning for Sarah. Isaac is a symbol of our own new beginnings. What is there in our life that we least expect will unfold? What 'child' has come forth out of our midlife womb of darkness? Our Isaacs are varied and many: mended or newly discovered relationships, old dreams dusted off and brought to life, creativity that we never believed in before, a view of ourselves that is both beautiful and bountiful, a spiritual path that energizes us, a work that never seemed possible. There may be many 'children' as a result of our midlife seeding – our 'Isaacs' have unlimited potential." From **Dear Heart, Come Home: The path of midlife spirituality**, Joyce Rupp 1997

Update on ISAAC Phase Two

The Phase Two of ISAAC is making good progress. The study protocol has been finalised and the Phase Two modules have been revised and extended. There is considerable interest in ISAAC Phase Two from many centres who had participated in Phase One. In addition, several countries who did not participate in Phase One are keen to conduct Phase Two studies. At present, Phase Two studies have been completed in Germany (2 centres), China (3), Sweden (2), Estonia (1), and the Netherlands (1). Phase Two field work is currently being conducted, or is about to get started, in Albania (1), Costa Rica (1), France (5), Iceland (1), and the UK (1). Firm plans or strong interest to conduct Phase Two studies have been expressed from colleagues in Barbados, Brazil, Canada, Finland, Georgia, Greece, India, Indonesia, Iran, Italy, Japan, Korea, Latvia, Lebanon, Norway, Poland, Portugal, Turkey, Spain and New Zealand.

Our efforts to raise funds for the support of field work in low income countries and for the Phase Two Data Centre in Münster have unfortunately not been very successful. However, we will continue to look for funding opportunities, because we trust

that an effort of such outstanding scientific importance will sooner or later find the necessary financial support. The standardisation of field work in Phase Two studies is essential for the comparability of data. We therefore conducted a Phase Two training seminar on March 11-13, 1999 in Münster where all the different aspects and techniques of Phase Two field work were discussed and trained in detail. The workshop was very successful and had 30 participants from 22 of the above countries!

For further information or copies of the ISAAC Phase Two modules contact

Phase Two Co-ordinator:

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Steering Committee Papers Accepted for Presentation at ERS Meeting: Madrid '99

The relationship of per capita gross national product to the prevalence of symptoms of asthma and other atopic diseases in children: The International Study of Asthma and Allergies in Childhood (ISAAC).

Presenter: Alistair Stewart

Diet, Asthma and Allergies: A further ecological study with ISAAC (International Study of Asthma and Allergies in Childhood) Phase One worldwide data.

Presenter: Innes Asher

Report from the Asia-Pacific Region

ISAAC Phase Two – There are three centres (Hong Kong, Guangzhou and Beijing) taking part in this project and data collection has been completed. I am now analysing the data. An abstract of the Hong Kong data entitled “Risk factors for asthma in Hong Kong schoolchildren” was presented as a poster at the ATS meeting. I am planning to hold a regional coordinators’ meeting during a regional chest meeting in the Phillipines in December (15th Asia Pacific Conference of Diseases of the Chest) to discuss Phase Three.

* **Chris Lai** <keilai@netvigator.com>

ISAAC PHASE THREE

Phase Three is important, not only to investigate whether asthma prevalence is increasing, but also to observe whether the increases are uniform throughout the world and to identify factors which may be related to these increases.

The main objective of Phase Three is to examine time trends in asthma, allergic rhinitis and atopic eczema in centres and countries which participated in ISAAC Phase One. To date over 80 centres from 47 countries that completed Phase One have expressed an interest in participating in Phase Three. Another objective of Phase Three is to describe the prevalence and severity of asthma, allergic rhinitis and atopic eczema in centres and countries which are of interest, but did not participate in ISAAC Phase One, and to obtain baseline measures for these new locations. In addition Phase Three may include examination of hypotheses which have been suggested by the findings of ISAAC Phase One and subsequent ecological analyses, through the use of additional tools and sources of data.

Centres are encouraged to collect Phase Three data in 2001 and 2002.

The Phase Three Manual

The Phase Three Manual will be prepared to explain all aspects of methodology. It will include:

- The relevant sections of the Phase One Manual, updated as necessary
- A copy of the questionnaires
- Field workers guidelines for the written questionnaires
- Guidelines for the video questionnaire
- Translation guidelines
- Any new modules
- A section on coding and data transfer (update of Phase One Coding and Data Transfer Manual)
- Centre Report Form, and instructions for completion

The Phase Three Manual will be supplied in electronic form as well as a bound printed copy. This will enable centres to have maximum flexibility in preparing the study, and study instruments, and supplying data and the requisite documents to the ISAAC Phase Three International Data Centre.

New Citations

Worldwide variations in the prevalence of symptoms of atopic eczema in the international study of asthma and allergies in childhood.

