

March 1985 Vol 39 No 1

753-30

Journal of

H

Epidemiology

and

Community Health

1985 12: 105

# Editorial Committee

H CAMPBELL (*Editor*)  
R M ACHESON (*Assistant Editor*)  
JOHN COLLEY  
J M ELWOOD  
P C ELWOOD

JOHN FOX  
PETER GENTLE  
GEOFFREY ROSE  
ESTLIN WATERS

EDITOR *British Medical Journal*  
JOCELYN CHAMBERLAIN } representing the  
IAN LECK } SOCIETY FOR  
BERYL FLITTON (*Technical Editor*) } SOCIAL MEDICINE

It is the policy of this Journal to publish original work in the field of epidemiology and community health which relates to a total defined population and which shall be numerically rated. The field of interest includes studies of the distribution and behaviour of disease in human populations; the definition of the agents responsible for the patterns observed; the modifying effect of social or environmental conditions on disease evolution; and the assessment of the health and efficiency of people exposed to various external circumstances. Linked with these subjects is the design of measures intended to control or prevent disease and the field assessment of their value in public health practice. Epidemiology and community health also encompasses the objective study of the organisation and functioning of medical services with particular emphasis on the measurement of their efficiency. Papers are accepted on their scientific originality and general interest, and ethical considerations will be taken into account.

**COMMUNICATIONS** Papers should be prepared in accordance with "Uniform requirements for manuscripts submitted to biomedical journals" *Br Med J* 1982; **284**: 1766-70. Two copies should be submitted to the Editor, *Journal of Epidemiology and Community Health*, Department of Computing and Medical Statistics, University of Wales College of Medicine, Heath Park, Cardiff CF4 4XN. Papers will be considered in accordance with the terms of the uniform requirements. Papers will be acknowledged if a stamped addressed envelope or an international postal coupon is enclosed. Papers will not be returned whether accepted or not, so copies should be retained by authors. The Editors cannot enter into correspondence about papers not accepted for publication but will convey to authors the general reasons for non-acceptance.

Summaries, Illustrations, Tables, Acknowledgments. References should be in accordance with the uniform requirements for manuscripts. References will not be checked by the editorial office as responsibility for the accuracy and completeness of references lies with the author.

**PROOFS** Contributors will receive one proof, and should read it carefully for printers' errors, and check the tables, figures, legends, and any numerical, mathematical, or other scientific expressions. Alterations to the original text should be kept to a minimum.

**REPRINTS** Twenty-five reprints will be supplied free of charge. A limited number of additional reprints may be ordered from the Publishing Manager when the proofs are returned.

**COPYRIGHT** © 1985 by the *Journal of Epidemiology and Community Health*. This publication is copyright under the Berne Convention and the International Copyright Convention. All rights reserved. Apart from any relaxations permitted under national copyright laws, no part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means without the prior permission of the copyright owners. Permission is not, however, required to copy abstracts of papers or of articles on condition that a full reference to the source is shown. Multiple copying of the contents of the publication without permission is always illegal.

**NOTICE TO ADVERTISERS** Application for advertisement space and for rates should be addressed to the Advertisement Manager, *Journal of Epidemiology and Community Health*, BMA House, Tavistock Square, London WC1H 9JR.

**NOTICE TO SUBSCRIBERS** The *Journal of Epidemiology and Community Health* is published quarterly. The annual subscription rates are available on request to the Subscription Manager, *Journal of Epidemiology and Community Health*, BMA House, Tavistock Square, London WC1H 9JR.

# JOURNAL OF EPIDEMIOLOGY AND COMMUNITY HEALTH

EDITORIAL BOARD

H CAMPBELL (*Editor*)

R M ACHESON (*Assistant Editor*)

JOHN COLLEY  
J M ELWOOD  
P C ELWOOD

JOHN FOX  
PETER GENTLE

GEOFFREY ROSE  
ESTLIN WATERS

EDITOR *British Medical Journal*

JOCELYN CHAMBERLAIN  
IAN LECK

} representing the SOCIETY FOR SOCIAL MEDICINE

BERYL FLITTON (*Technical Editor*)

**VOLUME 39**  
**1985**

BRITISH MEDICAL ASSOCIATION : TAVISTOCK SQUARE : LONDON WC1H 9JR

# Contents

## *No 1 March 1985*

- Social class mortality differentials: artefact, selection or life circumstances? A J FOX, P O GOLDBLATT, AND D R JONES *page 1*
- Social class, ethnic group, and male mortality in New Zealand, 1974–8 N E PEARCE, P B DAVIS, A H SMITH, AND F H FOSTER *page 9*
- Respiratory conditions: effect of housing and other factors P MCCARTHY, D BYRNE, S HARRISON, AND J KEITHLEY *page 15*
- Tuberculosis: spatial and demographic incidence in Bradford, 1980–2 KATHERINE FROGGATT *page 20*
- High liveborn birth weights in the Faroes: a comparison between birth weights in the Faroes and in Denmark SJURDUR F OLSEN AND HØGNI D JOENSEN *page 27*
- Mortality ratios and life expectancy in X chromatin positive males W H PRICE, J F CLAYTON, SUSAN COLLYER, AND RHONA DE MEY *page 33*
- Sib risk and dizygotic twin concordance rate for multiple sclerosis WILLIAM H JAMES *page 39*
- Cancer mortality in England in relation to levels of naturally occurring fluoride in water supplies CLAIR CHILVERS AND DEIRDRE CONWAY *page 44*
- Frequency of moles in a defined population K R COOKE, G F S SPEARS, AND D C G SKEGG *page 48*
- Childhood cancer in the Northern region, 1968–82: incidence in small geographical areas A W CRAFT, S OPENSHAW, AND J M BIRCH *page 53*
- Space-time interaction in Hodgkin's disease in Greater Manchester ABDULLAH MANGOUD, VALERIE F HILLIER, IAN LECK, AND R W THOMAS *page 58*
- Treatment delay in patients with bladder tumours CHRISTINE MACARTHUR, LAURA L PENDLETON, AND ALWYN SMITH *page 63*
- Malignant melanoma in Rome, Italy, 1970–9 G PETRELLI, M MAGGINI, F TAGGI, AND G MORPURGO *page 67*
- Seasonality of thyrotoxicosis D W PHILLIPS, D J P BARKER, AND J A MORRIS *page 72*
- Carbon monoxide levels in the breath of smokers and nonsmokers: effect of domestic heating systems B D COX AND MARGARET J WHICHELOW *page 75*
- Seasonal variation in carbon monoxide poisoning in urban Korea YOON SHIN KIM *page 79*
- Peptic ulcer in male factory workers: a survey of prevalence, incidence, and aetiological factors SHUNICHI ARAKI AND YOSHITAKA GOTO *page 82*
- Measuring disability after a stroke SHAH EBRAHIM, FIONA NOURI, AND DAVID BARER *page 86*
- Seasonal variations in the process of care in urban general practice L HALLAM AND D H H METCALFE *page 90*
- Society for Social Medicine *page 94*

