THE SERO-EPIDEMIOLOGY OF ENDEMIC DISEASES IN LIBYA

Thesis submitted in accordance with the requirements of the University of Liverpool for the degree of Doctor of Philosophy by

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June 1982.

ABSTRACT

The aim of this thesis is to investigate, for the first time in the history of public health services in Libya, the role of suitable serological methods in the study of the following endemic diseases : viral hepatitis, measles, rubella, malaria, leishmaniasis, echinococcosis and schistosomiasis. The serological study is considered to be valuable where vital statistics and morbidity data are scanty or non-existent. The findings are summarized below.

1. Random surveys in Gharian and Derna assessed by radio immune assay indicate that 100.0 per centum of children of 7 years and older, including adults, were HAV immune, as were 60.0 – 80.0 per centum of 3 year old children; revealing that infection occurs below the latter age.

2. HBV infection occurs erratically in time and appears to be uncommon in young children, affecting school children somewhat more frequently and adults more so.

3. Measles having been a serious problem in the past, a vaccination programme was initiated in 1972. Nineteen sera from 6 year old children at random revealed 100.0 per centum immunity by means of enzyme linked immunosorbent assay (ELISA).

4. Random rubella surveys in Benghazi and Gharian assessed by single radial haemolysis indicated that approximately 60.0 per centum of 6 year old children were immune, increasing to 80.0 - 90.0 per centum at 12 years.

5. Several hundred foreign immigrants were investigated for potential relapsing malaria by immuno-fluorescent antibody testing. It was concluded that Indians present 19.0 and non-Asians 5.0 per centum risk to the community. Native Libyan children were shown to be 100.0 per centum non-immune.

6. Skin testing indicated that cutaneous leishmaniasis remains endemic in north western Libya.

7. An ELISA system indicated echinococcosis to be endemic in the region of Benghazi in approximately 10.0 per centum of young persons.

8. An ELISA system, employing soluble egg antigen, detected 33.4 per centum prevalence rate of S.mansoni infection, in Tauorga; stool examination revealed 6.9 per centum.

CONTENTS

PREFACE

The aim of this thesis is to provide a general view of certain important endemic diseases by means of serological studies for the first time in the history of public health services in Libya.

Each chapter presents in an introduction a short description of the relevant disease, followed by an historical review of that disease in Libya. The serological study method and the subjects involved are described and the results presented. A discussion and related conclusion follow.

The serological survey is considered to be a method of great importance in Libya where vital statistics and morbidity data may be either scanty or completely lacking. It is stressed that the objective of such surveys is to identify public health problems and an approximation of their magnitude in particular populations, primarily to assist in the productive deployment of a public health staff inadequate in terms of numbers, efficiency and support.

The author hopes to point the way to programmes of surveillance which will serve to coordinate and consolidate knowledge which increasingly will become important in the control of endemic disease in Libya.

ACKNOWLEDGEMENTS

The work involved in this study was carried out under the supervision of Professor Chevalier H.M.Gilles, Dean and Professor of Tropical Medicine in the Liverpool School of Tropical Medicine to whom I am indebted for his wisdom and encouragement.

Despite the many difficulties encountered in the collection of serum samples, my thanks are due to the many people of Libya who willingly gave their blood.

I am grateful to the following persons for assistance and advice :

Miss Kate Bellamy, B.A., Standards Laboratory for Serological Reagents, Central Public Health Laboratory, London, for enzyme linked immunosorbent assay in respect of measles.

Professor M. Clarkson, Professor of Veterinary Preventive Medicine, Faculty of Veterinary Science, Liverpool University for the kind gift of experimental echinococcosis antigen.

Dr. D.S. Dane, Head of Virology, School of Pathology, Middlesex Hospital Medical School, London, and to his staff for radio-immuno-assay in respect of hepatitis.

Dr. C.C. Draper, Senior Lecturer (ODA), Ross Institute, School of Hygiene and Tropical Medicine, and to his staff for generous provision of both malaria and schistosomiasis antigens and for laboratory facilities.

Dr. Shamseddin El Gahmi for translation of Italian language literature.

Dr. Ahmed Sherif, Secretary General, Libyan Red Crescent Organisation for equipment and encouragement.

I am grateful for assistance given by the following :

Dr. Muftah Osta Omar, Secretary for Health and his staff, Secretariat for Health, Tripoli, Socialist People's Libyan Arab Jamahiriya.

Secretary for Health and his staff, Secretariat for Health, Derna.

Secretary for Health and his staff, Secretariat for Health, Kufra.

Secretary for Health and his staff, Secretariat for Health, Misurata.

Director and staff, Infectious Diseases Unit, Tripoli.

Head and staff, Endemic Disease Control Centre, Sebha.

Head and staff, Community Health Department, Benghazi.

Head and staff, Community Health Department, Derna.

Head and staff, Community Health Department, Gharian.

Head and staff, Health Department, Ghadames.

Head and staff, Health Department, Ghat.

Dr. Murad Lenghi, Dean, Faculty of Medicine, and his staff, Garyounis University, Benghazi.

Director and his staff, Research Centre, Garyounis University, Benghazi.

My warm thanks go to the following members of the School of Tropical Medicine, Liverpool :

Professor W.W. Macdonald, Professor of Medical Entomology, and Dr. R.W. Ashford, Senior Lecturer, Department of Parasitology, for advice freely given.

Miss Sarah Macfarlane, B.A.,MSc. Lecturer in Statistics, Department of Tropical Paediatrics, for statistical guidance.

Miss Olive Williams for her forbearance and accuracy in the efficient typing of this text.

Mr. Joe Brady and his staff of the Department of Medical Illustration for their expertise.

Finally, I wish to express my sincere thanks to Mr. James Prescott, MIST.,MRSH.,Dip.Hlth.Eng.(A), who assisted me in this work with his forty-five years experience of research in laboratory and field, with genuine interest, solid support and friendship.

ABBREVIATIONS

nm	...	nanometre
µl	...	microlitre
P	...	probability
χ^2	...	chi-squared
Z	...	normal deviate, derived on basis of McNemar's paired test
d.f.	...	degree of freedom
E_{490}	...	optical filter extinction value 490 nm.

CHAPTER 1.0 : THE LIBYAN ENVIRONMENT

1.1. Geography and climate of Libya

Libya lies on the north coast of Africa within latitudes 33° and 20° N and longitudes 10° and 25° E. It is bounded on the north by the Mediterranean sea, on the east and south-east by Egypt and Sudan, south and south-west by Chad and Niger, on the west and north-west by Algeria and Tunisia.