Hywel Williams, Colin Robertson, Alistair Stewart, Nadia Ait-Khaled, Gabriel Anabwani, Ross Anderson, Innes Asher, Richard Beasley, Bengt Björkstén, Michael Burr, Tadd Clayton, Julian Crane, Philippa Ellwood, Ulrich Keil, Chris Lai, Javier Mallol, Fernando Martinez, Edwin Mitchell, Stephen Montefort, Neil Pearce, Jayant Shah, Bonnie Sibbald, David Strachan, Erika von Mutius, & Stephan Weiland - J Allergy Clin Immunol 1999;103:125-38

Intake of trans fatty acids and prevalence of childhood asthma and allergies in Europe.

Stephan K Weiland, Erika von Mutius, Anika Hüsing, M Innes Asher, on behalf of the ISAAC Steering Committee - Lancet 1999, 353:2040-1

At this stage we would welcome having any further suggestions about the manual from Phase One collaborators who intend to do Phase Three. We want to make the manual as helpful as possible. Please send any suggestions to Richard Beasley.

Interest in Phase Three has been registered by the following centres:

Albania	Tiranë	Germany	Greifswald	Nigeria	I badan
Argentina	Rosario		Münster	Norway	Oslo
	Buenos Aires	Greece	Athens	Oman	Al-Khod
Australia	Perth	Italy	Ascoli Piceno	Pakistan	Karachi
	Sydney		Torino	Panama	David
	Melbourne		Firenze	Paraguay	Asuncion
Austria	Kärnten		Empoli	Peru	Lima
	Oberösterreich	India	Kottayam	Poland	Krakow
	Urfahr-umgebung		Chandigarh	Portugal	Lisboa
	Salzburg		Jodhpur	Romania	Cluj
Belgium	Antwerp		Pune	Singapore	Singapore
Brazil	Recife		Davangere	Spain	Almeria
	Curitiba	Iran	Tehran		Barcelona
	Salvador		Birjand		Pamploma
	Uberlândia		Zanjan		Castellon
Canada	Hamilton		Rasht		Valencia
Chile	Puntas Arenas	Rep. of Ireland	Dublin		Cartagena
	Valdivia	Japan	Fukuoka		Vallodolid
	Central Santiago	Kenya	Eldoret	Sweden	Stockholm/Uppsala
China	Beijing	Korea	Seoul		Linköping
	Guangzhou		Provincial Korea	Syria	Aleppo
	Wulumuqi	Kuwait	Kuwait	Thailand	Chiang Mai
	Hong Kong	Lebanon	Beirut		Bangkok
Ethiopia	Addis Ababa	Malaysia	Kota Bharu	UK	North Thames
Estonia	Tallinn		Klang Valley		South Thames
Finland	Kuopio County	Mexico	Tlalpan		Sunderland
	Turku & Pori County	Morocco	Rabat		Guernsey
France	West Marne	New Zealand	Auckland	Ukraine	Kharkov
	Pessac		Wellington	Uruguay	Montevideo
	Marseille		Bay of Plenty	USA	Birmingham
Georgia	Tbilisi		Nelson		
			Christchurch		

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ISAAC PHASE ONE ABSTRACTS FROM WORLD ASTHMA MEETING - December 1998

(published in *European Respiratory Journal* 1998; vol 12, supplement 29)

P035

NATIONAL CHILDHOOD IMMUNISATION RATES AND THE PREVALENCE OF CHILDHOOD ASTHMA. ECOLOGICAL ANALYSIS OF ISAAC DATA

H.R. Anderson. *On behalf of the ISAAC Steering Committee; Department of Public Health Sciences, St George's Hospital Medical School, London, United Kingdom*

It has been postulated that infections in early life may reduce the incidence of subsequent atopy. If so, immunisation could be related positively to the incidence of atopy by preventing certain infections or negatively by stimulating the immune system itself. To test these hypotheses we have examined the relationship between national immunisation rates and the prevalence of childhood wheezing in countries which collaborated in the International Study of Asthma and Allergies in Childhood (ISAAC). For 6-7 year olds, the correlations between wheezing in the past year and DPT, BCG and measles immunisation rates in 1995/96 tended to be positive but were weak and non significant (24-31 countries). The results were similar for 13/14 year-olds (37-47 countries). Controlling for an indication of development using GDP made little difference. The results do not support the theory that immunisation may be an important factor in geographical variations in asthma prevalence. However, limited information from participating centres indicates that local immunisation rates may differ considerably from national rates. Future analyses will also look at immunisation rates which relate to the infancy of ISAAC subjects, and to the area of the ISAAC centre.