## *No 2 June 1985*

- Economics of an aging population P M JACKSON *page 97*
- Mortality from congenital malformations by mother's country of birth R BALARAJAN AND M MCDOWALL *page 102*
- Visual acuity in a national sample of 10 year old children SARAH STEWART-BROWN AND NEVILLE BUTLER *page 107*
- Introduction of measles into a highly immunised West African community: the role of health care institutions PETER AABY, JETTE BUKH, IDA MARIA LISSE AND ARJON J SMITS *page 113*
- Serological hepatitis A virus infections and ratio of clinical to serological infections in a controlled trial of pre-exposure prophylaxis with immune serum globulin JEREMY D KARK, SHULSMITH BAR-SHANY, SMADAR SHOR, LEAH MERLINSKI AND ELIZER NILI *page 117*
- Hepatitis B infection in households of acute cases K T GOH, J L DING, E H MONTEIRO AND C J OON *page 123*
- Pregnancy and its outcome among hospital personnel according to occupation and working conditions M J SAUREL-CUBIZOLLES, M KAMINSKI, J LLADO-ARKIPOFF, C DU MAZAUBRUN, M M ESTRYN-BEHAR, C BERTHIER, M MOUCHET, AND C KEIFA *page 129*
- Comparison of birthweight and infant mortality between Singapore and England and Wales, 1980 K HUGHES *page 135*
- Spontaneous abortions and malformations in the offspring of nurses exposed to anaesthetic cases, cytostatic drugs and other potential hazards in hospitals, based on registered information of outcome KARI HEMMINKI, PENTTI KYRÖNEN, AND MARIA-LIISA LINDBOHM *page 141*
- Identification of cases of sudden infant death syndrome from death certificates JEAN W KEELING, JEAN GOLDING AND BETTINE SUTTON *page 148*
- Biosocial factors in the epidemiology of childhood asthma in a British national sample B A KAPLAN AND C G N MASCIE-TAYLOR *page 152*
- Patterns of cigarette smoking and trends in lung cancer mortality in Italy CARLO LA VECCHIA *page 157*
- Interaction of alcohol and tobacco as risk factors in cancer of the laryngeal region JØRN OLSEN, SVEND SABROE, AND ULLA FASTING *page 165*
- Relation between parents' and children's smoking behaviour and attitudes M MURRAY, S KIRYLUK, AND A V SWAN *page 169*
- Socioeconomic status and risk of multiple myeloma J MARTIN JOHNSTON, SEYMOUR GRUFFERMAN, CLAIRE C BOURGUET, ELIZABETH DELZELL, ELIZABETH R DELONG, AND HARVEY J COHEN *page 175*
- Do cholecystectomy rates correlate with geographic variations in the prevalence of gallstones? KLIM MCPHERSON, P M STRONG, LESLEY JONES, AND B J BRITTON *page 179*
- A useless raffle A K MORTAGY, J R L HOWELL, AND W E WATERS *page 183*

## No 3 September 1985

- Epidemiology and community health in the medical curriculum: the Nottingham experience J M ELWOOD *page* 185
- Epidemiology training: a necessity for primary health care USHA SHAH *page* 194
- Risk factors for ischaemic heart disease: the prospective phase of the British Regional Heart Study A G SHAPER, S J POCOCK, M WALKER, A N PHILLIPS, T P WHITEHEAD, AND P W MACFARLANE *page* 197
- The Tromsø heart study: coronary risk factors and their association with living conditions during childhood EGIL ARNESEN AND ANDERS FORSDAHL *page* 210
- Blood pressure in Papua New Guinea: a survey of two highland villages in the Asaro Valley HILARY KING, ANDREW COLLINS, LORRAINE F KING, PETER HEYWOOD, MICHAEL ALPERS, JANICE COVENTRY, AND PAUL ZIMMET *page* 215
- Automatic measurement of blood pressure: evaluation of the Copal UA-231 automatic sphygmomanometer J E J GALLACHER, J W G YARNELL, S ROGERS, AND P SWEETNAM *page* 220
- Fluoridation and cancer mortality in Anglesey G WYNNE GRIFFITH *page* 224
- Arsenic, syphilis, and cancer of the prostate R E M LEES, R STEELE, AND D WARDLE *page* 227
- Multiple myeloma in South Cumbria 1974-80: problems of health analysis in small communities E G JESSOP AND S D HORSLEY *page* 231
- Birth dates of men with cancer of the testis E G KNOX AND C CUMMINS *page* 237
- A case control study of lung cancer in Florence, Italy. I Occupational risk factors E BUIATTI, M GEDDES, D KRIEBEL AND N PUCCI *page* 244
- A case control study of lung cancer in Florence, Italy. II Effect of migration from the south E BUIATTI, M GEDDES, D KRIEBEL, M SANTUCCI, AND A BIGGERI *page* 251
- Lead levels on traffic-less islands PETER C ELWOOD, ROGER BLANEY, ROBERT C ROBB, ANTHONY J ESSEX-CATER, BRIAN E DAVIES, AND COLIN TOOTHILL *page* 256
- Comparison of food constituents in the diet of female agricultural workers in Japan with high and low concentrations of high density lipoprotein in their sera KEIKO CHIBA, MICHIKO MIYASAKA, AKIO KOIZUMI, MIHO KUMAI, TAKAO WATANABE, AND MASAYUKI IKA *page* 259
- Iodine deficiency, hypothyroidism, and endemic goitre in Southern Tanzania: a survey showing the positive effects of iodised oil injections by TSH determination in dried blood spots W WÄCHTER, M G MVUNGI, E TRIEBEL, D VAN THIEL, I MARSCHNER, W G WOOD, J HABERMANN, C R PICKARDT, AND P C SCRIBA *page* 263
- Height and weight in two English towns JANET O'CLAREY AND MICHAEL NELSON *page* 271
- Letters to the Editor *page* 273