The three historic regions of the country are Tripolitania in the west, having an area of 285,000 sq.kms., Cyrenaica in the east comprising 905,000 sq.kms. and Fezzan, in the south, of 570,000 sq.kms. The total land area is of the order of 1,760,000 sq.kms.; in comparative terms, two and a half times the size of Egypt, four times that of France and Spain together and fourteen times larger than England.

The coast line between Tunisia and Egypt is 1,900 kms in length and in most places the littoral is fertile. To the south of this coastal belt is a chain of mountains in the west, high ground to the east and between these a wide stretch of desert, the Sirte Depression. Further south, in Fezzan, the land is desert containing a number of oases of varying size.

Within Tripolitania there is a low lying coastal plain, Jefara, behind which lies a line of hills, known as the Jebel Nefusa, running straight from the Tunisian border in the west to the Menshar hills which jut northward and are limited by the Kikla trough on their eastern side. The Jefara plain and adjacent parts of the Jebel comprise the best watered area of the region and contain the major proportion of the population and the capital city,Tripoli. South of the Jebel Nefusa lies an upland plateau, Hamada El Hamra, a desert area of scrub, sand and scattered irregular masses of rock; after several hundred kilometres the plateau gives way to a series of depressions, running east/west where artesian water and, hence, oases are found ; this area constitutes the Fezzan. In the extreme south lie the central Saharan mountains, the Tibesti Range.

Cyrenaica has a somewhat different physical arrangement. The northern uplands are called the Jebel Akhdar where the bulk of the population lives in the two principal coastal towns, Benghazi and Derna. On the western side the Jebel Akhdar fall fairly steeply to the shores of the Gulf of Sirte whilst on the eastern side they fall more gradually as they extend to the Egyptian border. South of the Jebel Akhdar the land declines to produce an extensive lowland, mainly desert, in which Kufra constitutes the principal oasis.

The climate of the northern areas of Libya is temperate with a winter rainfall of 35.0 cm. In the south the climate is extremely hot with little or no rain. No permanent rivers exist but normally dry river beds (wadis) flood during rain and remain so for a few days. A hot, dry wind from the south (gibli),which can rapidly raise the temperature in the north,blows usually, for a day or so at a time, during spring and autumn although it may rise up suddenly at any time.

1.2. Demography

1.2.1. Census data

The total population derived from the most recent censuses was as follows :

1964 : 1,559,399 inhabitants

1973 : 2,257,000 inhabitants

The growth rate, elicited in 1973, being 3.9 per centum.

Related statistics per thousand

Crude birth rate	44.8
Death rate	8.0
Infant mortality	80.3

The figure for infant mortality relates only to registered cases and excludes neo-natal and peri-natal mortality and, also, still-births.

1.2.2. The age structure, derived from the 1964 census, being as follows.

*Below 15 years	43.69 per centum
15 - 64 years	51.14 per centum
65 years or more	5.17 per centum

Within the first category* the rate for children below one year being 3.52 per centum.

1.2.3. The population of the capital city Tripoli, in Tripolitania, is quoted by 1973 census as representing 31.4 per centum of the total : the second principal-city Benghazi, in Cyrenaica, contained 14.7 per centum of the total population according to the same census. Thus, these two urban centres represent 46.1 per centum of the national total.

1.2.4. Table En.1.presents a ranked list of urban centres in Libya. These being based upon the 1973 census of population and quoted by Saad Khalil Kezeiri (1981).

TABLE En.1.

URBAN CENTRES IN LIBYA 1973 (KEZEIRI,1981)

Urban Centre	Population	Rank
Gr.Tripoli	680,000	1
Gr.Bengahzi	297,000	2
Misurata	46,000	3
Ez-Zawiyah	42,000	4
Derna	35,800	5
El-Beida	34,000	6
Ejdabiah	33,700	7
Tobruq	33,000	8
Sebha	32,400	9
El-Merj	21,900	10
Gharian	17,000	11
Zliten	16,000	12
Zuara	13,500	13
El-Homs	13,000	14
Sirte	11,600	15
Sorman	11,200	16
El-Aziziah	11,000	17
El-Abiar	8,850	18
El-Harshah	8,150	19
Tarhuna	7,800	20
Nalut	6,500	21
El-Jof (Kufra)	6,300	22
El-Garabulli	6,000	23
El-Ajelat	5,500	24
Benina	5,430	25
Hoon	5,400	26
Bani Walid	5,350	27
El-Gubbah	4,750	28
Waddan	4,600	29
Shahat	4,400	30
Emm Sa'ad	4,320	31
ABrak	4,050	32
Ez Zahra	4,000	33
Mizdah	3,870	34
Ubari	3,500	35

MEDITERRANEAN

TRIPOLI

ZUARA

GHARIAN

MISURATA

TAUORGHA

SIRTE

DERNA

BENGHAZI

MAP En.1.

TUNISIA

GHADAMES

TRIPOLITANIA

BRAK

SEBHA

CYRENAICA

EGYPT

ALGERIA

LIBYA

MURZUK

FEZZAN

GHAT

EL-BERKT

KUFRA

NIGER

CHAD

SUDAN

CHAPTER 2.0 : VIRAL HEPATITIS

2.1 Introduction

The term viral hepatitis usually refers to a primary infection of the liver caused either by hepatitis A virus or by hepatitis B virus.

The development of specific laboratory tests enabling the identification of these two viruses has revealed that hepatitis can be caused by other agents, as yet uncharacterised, currently referred to as non-A, non-B virus.

A World Health Organisation Report (1977) presents the following standard nomenclature and definitions.

HAV : Hepatitis A virus. A small virus in the range 25-28 nm possessing cubic symmetry. Full and empty particles exist; both are identified by immune electron microscopy serological tests for HAV include complement fixation, immune adherence haemagglutination, radioimmunoassay and enzyme immunoassay.

anti-HAV : Antibody to hepatitis A virus.

HBV : Hepatitis B virus. A 42 nm double shelled virus, originally known as the Dane particle.

HBsAg : Hepatitis B surface antigen, originally known as Australia antigen. The hepatitis B antigen found on the surface of the virus and on the accompanying unattached 22 nm spherical particles and the tubular forms.

HBcAg : Hepatitis B core antigen. The hepatitis B antigen found within the core of the virus.

HBeAg : The e antigen which is closely associated with hepatitis B infection.

anti-HBs : Antibody to hepatitis B surface antigen.

anti-HBc : Antibody to hepatitis B core antigen.

anti-HBe : Antibody to hepatitis Be antigen.