P037

INVERSE RELATION BETWEEN TUBERCULOSIS AND CHILDHOOD ATOPIC DISEASES

Erika von Mutius, Ondine von Ehrenstein, Stephan Weiland, Neil Pearce, Richard Beasley. *On behalf of the ISAAC Steering Committee; Munich, Germany*

An inverse relationship between tuberculin skin test reactivity and the prevalence of atopic diseases has recently been reported in BCG immunized Japanese children. In animal models an infection with *Mycobacterium tuberculosis* has been shown to prevent the development of atopic sensitization and the eosinophilic infiltration (?) of the lungs.

The Aim: of this study was to investigate the association between tuberculosis and childhood atopic diseases on an ecological level.

Methods: All centres which contributed data to the ISAAC study were included. Weighted regression analysis was performed using TB notification rates from the WHO "Health for All" report.

Results: The prevalence of wheeze ever (coeff: -0.08, $p = 0.0001$), wheeze in the past 12 months (coeff: -0.03, $p = 0.005$), asthma ever (coeff: -0.03, $p = 0.0002$), nose problems in the past 12 months (coeff: -0.08, $p = 0.0001$), and eczema ever (coeff: -0.035, $p = 0.005$) were all significantly inversely related to TB notification rates. The associations were reduced when the analysis was further adjusted for GNP. However, the negative associations with wheeze ever (coeff: -0.03, $p = 0.03$) and asthma ever (coeff: -0.02, $p = 0.02$) remained significant. This analysis showed, for example, that an increase in TB notification rates of 100 per 100,000 was associated with a decrease in the prevalence of 'wheeze ever' of 3.5%.

Conclusion: The results suggest that on a population level the incidence of tuberculosis is inversely related to the development of childhood atopic diseases, particularly asthma.

P082

ANALYSIS OF RESULTS OF A VIDEO QUESTIONNAIRE USED FOR A SURVEY OF ASTHMA PREVALENCE IN SCHOOL CHILDREN

A. Bennis¹, Z. Sayah, M.T. El Fassy Fihry, S. Mouline, A. Badsı, M. El Ftouh, J. Benamor, J.E. Bourkadi, A. Benabdallah, M. Bouzekri. ¹*Résid Minaret, rue Ammane, Rabat, Morocco*

In studies of asthma prevalence performed with ISAAC protocol, a video questionnaire was established in the aim to minimize difficulties of comparison of results from different populations and to avoid translation problems. The aim of this study is to compare results of written and video questionnaires.

Our study has concerned 3276 schoolchildren aged 13-14 years. We used international version of the video questionnaire. Five video scenes were projected after the written questionnaire. The scenes depicted: V1: Moderate wheezing at rest. V2: Wheezing and shortness

of breath after exercise. V3: Night waking with wheezing. V4: Night waking with cough. V5: Severe asthma attack.

Results: Percentage of positive response to video-questionnaire is as follow:

V1. Moderate wheezing at rest	313 – 9.5%
V2. Wheezing after exercise	377 – 11.5%
V3. Night waking with wheezing	177 – 5.4%
V4. Night waking with cough	536 – 16.4%
V5. Severe asthma attack	225 – 6.9%

Among 367 patients who answered by 'yes' to written questionnaire on wheezing at any time in the past, 112 (30.5%) answered by 'yes' to one or more of the sequences V1, V2, V3, and V5. Among 466 children who answered by 'yes' to the written question on wheezing after exercise, 162 (34.7%) answered by 'yes' to the corresponding video-sequence (V2). Among 181 children who answered by 'yes' to the written question on the night waking with wheezing, 15 (8.2%) answered 'yes' to the corresponding video-sequence (V3). Among 476 children who answered 'yes' to the written question on night waking with dry cough, 197 (41.3%) answered 'yes' to the corresponding video-sequence (V4). Lastly, among 215 children who answered 'yes' to the written question on asthma attacks, 71 (33%) answered 'yes' to the corresponding video-sequence (V5).

Conclusion: Correlation between written and video questionnaires is weak. A deeper study of the reliability of the two questionnaires is needed.

P404

INCREASED PREVALENCE OF ASTHMA IN SCHOOL CHILDREN IN RABAT

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The prevalence of asthma seems to increase especially in Western countries. This study aims to determine the prevalence of asthma in schoolchildren in Rabat, Morocco, a developing country, and to make comparison with previous data. The survey was conducted with ISAAC (International Study of Asthma and Allergies in Childhood) protocol, between September and December 1995 and concerned schoolchildren aged 6 – 7 years (with questionnaire completed by parents) and 13 – 14 years (with self-completed questionnaire). Children were randomised from all pupils of the same school grades.