## No 4 December 1985

- An epidemiological application of Popper's method DOUGLAS WEED *page* 277
- Risks of lung cancer, chronic bronchitis, ischaemic heart disease, and stroke in relation to type of cigarette smoked M R ALDERSON, P N LEE AND R WANG *page* 286
- Occupation and bladder cancer in Boston, USA, Manchester, UK, and Nagoya, Japan ALAN S MORRISON, ANDERS AHLBOM, WENDY G VERHOEK, KUNIO AOKI, IAN LECK, YOSHIYUKI OHNO AND KOJI OBATA *page* 294
- High dietary fat intake and cigarette smoking as risk factors for ischaemic heart disease in Bangladeshi male immigrants in East London ALAN SILMAN, ELENA LOYSEN, WOUTER DE GRAAF AND MICHAEL SRAMEK *page* 301
- Effect of combined alcohol and tobacco exposure on risk of cancer of the hypopharynx JØRN OLSEN, SVEND SABROE, AND JOHANNES IPSEN *page* 304
- Cigarette smoking and benign breast disease GERTRUD S BERKOWITZ, PRISCILLA F CANNY, VIRGINIA A VIVOLSI, MARIA J MERINO, THERESA Z O'CONNOR, AND JENNIFER L KELSEY *page* 308
- Reading attainment and physical development after whooping cough I D A JOHNSTON, H R ANDERSON, H P LAMBERT, AND S PATEL *page* 314
- Changes in the characteristics of families with Down's syndrome children BILLIE SHEPPERDSON *page* 320
- Physical activity at work and job responsibility as risk factors for fatal coronary heart disease and other causes of death A MENOTTI AND F SECCARECCIA *page* 325
- Causes of death in X chromatin positive males (Klinefelter's syndrome) W H PRICE, J F CLAYTON, J WILSON, S COLLYER, AND R DE MAY *page* 330
- Factors predicting mortality in a total population sample of the elderly A JOHN CAMPBELL, C DIEP, J REINKEN, AND I MCCOSH *page* 337
- Long term effects of childbearing on health VALERIE BERAL *page* 343
- Hospital admission for acute stroke: who, for how long, and to what effect? DERICK T WADE AND RICHARD LANGTON HEWER *page* 347
- Trauma to the nervous system and its sequelae in a one-year birth cohort followed up to the age of 14 years PAULA RANTAKALLIO AND LENNART VON WENDT *page* 353
- Analysis of death rates in the population aged 60 years and over of Greater Glasgow by postcode sector of residence DAVID HUME AND JOHN WOMERSLEY *page* 357
- Estimating the sensitivity of a screening test NICHOLAS E DAY *page* 364
- Letter to the Editor *page* 367
- Index *page* 369

For example, long-distance runners<sup>21</sup> and cross-country skiers<sup>22</sup> have higher HDL levels than matched controls. It was also observed previously that the physical load in farming is presumably variable, depending on the type of agriculture, being heaviest in dairy farming and lightest in mechanised rice production.<sup>23</sup> No information was, however, available in the present study to suggest a possible difference in physical activity between members of the high and low groups; because the three volunteers from the high group and the three from the low group from a given region were engaged in the same form of agriculture. Nevertheless the possibility cannot be ruled out that those in the high group are physically more active than those in the low group, as the lower body weight and lower obesity index coupled with an essentially equal calorie intake suggest, and that such higher physical activity may result in raised HDL levels.

Thanks are due to Professor S Ito, of Miyagi College for Women, Sendai, Japan, for helpful discussion.

A part of this work was presented at the 53rd Annual Meeting of the Japanese Society for Hygiene, held in Osaka, on 5–7 April 1983.

Requests for reprints to: Professor M Ikeda, Department of Environmental Health, Tohoku University, School of Medicine, Sendai, 980 Japan.

## References

- <sup>1</sup>Miller GJ, Miller NE. Plasma-high-density-lipoprotein concentration and development of ischaemic heart disease. *Lancet* 1975; i: 16–9.
- <sup>2</sup>Blackburn H. Diet and atherosclerosis: Epidemiologic evidence and public health implications. *Preventive Med* 1983; **12**: 2–10.
- <sup>3</sup>Ueshima H, Shimamoto T, Konishi M, *et al.* High-density lipoprotein-cholesterol levels in Japan. *J Am Med Ass* 1982; **247**: 1985–7.
- <sup>4</sup>Chiba K, Koizumi A, Kumai M, Watanabe T, Ikeda M. Nationwide survey of high density lipoprotein cholesterol among farmers in Japan. *Preventive Med* 1983; **12**: 508–22.
- <sup>5</sup>Katsura, 1970: Cited from: Physical Fitness Laboratory, Tokyo Metropolitan University, *Physical Fitness Standards of Japanese People*, 3rd edition, Tokyo, Fumai-do Publishing Co, 1980, 346–7 (in Japanese).
- <sup>6</sup>Acheson KJ, Campbell IT, Edholm OG, Miller DS, Stock MJ. The measurement of food and energy intake in man—an evaluation of some techniques. *Am J Clin Nutr* 1980; **33**: 1147–54.
- <sup>7</sup>Yamagata N, Iwashima K. Average cadmium intake of the Japanese people. *Bull Inst Public Health* 1975; **24**: 18–24.
- <sup>8</sup>Resources Council, Science and Technology Agency, the Government of Japan, ed., *Standard Tables of Food Composition in Japan*, 4th revised edition, Ministry of Finance Printing Bureau, Tokyo, Japan, 1982 (in Japanese).
- <sup>9</sup>Resources Council, Science and Technology Agency, the Government of Japan, ed., *Nippon Shokuhin Seibunhyo* (Japanese Food Composition Table), 4th edition, Ishiyaku Shuppan Publishing Co, Tokyo, 1982, 295–302 (in Japanese).
- <sup>10</sup>Fristrom GA, Weihrauch JL. Comprehensive evaluation of fatty acids in foods. IX Fowl. *J Am Diet Ass* 1976; **69**: 517–22.
- <sup>11</sup>Exler J, Avena RM, Weihrauch JL. Comprehensive evaluation of fatty acids in foods. XI Leguminous seeds. *J Am Diet Ass* 1977; **71**: 412–5.
- <sup>12</sup>Exler J, Weihrauch JL. Comprehensive evaluation of fatty acids in foods. XII Shellfish. *J Am Diet Ass* 1977; **71**: 518–21.
- <sup>13</sup>Anderson BA. Comprehensive evaluation of fatty acids in foods XIII Sausages and luncheon meats. *J Am Diet Ass* 1978; **72**: 48–52.
- <sup>14</sup>Hulley SB, Cohen R, Widdowson G. Plasma high-density lipoprotein cholesterol level. Influence of risk factor intervention. *J Am Med Ass* 1977; **238**: 2269–71.
- <sup>15</sup>Rhoads GG, Gulbrandsen CL, Kagan A. Serum lipoproteins and coronary heart disease in a population study of Hawaii Japanese men. *N Engl J Med* 1976; **294**: 293–8.
- <sup>16</sup>Fukuba H. Future aspect of Japanese food life from the view point of Japanese style diet. *Shokuhin Kogyo* (Food Industries) 1982; **25**(21): 64–9 (in Japanese).
- <sup>17</sup>Organisation for Economic Co-operation and Development. *Food consumption statistics 1964–1978*, Paris, OECD, 1981, 123–40, 177–210, 353–70.
- <sup>18</sup>Keys A, Aravanis C, van Buchem FSP, *et al.* The diet and all-causes death rate in the Seven Countries Study. *Lancet* 1981; ii: 58–61.
- <sup>19</sup>Shekelle RB, Shryock AM, Paul O, *et al.* Diet, serum cholesterol, and death from coronary heart disease. The Western Electric Study. *N Engl J Med* 1981; **304**: 65–70.
- <sup>20</sup>Becker N, Illingworth DR, Alaupovic P, Conner WE, Sundberg EE. Effects of saturated, monounsaturated and  $\omega$ -6 polyunsaturated fatty acids on plasma lipids, lipoproteins, and apoproteins in humans. *Am J Clin Nutr* 1983; **37**: 355–60.
- <sup>21</sup>Wood PD, Haskell WL. The effect of exercise on plasma high density lipoproteins. *Lipids* 1979; **14**: 417–27.
- <sup>22</sup>Enger SC, Herbjørnsen K, Erikssen J, Fretland A. High density lipoproteins (HDL) and physical activity: the influence of physical exercise, age and smoking on HDL-cholesterol and the HDL-/total cholesterol ratio. *Scand J Clin Lab Invest* 1977; **37**: 251–5.
- <sup>23</sup>Watanabe T, Ishihara N, Miyasaka M, Koizumi A, Fulita H, Ikeda M. Haemoglobin levels among Japanese farmers with special references to climate and physical load. *Human Biology*, submitted for publication.