Other hepatitis viruses : a form of hepatitis indistinguishable clinically from type A or type B infection but is antigenically unrelated to either type.

(In this text NANB will be used to indicate other hepatitis viruses)

In 1944 human volunteers studies carried out by MacCallum and Bradley revealed that hepatitis could be caused by at least two agents; one designated as type A (infectious hepatitis) and another designated as type B (serum hepatitis).

In 1967 Krugman, Giles and Hammond confirmed the existence of two types of viral hepatitis; one designated Ms-1 type, later proved to be hepatitis A, and the other Ms-2 type, to be hepatitis B.

It is noteworthy that long before the development of serodiagnostic technique in respect of hepatitis types A and B Havens (1956) suggested that the occurrence of a series of three attacks of acute viral hepatitis in a drug addict might point to the existence of a third form of the disease.

In 1970 (Dane et al.) proposed a particle 42 nm in size, having an inner core of 28 nm, as a hepatitis B virus candidate. This became generally accepted and became known as the Dane particle, now HBV. Blumberg (1964) first detected HBsAg by means of the Ouchterlony technique of two dimensional double immunodiffusion (ID) in agar gel; a simple, cheap but relatively insensitive method. The methods currently in use comprise complement fixation, immuno-electro-osmophoresis, immuno-electron-microscopy, a number of agglutination tests and several radio-immuno-assay techniques (RIA) : most of the agglutination and RIA tests appear to be extremely sensitive and highly specific (WHO Technical Report 1977). In addition to HBsAg, once known as Australia antigen, there exists an antigen contained within the core of the HBV, now known as HBcAg. The serum antibodies to these antigens are

known as anti-HBs and anti-HBc respectively (Weekly Epidemiological Record, WHO 1976). Anti-HBc appears early in HBV infection and is regularly found at the onset of illness, whilst anti-HBs appears later (Hoofnagle et al. 1973).

In 1972 Magnius and Espmark described a new antigen antibody system associated with hepatitis B infection, referred to as the e system (HBeAg). It was suggested that HBeAg represents a marker of infectivity and that conversely anti-HBe indicates non-infectivity.

The large reservoir of HBV in the human population of the globe is indicated by the prevalence of HBsAg in apparently healthy adults, as follows : in parts of Europe, North America and Australia, 0.02 - 0.1 per centum; in parts of eastern and southern Europe, the Middle and Far East 3.0 - 5.0 per centum, and in tropical Asia and Africa 20.0 per centum (WHO Technical Report, 1975).

Usually HBV is spread parenterally, e.g. by blood transfusion or by contaminated syringes and needles. It is also spread by homosexuals and from HBsAg carrier mothers, especially those with HBeAg, to their newborn children. HBV represents an occupational hazard for hospital personnel, particularly those working in renal dialysis units, surgery, obstetrics and laboratories.

The incubation period of HBV infection has been shown experimentally to range from 60 - 180 days.

HBV infection is not common in children in developed communities except under certain particular circumstances such as where children with Down's syndrome or mental retardation are confined to institutions.

There is a general increase in the incidence of HBV among adults in developed communities.

The epidemiological situation differs in tropical and in developing countries where a significant proportion of clinically well children are known to carry HBsAg in their serum or show evidence of previous exposure to HBV in the form of anti-HBs and anti-HBc.

Hepatitis A virus (HAV) was first identified in 1973 (Feinstone et al.) appearing as a 27 nm particle in human stools by means of immune electron-microscopy. Serological tests for HAV include complement fixation, immune adherence haemagglutination, radio-immuno-assay and enzyme immuno-assay (Weekly Epidemiological Record, WHO 1976).

A high incidence of HAV is observed in developing countries in children of school age, whereas in developed countries cases occur more frequently in adults, presumably this shift reflects improvements in socio-economic conditions.

HAV is spread by the intestinal/oral route, most commonly by close contact, and, accordingly, infection occurs readily in conditions of poor sanitation and overcrowding; vehicles of infection such as contaminated food, shellfish and water have been implicated (WHO Technical Report, 1977). However, even in large waterborne outbreaks, HAV is not always the cause. Recent evidence has implicated NANB in such situations (Wong et al. 1980).

HAV is not transmitted by blood or blood products and rarely, if ever, by the parenteral route (Szmuness et al. 1977), although this has been achieved experimentally in volunteers (Zuckerman and Howard, 1979).

The incubation period of HAV has been established experimentally as between 3 and 5 weeks, most commonly 4 weeks; the range being from 15 - 40 days.

Following the development of sensitive techniques for the identification of HAV and HBV, evidence has accumulated concerning the existence of a new type of agent, or agents, causing hepatitis (NANB) (Feinstone et al.1975). The agent has not been identified or characterised to date and the diagnosis is essentially one of exclusion. Recent studies involving chimpanzees have

verified the existence of a transmissible non-A, non-B agent (Tabor et al. 1978).

The development of serological techniques directed towards the identification of NANB is in process (Shirachi et al. 1978).

NANB has been implicated in the occurrence of fifteen cases of fulminant hepatic failure, with greater than 50.0 per centum mortality rate (Rakela et al. 1975).

The clinical course in NANB infection is somewhat similar to that of HBV, although generally milder.

The incubation period is again similar to that of HBV infection ranging from 18 - 100 days.

2.2 Historical Review

Prior to 1959 virtually nothing was known concerning viral hepatitis in Libya. Since that time records of hospital admissions have been available and Figure H.1 presents the data for the period 1959 - 1973; wherein following a fairly steady annual incidence fluctuating about 100 cases between 1959 and 1964 an upward trend, with cyclical variation, developed to the point of 2236 in 1973, an incidence approximating to 1 : 1000 of the entire population and 1 : 500 of the urban population.

Nothing concerning the nature of virus type was available until 1976 when Christie et al. reported upon a severe outbreak among pregnant women in Tripoli during 1975; although it was established that the mortality rate of 13.0 per centum was not due to HBV, despite the occurrence of some cases of that type, the state of laboratory methods at that time prevented the implication of either HAV or NANB. A similar outbreak in 1970, also in Tripoli, was reported retrospectively in 1977 by Wyatt; the mortality rate on this occasion being 26.0 per centum with no virus typing being possible.

2.3 Methods and Subjects

In view of the high incidence of viral hepatitis in general and the severe outbreaks among pregnant women in particular, it was thought to be valuable to attempt definition of the age of onset of the virus type or types involved.