Results: For the 6-7 years group, 3052 children were randomised, 2612 parents have answered, 2549 questionnaires were included in analysis. For the 13-14 years group, 3449 pupils were randomised, 3335 have answered. 3276 questionnaires were included. The percentage of answers by 'yes' were as follow:

P403

PREVALENCE OF ASTHMA AND ALLERGY IN 6-7 YEARS OLD KUWAITI SCHOOL CHILDREN; AN ISAAC STUDY

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International Study of Asthma and allergy in childhood (ISAAC) is an international study using both written and video questionnaires to determine the prevalence of asthma, allergic rhinitis (AR) and eczema in countries all over the world. We used the ISAAC protocol to determine the prevalence of asthma, AR and eczema in 6-7 years old children in Kuwait (these children were born during the Gulf war and exposed to the oil fires of Kuwait).

Methods and Results: 2117 (45% females) students were surveyed. The prevalence rates (with 95% CI) for wheezing ever, current wheeze (within the last year) and physician diagnosis of asthma were 22.4%, 13.4% and 16.1% respectively. The prevalence rates for symptoms of AR, current symptoms and physicians diagnosis of AR were 23%, 65% and 11% respectively. The prevalence rates of rash ever, current rash and physicians diagnosis of eczema were 17%, 13% and 10.5% respectively. The prevalence of physicians diagnosis of asthma was higher in males (20%) compared to females (12%) (P = 0.001).

Conclusion: Kuwait has a moderate prevalence of asthma in school children according to ISAAC criteria. We can not draw conclusions regarding the effect of the oil fires on asthma prevalence due to the lack of pre-exposure data, but the results serve as a base line for future reference.

	6-7 yrs	13-14 yrs
Wheezing at any time in the past	13.2%	11.2%
Wheezing in the last 12 months	7.7%	6.8%
Asthma	5.0%	6.6%
Exercise wheezing in the past 12 months	5.6%	14.2%

In 1986 we have performed studies on asthma prevalence in children aged 6 – 15 yrs with a parents' questionnaire (Bennis A et al. Eur Resp J 1990; 3 suppl 10: 167s) and in adolescents aged 11-20 yrs with a questionnaire completed by an interviewer (Bennis A. et al. Rev Fr Mal Resp 1992; 9: 163 – 9). Questions about wheezing at any time in the past and about asthma (has your child -or have you- ever had asthma?) were the same in the two studies. Comparative results are showed in the following table:

	1986		1995	1986		1995
	6-15 yrs n = 1799	6-10 yrs n = 470	6-7 yrs n = 2549	12-20 yrs n=1464	13-15 yrs n = 438	13-14 yrs n = 3278
Wheezing in the past	8.3%	8.6%	13.2%	6.0%		11.2%
Asthma	3.1%	2.9%	5.0%	3.3%	3.7%	6.6%

Despite differences in methods, we can conclude that prevalence of reported wheezing and asthma in schoolchildren has increased between 1986 and 1995.

P420

ATOPIC SENSITIZATION AMONG 10-12 YEAR OLD SCHOOLCHILDREN IN TALLINN IN TWO STUDIES 5 YEARS APART

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Introduction: The prevalence of atopic sensitization and atopy related diseases in children is increasing in many countries.

Methods: As a part of ISAAC II (questionnaires, lung function tests, BHR), sensitization to 7 inhalant allergens (ALK, Denmark) was studied in 643 schoolchildren aged 10-11 years in 1997 Jan-April. SPT > 3 mm was considered as positive.

Results: The SPT was positive in 14.8%, (14.3% in 1992) of the children. A skin prick test (SPT) sensitivity to cat was seen in 7.2% (6.1%), to timothy in 4.8% (4.8%), to dog in 4.7% (2.0%), to *D. pteronyssinus* in 4.4% (6.1%), in birch in 4.1% (2.5%) and to *D. farinae* in 4.0% of children. The lifetime prevalence of diagnosed asthma was 2.4% and 12 month prevalence of wheezing was 8.3%.

Discussion: The prevalence of atopic sensitization to inhaled allergens in Estonian schoolchildren during the 5 year period from 1992 has not changed. Among the 7 inhalant allergens, the only statistically significant difference ($p > 0.01$) was for dog allergen. The prevalence of diagnosed asthma and 12 month wheezing were also similar in 1992 and 1998. The trend for decrease of mite sensitivity along with the increase in dog, birch and cat sensitivity could be a mark for the beginning of changes in the atopic sensitivity, similar to Nordic countries, in Estonia.

Conclusion: The introduction of western lifestyle (foods, modern building materials, cars) in Estonia during the last 7 years has so far not resulted in any change in the prevalence of allergic symptoms and atopic sensitivity.

Address Database Revision

It is many years since we have revised our address database and we would be grateful if you would record any changes in your details on the enclosed form and return by fax or email (as indicated on the form). Every time we send out reprints or a newsletter we find some are returned so please help us to keep in touch with you!