# Iodine deficiency, hypothyroidism, and endemic goitre in Southern Tanzania\*

## A survey showing the positive effects of iodised oil injections by TSH determination in dried blood spots

W WÄCHTER,<sup>1</sup> M G MVUNGI,<sup>1</sup> E TRIEBEL,<sup>2</sup> D VAN THIEL,<sup>2</sup> I MARSCHNER,<sup>2</sup> W G WOOD,<sup>3</sup> J HABERMANN,<sup>2</sup> C R PICKARDT,<sup>2</sup> AND P C SCRIBA<sup>3</sup>

From Lutheran Hospital,<sup>1</sup> Ilembula via Iringa, Tanzania; Medizinische Klinik Innenstadt der Universität München,<sup>2</sup> Ziemssenstr 1, D-8000 München 2, FRG; and Klinik für Innere Medizin der Medizinischen Universität Lübeck,<sup>3</sup> Ratzeburger Allee 160, D-2400 Lübeck 1, FRG

**SUMMARY** The Ukinga and Uwanji regions, located in the southern highlands of Tanzania, were studied for the degree of iodine deficiency and the incidence of goitre and hypothyroidism, respectively. A urinary iodine excretion as low as  $17.6 + 9.3 \mu\text{g/g}$  creatinine was observed in Wangama village. The mean goitre prevalence in 27 villages in Uwanji ranged between 65 and 96% ( $n=3031$  schoolchildren). Of 681 pregnant women from Ukinga 79.6% had goitre. The prevalence of cretinism as estimated on clinical criteria was 3% in Magoye (Uwanji). A normal serum TSH (below 2.1 mU/l) was observed in only 12 out of 66 school children before iodine prophylaxis, whereas the  $T_4/\text{TBG}$  ratio was decreased in 36 of 63 cases. Blood spot TSH levels in newborn infants ( $n=219$ ) from mothers without iodine supplementation were above 12 mU/l in 45%. In contrast, only 20.3% of the newborn ( $n=118$ ) had elevated blood spot TSH ( $p<0.002$ ) when the mothers had received an iodised oil injection during pregnancy. Most of the newborn ( $n=18$ ; 75%) of the latter group with elevated TSH ( $n=24$ ) came from mothers who had received the iodine injection only 1-25 days before delivery. Maternal iodine prophylaxis in late pregnancy does not increase the rate of neonatal hypothyroidism.

Conclusions: (1) It has been confirmed that severe iodine deficiency resulting in endemic goitre, cretinism, and hypothyroidism is prevalent in the regions studied. (2) Dried blood spot TSH determinations may serve as an index for the efficiency of iodine prophylaxis programmes. (3) Such a programme was carried out with relatively little expenditure and effort on a large scale basis.

Numerous areas of endemic goitre and cretinism throughout the world<sup>3 8 12 13</sup> have been studied. Unfortunately, both diseases have not yet been eradicated, although preventive programmes have been convincingly suggested and introduced in many countries known to have areas of endemic goitre and iodine deficiency.<sup>3 8 12</sup> Two different areas of the southern Highlands of Tanzania, Ukinga, and Uwanji, having a mean altitude of 2000 m were surveyed for the prevalence of endemic goitre. Iodine was measured in urine specimens from

schoolchildren, in samples of drinking water, and in non iodised salts in order to confirm iodine deficiency in this area. Target populations such as pregnant women, newborn, and schoolchildren were also studied for the incidence of hypothyroidism before and after iodine supplementation.

The aims of this study were (1) to confirm the areas of Ukinga and Uwanji as areas of endemic goitre and cretinism due to iodine deficiency, according to the PAHO-criteria;<sup>3</sup> (2) to perform a preliminary study with iodine prophylaxis in order to show its effectiveness in decreasing hypothyroidism; (3) to explore to what extent a decrease in blood spot TSH as compared to serum TSH may serve as an

\*Supported by the Bundesministerium für Forschung und Technologie and by the Federico Foundation

indicator of the effectiveness of iodine prophylaxis in areas with limited technical facilities; and (4) to convince the authorities of the need to install an effective preventive programme.

## Methods

### POPULATION STUDIED

In both areas, Uwanji and Ukinga, Cassava<sup>2</sup> is only a minor constituent of the diet but exact data are lacking for these regions.

**Uwanji** Altogether 3031 schoolchildren aged 6 to 18 years, 118 pregnant women (table 1), and 29 children under the age of 6 years were examined for thyroid enlargement by palpation. The goitres were graded according to the WHO classification of endemic goitre<sup>12</sup> with the modification that grade OB was included in grade I.

Table 1 Gradation of thyroid enlargement in young women (n=681) in Ukinga and schoolchildren (n=3031) in Uwanji.

Grade	Women		Schoolchildren	
	n	%	n	%
0	139	20.4	255	8.4
I	225	33.0	1591	52.5
II	287	42.2	752	24.8
III	30	4.4	433	14.3
I-III	542	79.6	2776	91.6
Total	681	100	3031	100

In one village (Magoye), 700 inhabitants were investigated for signs of deaf mutism, growth and mental retardation in an attempt to estimate the prevalence of clinically overt cretinism.

**Ukinga** In 1979, 371 pregnant and 221

non-pregnant women attending Consolata Fathers' Hospital in Ikonda were investigated for goitre. All the newborn as well as all babies up to 4 months of age brought to the Maternity and Child Health Clinics (MCH) were included in the survey, which comprised physical examination of the thyroid and determination of TSH levels.

### IODINE SUPPLEMENTATION

Iodised oil injections were given intramuscularly in doses of 1 ml each (Lipiodol<sup>R</sup>, Byk-Gulden, Constance FRG), which contained 480 mg iodine bound to the ethyl ester of oleum papaveris. This dose was reported to provide adequate iodine supplementation for approximately three to five years.<sup>8</sup> Iodised oil injections were given to all 371 pregnant women from Ukinga 1 to 230 days before delivery, where the injections were recorded in the antenatal records, and to approximately 12 000 inhabitants of Uwanji, including 8000 schoolchildren 6-18 years of age, representing approximately 60% of all schoolchildren in this area.