It was considered that radio-immuno-assay would be the method of choice for this objective and, since this technique would be both too complex and costly for short-term operation, an approach for assistance was made to Dr. D.S. Dane, Head of Virology, School of Pathology, Middlesex Hospital, London. Dr. Dane kindly agreed to participate and use methods developed and established in his laboratory.

In the author's experience, Gharian, a rural town some 100 kms south of Tripoli, suffered considerable incidence of viral hepatitis, especially in 1975. The age/sex analysis of case notifications (Table H.1) supported this view, indicating an incidence ranging from 20.4 per thousand in 1975 to 3.4 per thousand in other years throughout the period 1974-1978, with population adjusted by the annual growth rate (see I .2.1.); whilst calendar month analysis (Table H.2) indicated a tendency toward outbreaks following the cessation in September of the hot, dry summer. Accordingly, this town, Gharian, was selected as the initial location for a random serological survey. In 1979 approximately 400 subjects were bled, the majority being school children in the age range 6 - 18 years; in the event, not all sera were tested in the interests of the conservation of time, effort and reagents. In 1980 and 1981 some 40 young children below the age of 6 years were bled.

In 1980 36 children, of the age of 5 years or less, known to have suffered hepatitis in the recent past were bled for the purpose of a retrospective serological survey to supplement the random survey.

During 1981 a random survey was undertaken in Derna, a coastal town some 1500 kms east of Tripoli, where the age/sex analysis of case notifications (Table H.3) indicated an incidence ranging from 2.2 per thousand to 1.3 per thousand throughout the period 1975-1978 in respect of the adjusted population levels; whilst the calendar month analysis (Table H.4) revealed little tendency to outbreaks at any point in the year.

It was...

hoped that this location might provide an epidemiological contrast to the situation obtaining in Gharian. Accordingly, some 250 subjects were bled, the majority being school children in the age range 6 - 18 years with some 52 being of 5 years or less; in the event, not all of these sera were tested.

Throughout the study period 22 children were bled whilst actually suffering acute hepatitis; one being in Derna and the remainder in Gharian.

From all subjects approximately 10.0 ml blood was withdrawn from the median cubital vein; following natural clotting at ambient temperature all samples were refrigerated at + 4°C and the separated serum transferred, within twelve hours of withdrawal, to new, clean, glass, screw-capped bottles (Bijou type ¼ oz. capacity) by means of sterile, plastic Pasteur type pipettes. These samples were stored locally at -20°C until convenient for transport, chilled, in insulated containers by direct flight to London where they were stored finally at -20°C. The transport time being not in excess of twelve hours, frequently less.

2.4 Related Studies in Progress

Separate studies are currently in progress, as follows :

2.4.1. Hepatitis virus type in pregnant women.

2.4.2. Serological and electron microscopic investigation of the children of families having a single child index case of acute hepatitis.

2.5 Results

2.5.1. HAV studies

Laboratory testing of selected subjects from the random serological survey in Gharian indicated that 100.0 per centum of those aged 7 years or more were anti-HAV positive and that this rate declined, though remaining high, in children aged 6, 5, 4 and 3 years being 96.0, 87.0, 90.0 and 60.0 per centum respectively (Table H.5). It was not possible to

obtain a larger sample of children of three years nor could samples be obtained from younger children.

The retrospective study in Gharian, involving young children known to have suffered acute hepatitis in the recent past, indicated that all subjects, 100.0 per centum, totalling 36 within the age range 1 - 5 years inclusive, were anti-HAV positive. These results matched with similar age groups involved in the random study are presented in Table H.6. The majority of the children constituting the retrospective survey had been admitted to hospital during October, November 1977; figure H.2 gives a graphic view of the calendar month analysis of case notifications for 1977, extracted from Table H.2. The ages given for retrospective cases refer to their admission to hospital.

In the light of the results arising from the random survey of Gharian only those specimens from subjects of seven years of age or less were tested in connection with the random survey of Derna (Table H.7). These yielded anti-HAV positive rates of 100.0, 75.0, 97.0, 100.0 and 86.0 per centum in respect of children aged seven, six, five, four and three years.

The random survey results from both Gharian and Derna are compared in Table H.8 and compared graphically in Figure H.3. Taking all results from age seven years and below together the 87 subjects from Gharian yielded a positive rate of 92.0 per centum, as did the 75 subjects from Derna.

Table H.9 indicates the results concerning twenty-two young children bled throughout the period 1979-1981 when encountered whilst actually suffering acute hepatitis in hospital; one of these, DO513, being from Derna and the remainder from Gharian. The anti-HAV IgM positive rate of 81.8 per centum indicated those suffering acute HAV infection, whilst the remainder, 18.2 per centum, are considered as NANB cases by exclusion, since no case carried any of the markers indicating HBV infection : G0591, a four year old male, was the only case positive for HBsAg only indicating the HBV carrier state but not acute infection, either current or past. Sixteen of these children were bled during an outbreak in Gharian in October 1981, the anti-HAV positive rate being 81.3 per centum, the remaining 18.7 per centum being classed as NANB.

2.5.2. HBV studies

Table H.10 presents the age/sex analysis of 321 children from the random study of Gharian. The positive rate for HBV markers (HBsAg positive with anti HBc positive, or anti-HBc positive with anti-HBs positive or anti-HBc positive only) being 2.5 per centum for children in age range 3 - 5 year and 12.1 per centum for school children in the age range 6 - 16 years; little difference occurred between 6 - 11 years group of primary school children and the 12 - 16 years secondary school group.

Table H.11 presents the similar age/sex analysis in respect of the Derna random survey. Here, the positive rate is seen as 5.8 per centum for age group 2 - 5 years and 6.2 per centum for school children of 6 - 16 years; a more marked difference occurred between the primary school group, where the positive rate stands at 1.8 per centum, and the secondary school group yielding 13.4 per centum.

Table H.12 presents the age/sex analysis for 57 adults from the random survey of Gharian indicating that 75.0 per centum of 24 males were positive for HBV markers whilst 24.2 per centum of 34 females were positive.

2.6 Discussion

2.6.1. Viral hepatitis - general

The data presented in Figure H.1 indicate the cyclical variation of viral hepatitis on a rising trend between 1964 and 1970 with a continued rise to 1973.

The probable reasons for this pattern being as follows -

i. The gradual improvement in case notification arising from health service development.

ii. The migration of population, especially since 1970, from rural areas to urban centres, with consequent pressure upon water supply and disposal systems for excreta and other wastes, coupled with poor personal and food hygiene.

iii. A further increase in the population density of urban centres resulting from a high birth rate; the 1973 census elicited a national crude birth rate of 44.8 per thousand.

iv. A heavy increase in the immigration of foreign labour, especially from Tunisia and Egypt.