Iodised salt was distributed in a pilot study to all families in Wangama village (Uwanji) with the advice to use only this salt (50 mg KI/kg NaCl).

### BLOOD SPOT TSH SAMPLING IN BABIES AND NEONATES

Blood spot samples for TSH analysis were taken by heel-prick from 224 babies up to age 4 months and from 304 newborn in the first four days of life (Uwanji and Ukinga; table 2). Because the mothers usually leave the Maternity Unit early, it was not possible to perform a sampling for neonatal TSH on day 5 as optimal.<sup>1</sup>

In 191 cases the mothers had received iodine prophylaxis during pregnancy whereas 219 mothers had not received iodine because they attended the MCH clinic only late in pregnancy (table 2).

Table 2 Distribution of elevated blood spot TSH levels in children of mothers without and with iodine supplementation during pregnancy, compared with two Munich control groups.

The mean calculated iodine intake of adults is  $32 \pm 15 \mu\text{g/d}$  in Munich.<sup>7</sup>

Blood samples taken on:	Children of:								
	Untreated mothers			Treated mothers			Munich control group		
	n	TSH>12 mU/l	%	n	TSH>12 mU/l	%	n	TSH>12 mU/l	%
<b>Newborn</b>									
Day zero	13	8	61	40	12	30	18	9	50
1	42	19	45	55	8	15	65	11	17
2	6	2	33	17	3	18	20	0	—
3	8	2	25	5	1	20	—	—	—
Total	69	31	45	117	24	21	103	20	19
<b>Babies</b>									
5 days to 4 months	150	4	2.7	74	0	—	127	0	—



## TSH DETERMINATION IN DRIED BLOOD SPOTS

The radioimmunological TSH determination in dried blood spots on filter paper (filter paper method, FPM) was performed by modification of a published radioimmunological determination for serum TSH.<sup>4 14 16</sup> The interassay coefficients of variation were 14.3% for 54.2 mU TSH/l (n=12) and 16.7% for 34.8 mU TSH/l (n=16). The lower limit of detection was 6.4 mU/l, the 50% inhibition of tracer binding 31.3 mU/l (n=15). WHO 68/38 TSH standard, dissolved in TSH-free human blood, was used as material for the standard curve.

## STABILITY OF TSH IN DRIED BLOOD SPOTS ON FILTER PAPER AND IN SERUM

Blood spots on filter paper with a known TSH content were subjected to different storage conditions and then measured in a serial assay. The storage time was four months at  $-20^{\circ}\text{C}$ , one week, two and six weeks at room temperature, and one week at  $+37^{\circ}\text{C}$  (fig 1). TSH remained almost stable at  $-20^{\circ}\text{C}$  over four months but the activity decreased by approximately 25% after one or two weeks at room temperature and by about 75% after one week at  $+37^{\circ}\text{C}$ . In order to investigate the loss of activity during transport from Tanzania to Germany, freshly dried blood spots with a known TSH content were transferred by air directly to Tanzania and returned by the usual postal service. The delivery from Tanzania to Munich took six weeks, the decrease of TSH activity being approximately 50% (fig 1).

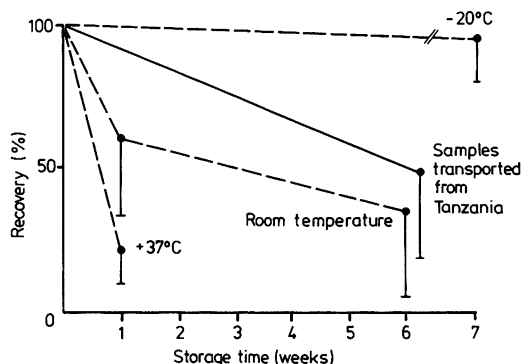


Fig 1 Dependence of TSH recovery on storage time and temperature.

The level (100%) ranged from 31 to 200 mU/ml.

The fall of TSH reactivity is based on the TSH measurement of seven filterpapers, each in triplicate ( $\pm$ SD). TSH recovery after storage of the samples under different temperature conditions (dotted line) and after transport from Tanzania to Munich (solid line).

Furthermore, serum samples of eight patients with serum TSH levels from 1.0 to 41.0 mU/l stored at  $+20^{\circ}\text{C}$  on day zero and at 1, 2, and 6 weeks showed no loss of hormonal activity when measured serially in a routine TSH radioimmunoassay.

Filter paper samples collected in Tanzania were dried and stored at  $4^{\circ}\text{C}$  until the transfer by air to Munich, where they were stored at  $-20^{\circ}\text{C}$  before determination. Thus losses of TSH immunoreactivity as described above have to be taken into consideration, and an underestimation of the prevalence of hypothyroidism in the Tanzanian children may be possible.

The analysis of thyroxine ( $\text{T}_4$ ), triiodothyronine ( $\text{T}_3$ ), thyroxine binding globulin (TBG), and thyrotrophin (TSH) in serum samples as well as the determination of iodine in urine, salt, and drinking water were performed by published methods.<sup>4 6 7 10 16</sup>

## Results

## IODINE DEFICIENCY IN UWANJI

The iodine content in seven local non iodised salt samples from different Uwanji villages was found to be in the range 0.7–9.4 mg iodine/kg salt with the exception of one sample which inadvertently contained as much as 85 mg iodine/kg salt.

Urinary iodine excretion was assessed in 23 individuals before iodine supplementation in Wangama village and found to be  $17.6 \pm 9.3 \mu\text{g}$  (mean  $\pm$  SD) per g creatinine.<sup>7</sup> After replacement of the local salts by the iodised salt the mean iodine excretion increased to  $93.3 \pm 59.0 \mu\text{g}$  iodine/g creatinine in 13 reinvestigated subjects.

## PREVALENCE OF ENDEMIC GOITRE AND CRETINISM IN UWANJI AND UKINGA

The goitre prevalence was 79.6% in 681 young women during pregnancy or shortly after delivery (table 1). Among the 3031 schoolchildren examined, the mean goitre prevalence was 91.6%; the mean values for 27 villages ranged from 65 to 96.5%.

The clinical investigation of approximately 700 inhabitants of Magoye village led to a rate of assumed cretinism of 3%. The 23 individuals with the clinical diagnosis of cretinism had normal TBG levels, the serum thyroxine was decreased in 20 cases, and the serum TSH levels were raised in 12 (range 4–60 mU/l).

HYPOTHYROIDISM IN SCHOOLCHILDREN; COMPARISON OF  $\text{T}_4$ /TBG RATIO AND TSH BEFORE AND AFTER IODINE SUPPLEMENTATION

The blood spot TSH levels were elevated (range 20–200 mU/l) in 10 out of 101 schoolchildren before iodine oil injections. In contrast, TSH levels were

below 12 mU/l in all 123 investigated subjects three months after iodine injection.

The situation appeared more dramatic when the serum TSH levels were determined. Before iodine injection only 12 out of 66 children had normal TSH levels below 2.1 mU/l, whereas the levels were moderately elevated (range 2.1–10.0 mU/l) in 29 and markedly elevated (range 10–200 mU/l) in 25 of the children. The  $T_4$ /TBG ratio was decreased in 36 out of 62 investigated children (fig 2).

Three months after iodine injection, the TSH levels were moderately elevated in 16 and grossly elevated in only 1 out of 69 children. The  $T_4$ /TBG ratio was decreased in only 2 out of 71 children. An elevated  $T_4$ /TBG ratio, suggesting hyperthyroidism, was found in one child before and in four children after iodine supplementation.

A special group of 23 pupils in Wangama with goitre grade III and a marked growth retardation was assumed to have borderline cretinism (fig 3). Whereas the TSH levels were increased in all but two, the  $T_4$ /TBG ratio was low in 15, the  $T_3$  levels being elevated in nine of this group. However, the increases in  $T_3$  levels did not compensate for the thyroxine deficiency as concluded from the elevated TSH levels. The urinary iodine excretion was below 45  $\mu\text{g/g}$  creatinine in all but one, who seemed to have an exogenous iodine contamination, as the urinary iodine excretion was 239  $\mu\text{g/g}$  creatinine. Of these 23 children, 17 were reinvestigated three months after the distribution of iodised salt. The TSH levels were found to be in the range 1.5–5.0 mU/l in 16 cases. The  $T_4$ /TBG ratio was normal in all except two (fig 3).

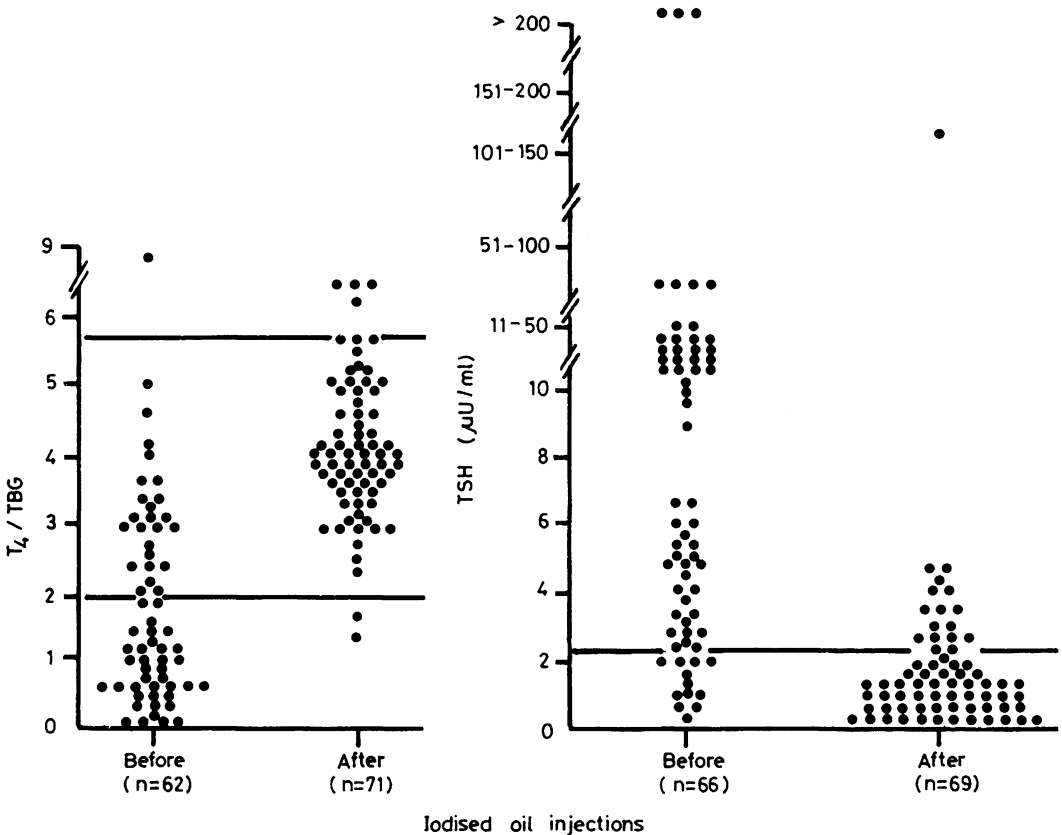


Fig 2 Serum TSH levels and  $T_4$ /TBG ratio in schoolchildren before and three months after iodised oil injection. The upper limit of the normal range of serum TSH is 2.1 mU/l; the normal range of  $T_4$ /TBG ratio is 1.8–5.7.

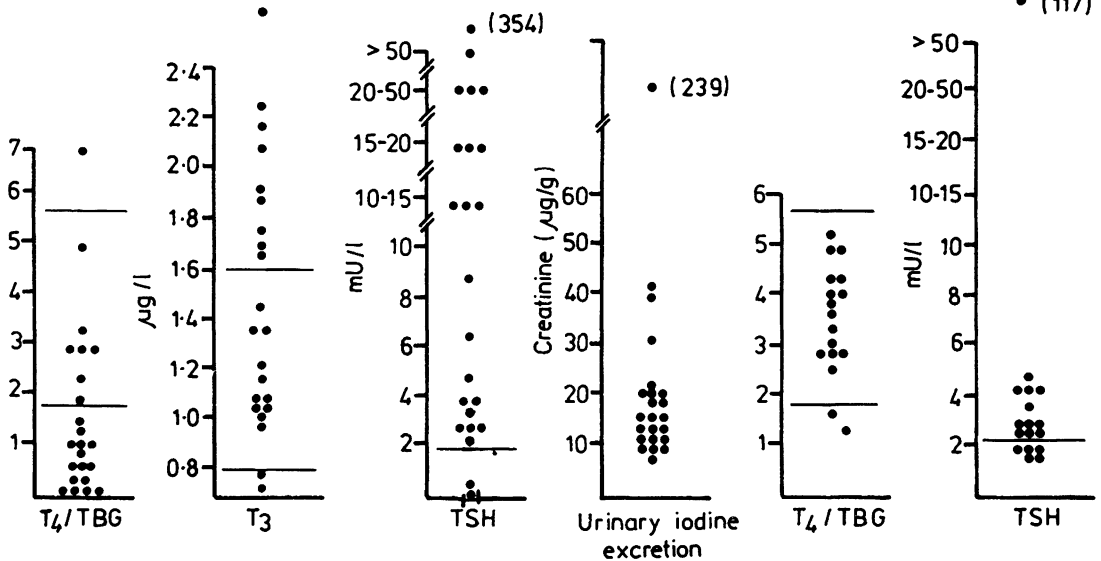


Fig 3 Thyroid function and urinary iodine excretion in 23 selected schoolchildren with goitre grade III and growth retardation in Wangama.