Prior to 1974, no data were available in respect of age, sex or point of incidence thus preventing any analysis of case figures. Virus typing has become possible only recently.

2.6.2. HAV studies

The random survey of Gharian indicated that all children of seven years and above were HAV immune (Table H.5); although serum samples were not obtained from children below the age of three years it was shown that 60.0 per centum of three year old subjects were immune. It would seem that infection takes place at an earlier age.

The retrospective survey (Table H.6.) supports this view since, although a small sample, both children of one year of age were shown to be immune as well as all five three year old children. Most of the children in this survey had been admitted to hospital during October and November 1977. The hospital notifications of hepatitis in Gharian for that year (Table H.1.) reveal a high incidence in children under five and that a majority of cases occurred in September, October and November (Table H.2. and Figure H.2.).

This evidence appears to suggest that HAV causes outbreaks among young children in Gharian from time to time. Reinforcing evidence arose when 16 cases of acute hepatitis in children of five years or less were bled, among others, during an outbreak in Gharian during October 1981; of these, 13 (81.3 per centum) were diagnosed serologically as having acute HAV infection (Table H.9.).

Despite the indication of the hospital notifications in Derna (Tables H.3 and H.4) the random survey in that location indicated a similar pattern of incidence in young children (Table H.7.) to that in Gharian.

A comparison of the random surveys in both locations (Table H.8 and Figure H.3) in respect of children of seven years, the point at which 100.0 per centum are shown to be immune, or less reveals an immune positive rate of 92.0 per centum in both groups of 87 subjects from Ghárian and 75 from Derna.

It can only be assumed that the apparent dissimilarity of the notifications from these two locations arises either from faulty data transmission between hospital and Community Health Department in Derna, or from some cultural attitude causing Derna parents not to send their young children to hospital unless very seriously ill.

2.6.3. HBV studies

A random survey of 321 children in Gharian (Table H.10) revealed that young children in the age range 3 – 5 years yielded an HBV immune positive rate of 2.5 per centum, whilst school children in the age range 6 - 16 years gave a positive rate of 12.1 per centum. No striking difference appears as between males and females nor between the component age groups of 6 - 11 years and 12 - 16 years. It should be explained here that subjects giving low titre positive anti-HBs reactions only were classed as negative due to doubt as to the validity of such results.

The similar survey of 230 children in Derna (Table H.11) showed that young children in the age range 2 - 5 years yielded an HBV immune positive rate of 5.8 per centum, whilst school children in the age range 6 - 16 years gave a positive rate of 6.2 per centum. In this case the positive rates for age groups 6 - 11 and 12 - 16 years were 1.8 and 13.4 per centum respectively; again, there was no especially marked difference between the sexes.

The number of children in each survey was reasonably large and the age distribution reasonably similar; presumably, the variations in positive rates reflect local epidemiological factors affecting one age group rather than another instead of a fundamental difference between the geographical locations.

A small number of adults, 57 in all, deriving from the random survey in Gharian were tested for HBV markers : these yielded positive rates of 75.0 and 24.2 per centum for males and females, respectively. The disparity between the sexes may have been affected by the age distribution; the average age of the women being 34 years and that of men 43 years.

Of the 551 children from Gharian and Derna 12 (2.2 per centum) proved to be HBsAg positive carriers. All were sub-type ay. There were no HBsAg carriers among the 57 adults. Blood bank screening figures give a national rate between 3.0 and 4.0 per centum for HBsAg carriers in Libya.

2.7 Conclusions

2.7.1. HAV studies

HAV is a common virus in Libya infecting small children but not older children and adults who remain immune as a result of their infection early in life. There is evidence from Gharian that outbreaks in the very young tend to occur at the end of the dry, hot summer : more epidemiological research is needed to determine the factors involved in these outbreaks.

This situation is more satisfactory than that existing in Britain and the United States of America (MMRW 1981), for example, where less than half of young adults are HAV immune; since HAV does not give rise to chronic liver disease there is no price to be paid, in the long term, for childhood infection.

Immune serum globulin (ISG) or gammaglobulin is seldom used in developed countries to protect young children from HAV. There appears to be no reason for such use in Libya and, clearly, its use in the case of adults would be pointless since they are already immune.

It is unlikely that an HAV vaccine (Zuckerman and Howard, 1979) will be of value in Libya since the infection occurs so early in life, the period of viraemia is short and not particularly severe, and there is no evidence to date of the development of a carrier state.

2.7.2. HBV studies

HBV infection appears to be uncommon in small children but affects school children and adults more frequently, although not dramatically, since only about half of the adult population is immune; this, of course, is consistent with the fact of the parenteral mode of spread of HBV.

However, the risk of HBV infection is high in hospital as, for example, by means of blood transfusion, during renal haemo-dialysis, or during surgery; these risks apply to both patients and staff involved.