$T_4$ /TBG and TSH levels on the left represent the data before, the respective value on the right side the data three months after the use of iodised salt.

$T_3$  levels could be determined in only 22 serum samples.

#### BLOOD SPOT AND SERUM TSH LEVELS IN WOMEN BEFORE AND SHORTLY AFTER DELIVERY AND BLOOD SPOT TSH IN THEIR BABIES

The blood spot TSH levels were below the limit of detection both in pregnant women from Tanzania ( $n=66$ ) and in the Munich control group ( $n=26$ ). In contrast, the serum TSH levels were found to be above 2.1 mU/l in 24 (72.9%) out of 33 pregnant women and in 6 (33.3%) of the 18 women after delivery in Ukinga. The serum TSH levels and the  $T_4$ /TBG ratio of 29 mothers were compared with the blood spot TSH levels of their babies on days 11 to 93 after birth. No significant correlation could be shown between the individual maternal  $T_4$ /TBG ratio and the blood spot TSH levels of their babies; however, 14 of 29 babies with an elevated TSH were born to mothers with a subnormal  $T_4$ /TBG ratio and thyroid enlargements grade I–III.

#### BLOOD SPOT TSH LEVELS IN THE NEWBORN AND BABIES: EFFECT OF IODINE PROPHYLAXIS IN THE MOTHERS

The TSH values of babies born to mothers without iodine supplementation were elevated in 45% of the 69 newborn (range 12–200 mU/l) and in 2.7% of the 150 older babies (table 2). In contrast, the TSH levels

of babies born to mothers after iodised oil injection during pregnancy were above 12 mU/l in only 21% of the 117 newborn and in none of the 84 older babies (table 2). The difference between the TSH levels of the children of iodine treated and untreated mothers was highly significant ( $p < 0.001$ ).

For comparison, the blood spot TSH levels of two Munich control groups of newborn from mothers living in the iodine deficiency area of Munich were determined. In this region the mean calculated iodine intake of adults is  $32 \pm 15 \mu\text{g}/\text{d}$ .<sup>7</sup> On zero to 5 days of age ( $n=103$ ) and on day 5 ( $n=127$ ) TSH levels were above 12 mU/l but below 50 mU/l in only 20 of the 103 newborn in the first two days of life. All TSH levels were found to be below 12 mU/l in Munich after the second day of life.

The date of iodine injection in relation to the gestational age was found to influence the prevalence of elevated TSH in the newborn. Iodine injection given at the end of the last trimester was accompanied by an elevation of TSH level in 33.9% of the babies, range 12–70 mU/l (fig 4). In contrast, iodine supplementation given earlier during pregnancy resulted in only 9.2% of cases with elevated TSH. In other words, 75% of the newborn with elevated TSH levels were born to mothers who

had received iodine supplementation only shortly before delivery.

### Discussion

This survey shows the persistence of severe goitre endemia in the southern highlands of Tanzania documented earlier by Latham,<sup>11</sup> which is due to the lack of a systematic iodine prophylaxis programme. Concomitantly, the prevalence of hypothyroidism was deduced from elevated serum TSH levels in 82% and decreased  $T_4$ /TBG ratios in 58% of the schoolchildren.

In one village (Magoye), cretinism was suspected in 3% of the inhabitants. In another village, a group of

23 schoolchildren was assumed to have borderline cretinism because of marked growth retardation, goitre grade III, and hypothyroidism (fig 3). Although these data allow only a rough approximation of the prevalence of cretinism in these regions, they indicate the significance of iodine deficiency for the regional public health.

In this study, the simple method of TSH determination in dried blood spots was used for an approximate estimation of severe hypothyroidism. The filter paper cards are easily transportable to laboratories capable of performing the TSH radioimmunoassay. However, using the filter paper method, a loss of TSH immunoactivity<sup>15</sup> due to prolonged storage of the filter paper and to environmental temperature and humidity has to be taken into account. This problem was not discussed in another publication<sup>5</sup> describing severe iodine deficiency goitre prevalence of 86% and elevated blood spot TSH above 7.5 mU/l in 40% of schoolchildren in a mountain area in Spain. In this study, clearly elevated TSH levels were found in 10% of the schoolchildren, in 45% of the newborn, and in 2.7% of babies up to the age of 4 months born to mothers without iodine prophylaxis. In addition, it could be documented that the prevalence of elevated TSH levels decreased after iodine supplementation. Undoubtedly, however, blood spot TSH levels below 12 mU/l do not necessarily exclude moderate and mild hypothyroidism under the conditions of our study. By shortening the transport time and introducing a more sensitive TSH assay this method could become even more useful for epidemiological investigations in areas of severe iodine deficiency and limited technical facilities.

The use of iodised oil has already been shown to be superior to iodised salt wherever economic and geographical obstacles are the dominant factors in developing countries.<sup>3,8,12</sup> Nevertheless, special attention was again given to this problem:

(1) Determination of the iodine content of locally produced salts which were said to be "valuable for goitre patients" showed a sufficiently high iodine content in only a single sample. This salt, however, originated from an area where endemic goitre was not noted by the local health authorities; it was produced in only small amounts for a fairly high price. As a result, this local salt preparation cannot be used as an effective permanent prophylaxis in this region.

(2) The regular salt was replaced completely by a reliably iodised salt over a period of several months in a rather isolated village (Wangama) within the mountain region. Serum TSH levels were investigated in a group of grammar schoolchildren

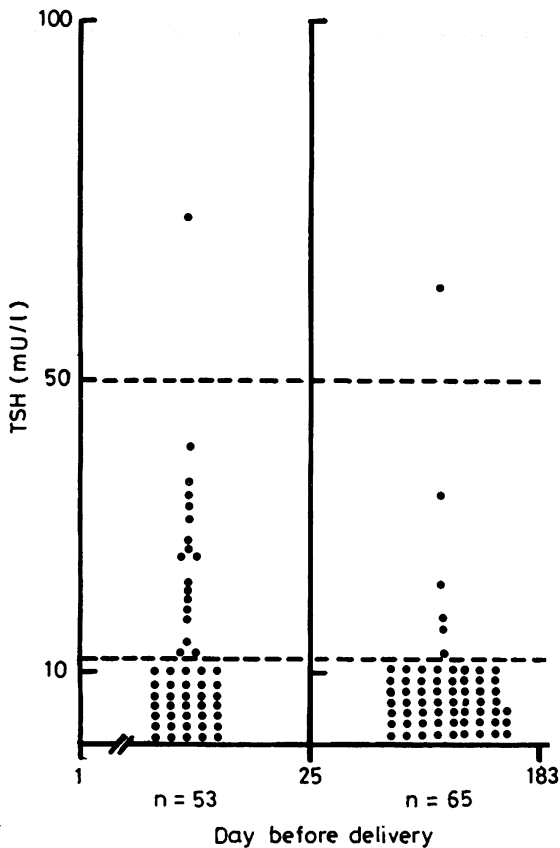


Fig 4 Comparison of the blood spot TSH levels in the newborn.

Left: newborn of mothers who received iodine only 1 to 25 days before delivery.

Right: newborn of mothers who received iodised oil injection 25 to 183 days before delivery.

before and after the introduction of this salt. The efficiency of this kind of prophylaxis could be documented in this village. However, a regular distribution of iodised salts is not feasible in these remote areas due to the insufficient road network and the lack of local salt factories.

In contrast, iodine supplementation using an oil preparation led to both a significant decrease of elevated serum TSH levels and an increase in T<sub>4</sub>/TBG ratios in schoolchildren and in young women. Moreover the incidence of elevated TSH levels in the newborn and in older babies could be lowered by iodine supplementation of the mothers during pregnancy. The prevalence of elevated TSH levels in the newborn was lower when iodine was given during early pregnancy. Further, it should be recognised that neither the prevalence nor the range of elevated TSH of the newborn from mothers who received iodine late in pregnancy were higher compared to that of the newborn from untreated mothers. Thus, there is no aggravation of neonatal hypothyroidism by a large amount of iodine administered to the mother. These results demonstrate again the undeniable advantage of iodised oil for prophylaxis of endemic goitre and cretinism in remote areas.<sup>2 8 13 14</sup>

The data in this paper document the fact that iodine deficiency is a serious public health problem in the highlands of Tanzania. The extent of physical and mental handicap related to iodine deficiency cannot be expressed fully in this investigation. It is evident that the institution of an iodine supplementation programme will result in regression of thyroid hormone deficiency and associated disorders. It can be foreseen that endemic cretinism will decrease and may even vanish. We therefore recommend iodine supplementation using iodised oil injection in pregnant women in the first and second trimesters in under-5s and pre-school age children, in schoolchildren, and in younger women during the fertile decades of life. Using this method of prevention, the prevalence of endemic goitre in young adults should be reduced from the present 90% to hopefully about 3%. Such a programme is in accordance with the recommendations of the Pan-American Health Organization of 1974.<sup>3</sup> This committee has pointed out that iodised oil prophylaxis together with correctly organised follow-up programmes should be conducted by local public health authorities. Our study supports Hetzel's postulation<sup>9</sup> for eradicating iodine deficiency disorders throughout the world.

We thank the German Red Cross, Berlin, for donating iodised oil (Lipiodol) and the Tanzanian Food and Nutrition Centre-Laboratories for iodine

analysis in urine and water and for providing the iodised salt. Thanks is expressed to all the staff of Ilembula Lutheran Hospital who took part in the programme. We acknowledge the help of Professor Dr Klaus Riegel, Abteilung für Neonatologie, Kinderklinik der Universität, and Dr med Gertrud Gressel, I Frauenklinik der Universität München, in providing the Munich control blood spot samples from mothers and their newborn.

Requests for reprints to: Peter C Scriba, MD, Klinik für Innere Medizin, MHL, Ratzeburger Alle 160, D-2400 Lübeck 1, FRG.

## References

- Delange F, Camus M, Winkler M, Dodion J, Ermans A M. Serum thyrotrophin determination on day 5 of life as screening procedure for congenital hypothyroidism. *Arch Dis Child* 1977, **52**: 89-96.
- Delange F, Iteke SB, Ermans AM. Nutritional factors involved in the goitrogenic action of Cassava. IDRC-194 e, Ottawa, Ontario, 1982.
- Dunn JT, Medeiros-Neto GA. Endemic goiter and cretinism: Continuing threats to world health. *Pan American Health Organization Scientific Publication no. 292*, 1974.
- Erdhardt F, Marschner I, Pickardt CR, Scriba PC. Verbesserung und Qualitätskontrolle der radioimmunologischen Thyrotrophin-Bestimmung. *J Clin Chem Clin Biochem* 1973, **11**: 381-7.
- Escobar del Rey F, Gomez-Pan A, Obregon MJ, Mallol J, Arnao MDR, Aranda A, Morreale de Escobar G. A survey of school children from a severe endemic goitre area in Spain. *Q J Med NSL* 1981, **198**: 223-46.
- Gärtner R, Kewenig M, Horn K, Scriba PC. A new principle of thyroxine (T<sub>4</sub>) and triiodothyronine (T<sub>3</sub>) radioimmunoassay in unextracted serum using antisera with binding optima at extreme pH ranges. *J Clin Chem Clin Biochem* 1980, **18**: 571-7.
- Habermann J, Heinze HG, Horn K, Kantlehner R, Marschner I, Neumann J, Scriba PC. Alimentärer Jodmangel in der Bundesrepublik Deutschland. *Dtsch med Wschr* 1975, **100**: 1937-45.
- Hetzel BS, Thilly C, Fierro-Benitez R, Petrell EA, Butterfield JH, Stanbury JB. Iodized oil in the prevention of endemic goiter and cretinism. In: *Endemic goiter and cretinism—iodine nutrition in health and disease* JB Stanbury, BS Hetzel (eds) New York, Chichester, Brisbane, Toronto: John Wiley 1980, 513-32.
- Hetzel BS. Iodine deficiency disorders (IDD) and their eradication. *The Lancet* 1983, **II**: 1126-9.
- Horn K, Kubiczek Th, Pickardt CR, Scriba PC. Thyroxin-Bindendes Globulin (TBG): Präparation, radioimmunologische Bestimmung und klinisch-diagnostische Bedeutung. *Klin Wschr* 1977, **55**: 881-94.
- Latham MC. The aetiology, prophylaxis and treatment of endemic goitre in Ukinga, Tanzania. *East Afr Med J* 1965, **42**: 489-501.
- Perez C, Scrimshaw NS, Munoz JA. Technique of endemic goitre surveys. In: *Endemic goiter. Monograph series no. 44* Geneva: World Health Organization; 1960: 369-84.

- <sup>13</sup> Stanbury JB, Hetzel BS. Endemic goiter and endemic cretinism—iodine nutrition in health and disease. New York, Chichester, Brisbane, Toronto: John Wiley 1980.
- <sup>14</sup> Thilly CH, Delange F, Ramioul L, Lagasse R, Luvivila K, Ermans EM. Strategy of goitre and cretinism control in Central Africa. *Int J Epidemiol* 1977, **6**: 43–54.
- <sup>15</sup> van Thiel D, Marschner I, Wood WG, Habermann J, Scriba PC. Methodische Untersuchungen und Vergleich von 7 kommerziellen Kits zur radioimmunologischen Thyrotropin-Bestimmung aus getrocknetem Blutstropfen. *J Clin Chem Clin Biochem* 1980, **18**: 807–16.
- <sup>16</sup> Wood WG, Habermann J, Marschner I, Scriba PC. The validity of serum TSH measurements by immunoassay. *Excerpta Medica, International Congress Series no. 528*; 1980: 39.