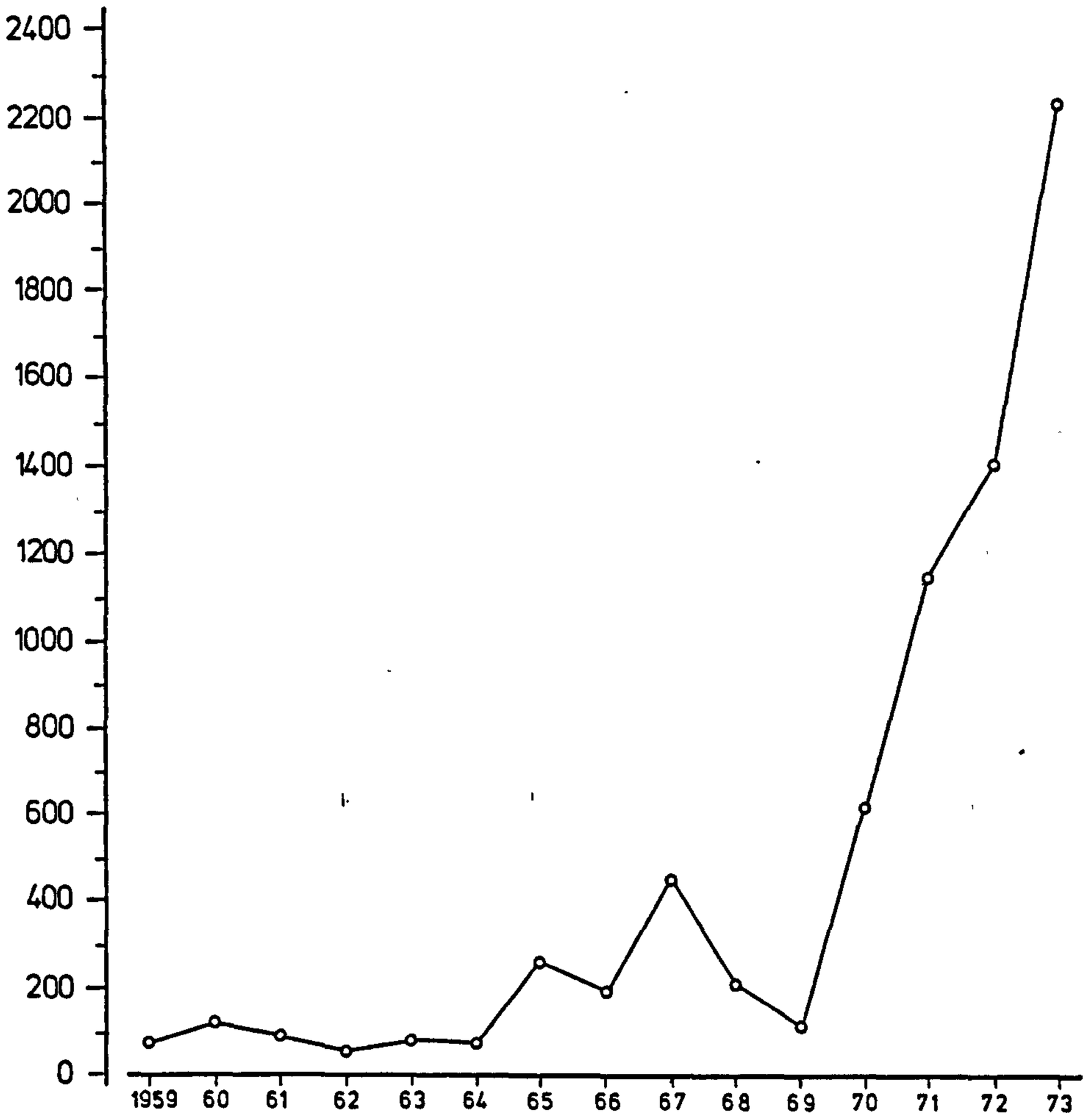
In Britain (B.M.J. editorial, 1980) the HBsAg carrier rate is about 0.2 per centum but in large areas of Africa and Asia it exceeds 10.0 per centum : the total number of carriers in the world has been estimated to be in excess of 200 millions. Those countries having high carrier rates also have a high incidence of HBsAg positive chronic liver disease and hepatocellular carcinoma. Infants born to HBsAg positive mothers are at risk of HBV infection and becoming chronic carriers; such children tend to a high incidence of fatal hepatoma in young adulthood.

Thus, an HBV vaccine is needed urgently for groups at high risk of infection; such as, surgeons, gynaecologists, renal haemo-dialysis unit staff, infants of HBsAg positive mothers and of HBeAg positive mothers, and mothers infected with HBV in the late stages of pregnancy.

figure H.1

VIRAL HEPATITIS in LIBYA

1959/73 notified cases



age/sex analysis not available

table H.1

HEPATITIS in GHARIAN : age/sex analysis

Notifications: hospital to Community Health Department

	AGE GROUP years														
	<5		5-14		15-24		25-34		35-44		>45		TOTAL		
	m	f	m	f	m	f	m	f	m	f	m	f	m	f	m+f
1974	11	6	31	27	35	27	24	46	15	14	9	5	125	125	250
1975	45	32	38	24	44	33	45	52	19	11	16	16	207	168	375
1976	5	5	11	7	9	13	11	17	4	8	5	5	45	55	100
1977	82	50	12	12	9	6	3	7	5	5	5	8	116	88	204
1978	3	4	6	6	17	5	8	5	3	5	3	4	40	29	69

table H.2

HEPATITIS in GHARIAN: calendar month analysis

Notifications: hospital to Community Health Department

	Jan	Feb	Mar	Apr	May	Jun	Jly	Aug	Sep	Oct	Nov	Dec	TOTAL
1974	32	18	25	19	21	19	6	20	6	20	25	39	250
1975	38	34	33	39	41	33	14	16	42	37	29	19	375
1976	12	12	10	3	8	10	7	3	9	8	8	10	100
1977	10	6	9	9	8	8	16	17	36	46	28	11	204
1978	analysis not available												69

table H.3

HEPATITIS in DERNA : age/sex analysis

Notifications: hospital to Community Health Department

	AGE GROUP years														
	<5		5-14		15-24		25-34		35-44		>45		TOTAL		
	m	f	m	f	m	f	m	f	m	f	m	f	m	f	m+f
1974	data not available														
1975	6	4	7	4	17	12	11	13	2	4	2	nil	45	36	81
1976	6	5	4	5	6	5	8	5	6	2	nil	1	30	23	53
1977	8	6	15	11	13	6	10	3	7	3	7	2	60	31	91
1978	8	5	10	7	5	3	4	6	2	1	nil	3	29	25	54

table H.4

HEPATITIS in DERNA: calendar month analysis

Notifications: hospital to Community Health Department

	Jan	Feb	Mar	Apr	May	Jun	Jly	Aug	Sep	Oct	Nov	Dec	TOTAL
1974	data not available												
1975	analysis not available												81
1976	6	5	5	6	2	3	nil	5	3	3	9	6	53
1977	16	6	5	10	11	12	2	1	9	9	7	3	91
1978	5	1	5	6	7	4	5	6	3	5	5	2	54

table H.5

HEPATITIS A ANTIBODY in GHARIAN

random survey 1979/81

		age / years								
		3	4	5	6	7	8	9	10-18	18+
POSITIVE	number	3	9	20	26	22	24	29	40	32
	per centum	60	90	87	96	100	100	100	100	100
NEGATIVE	number	2	1	3	1	nil	nil	nil	nil	nil
	per centum	40	10	13	4	-	-	-	-	-
TOTAL	number	5	10	23	27					
	per centum	100	100	100	100					

table H.6

HEPATITIS A in GHARIAN

antibody in children ≤ 5 years

		1	2	3	4	5	TOTAL number	TOTAL per centum
RETROSPECTIVE SURVEY *acute hepatitis previously	+	2	nil	5	16	13	36	100·0
	-	nil	nil	nil	nil	nil	-	-
RANDOM SURVEY history unknown	+	nil	nil	3	9	20	32	84·2
	-	nil	nil	2	1	3	6	15·8

*OLD HOSPITAL CASES

figure H.2

HEPATITIS in GHARIAN : total notifications 1977

calendar month analysis

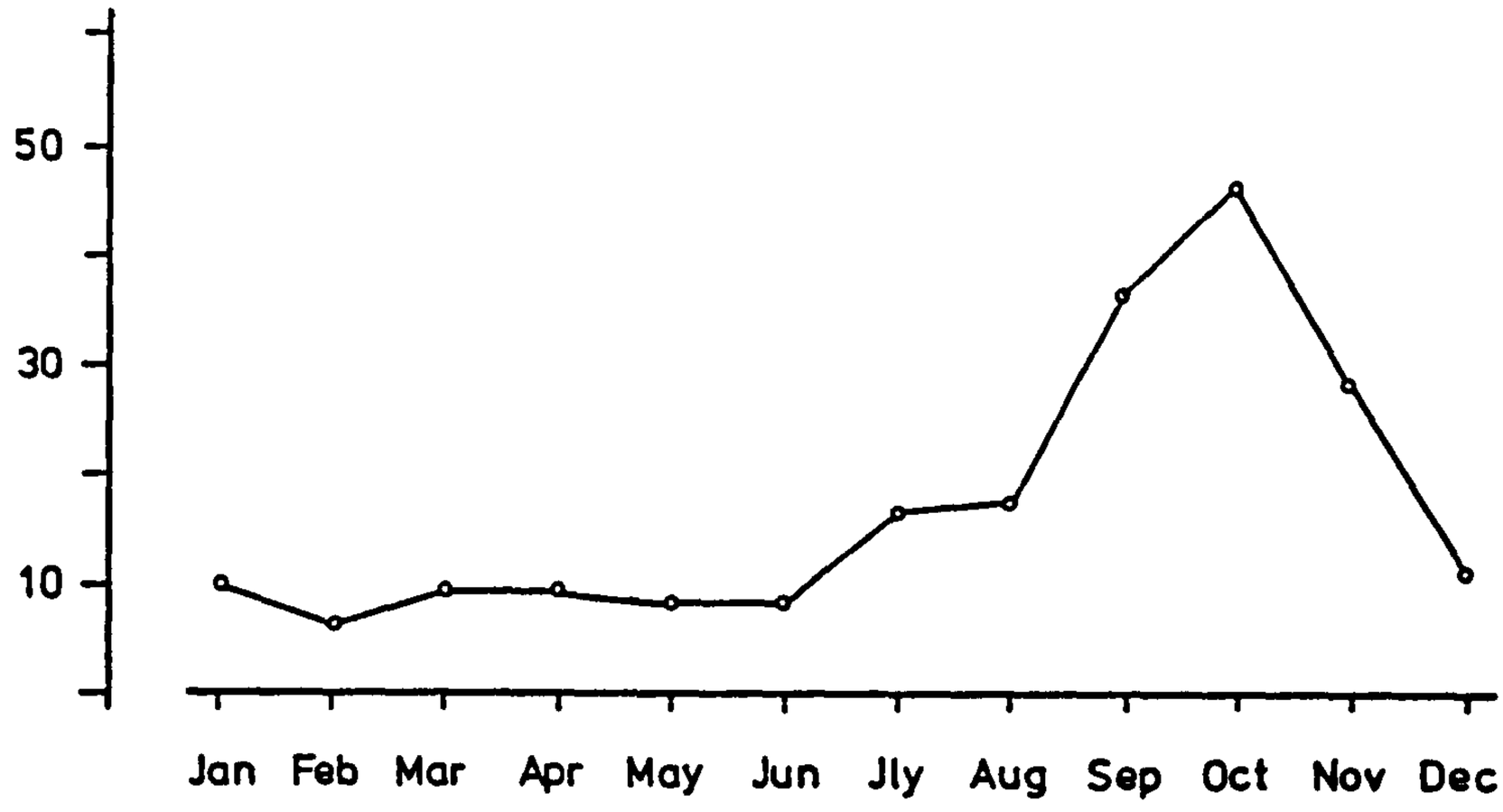


table H.7

HEPATITIS A ANTIBODY in DERNA

random survey 1981

		age /years					
		2	3	4	5	6	7
POSITIVE	number	nil	6	14	28	9	12
	per centum	-	86	100	97	75	100
NEGATIVE	number	1	1	nil	1	3	nil
	per centum	100	14	-	3	25	-
TOTAL	number	1	7	14	29	12	12
	per centum	100	100	100	100	100	100

figure H.3

HEPATITIS A ANTIBODY : random survey / per centum

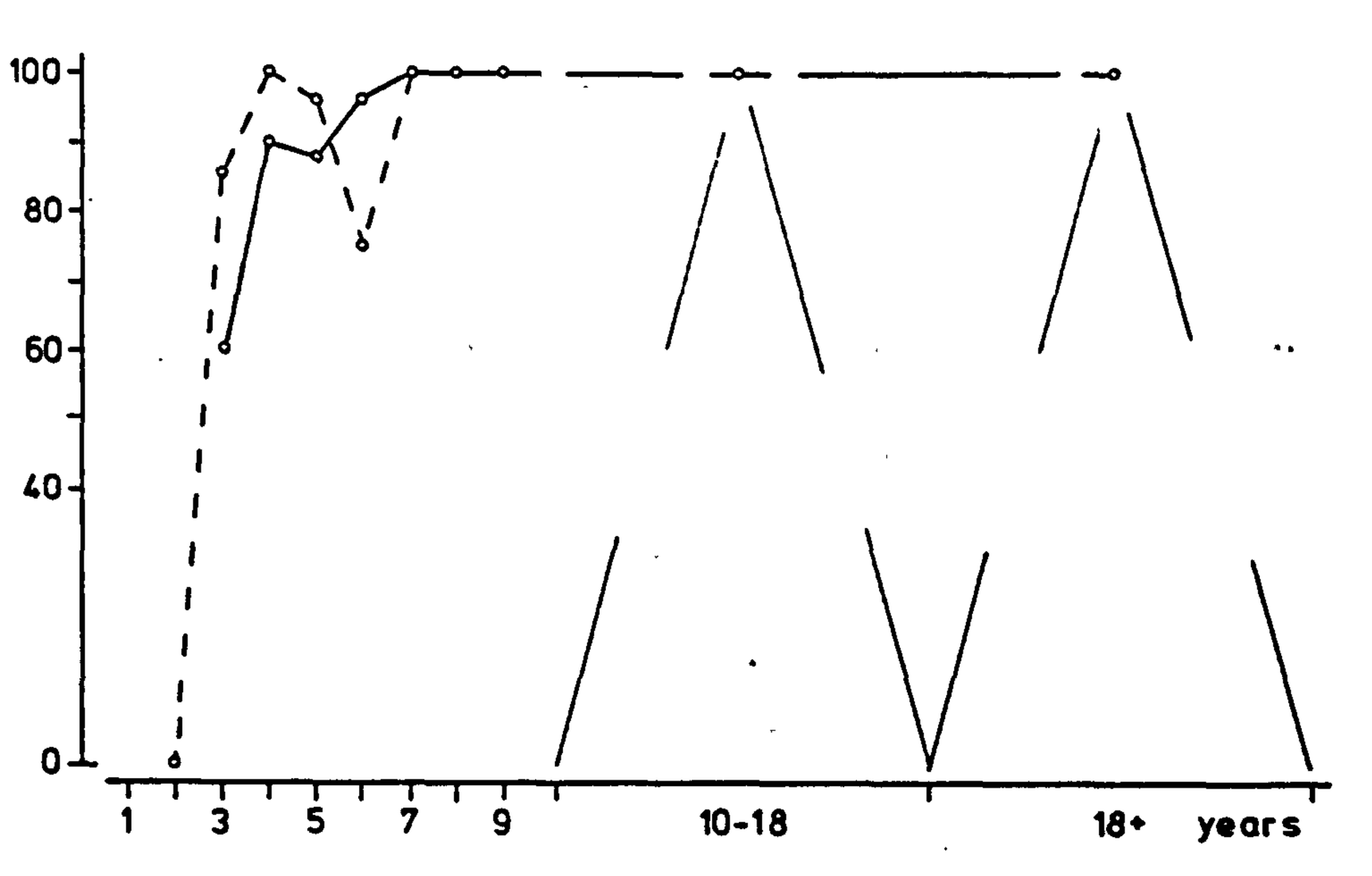


table H.8

HEPATITIS A ANTIBODY : random survey

two locations compared

		2	3	4	5	6	7	< 7 TOTAL number	< 7 TOTAL per centum	8	9	10-18	18+
GHARIAN	+	nil	3	9	20	26	22	80	92·0	24	29	40	32
	−	nil	2	1	3	1	nil	7	8·0	nil	nil	nil	nil
DERNA	+	nil	6	14	28	9	12	69	92·0	/	/	/	/
	−	1	1	nil	1	3	nil	6	8·0	/	/	/	/

table H.9

ACUTE HEPATITIS in YOUNG CHILDREN

ONSET	CODE	Age	Sex	HBsAg	anti-HAV IgM	causative virus
Oct 79	G0379	1·5	f	-	+	A
Dec 79	G0404	1·5	m	-	+	A
Mar 80	G0450	1·5	m	-	+	A
Apr 81	G0559	4	m	-	-	non-A,non-B
Apr 81	G0560	3	f	-	+	A
Oct 81	D0513	3	m	-	+	A
-	G0590	2	m	-	+	A
	G0591	4	m	°+	+	A
-	G0592	2	f	-	-	non-A,non-B
	G0593	2	f	-	+	A
-	G0594	2	f	-	+	A
	G0595	3	f	-	+	A
-	G0596	2	f	-	+	A
	G0597	5	m	-	+	A
-	G0600	2	f	-	+	A
	G0601	5	m	-	-	non-A,non-B
-	G0603	2	f	-	+	A
	G0612	3	f	-	+	A
-	G0613	3	f	-	+	A
	G0615	2	m	-	+	A
-	G0617	5	f	-	-	non-A,non-B
Oct 81	G0618	2	f	-	+	A

°carrier

table H.10

HEPATITIS B MARKERS in SCHOOLCHILDREN

GHARIAN
1979,1980,1981

AGE group	males		females		total	
	positive	negative	positive	negative	positive	negative
	number per centum	number per centum	number per centum	number per centum	number per centum	number per centum
3- 5	1 4.4	22 95.6	nil -	17 100.0	1 2.5	39 97.5
6-11	12 13.2	79 86.8	6 8.6	64 91.4	18 11.2	143 88.8
12-16	8 11.9	59 88.1	8 15.1	45 84.9	16 13.3	104 86.7
6-16	20 12.7	138 87.3	14 11.3	110 88.7	34 12.1	247 87.9

positive = HBs Ag+, anti-HBc+
or anti-HBc+, anti-HBs+
or anti-HBc+

negative = anti-HBs+ only, or all negative

table H.11

HEPATITIS B MARKERS in SCHOOLCHILDREN

DERNA

1981

AGE group	males		females		total	
	positive	negative	positive	negative	positive	negative
	number per centum	number per centum	number per centum	number per centum	number per centum	number per centum
2- 5	1 3.9	25 96.1	2 7.7	24 92.3	3 5.8	49 94.2
6-11	1 1.8	54 98.2	1 1.8	55 98.2	2 1.8	109 98.2
12-16	3 10.7	25 89.3	6 15.4	33 84.6	9 13.4	58 86.6
6-16	4 4.8	79 95.2	7 7.4	88 92.6	11 6.2	167 93.8

positive = HBs Ag+, anti-HBc+
or anti-HBc+, anti-HBs+
or anti-HBc+

negative = anti-HBs+ only, or all negative

table H.12

HEPATITIS B in GHARIAN

random survey: adults

		AGE GROUPS											TOTAL	
		21-25	26-30	31-35	36-40	41-45	46-50	51-55	56-60	61-65	66-70	71-75	number	per centum
male	+	nil	3	1	3	1	1	4	2	1	1	1	18	75.0
	–	2	nil	2	nil	1	1	nil	nil	nil	nil	nil	6	25.0
female	+	1	2	1	1	nil	–	1	–	1	1	–	8	24.2
	–	7	9	5	2	2	–	nil	–	nil	nil	–	25	75.8

NO HBsAg CARRIERS PRESENT

HBV+ refers to S+C or C only antibody

CHAPTER 3.0 : MEASLES

3.1 Introduction

Measles is prevalent worldwide as an endemic disease of children : thousands of infants and small children die yearly as a result of this infection in developing countries. In densely populated areas it is subject to epidemic fluctuation and seasonal variation.

In the old world the disease had been long documented notably by the Arabian physician Rhazes in AD850 thus :

"When the summer is hot and dry..... and the rains come on very late, then the measles quickly seize those who are disposed to them, but all these things admit of great differences by reason of the diversity of countries..... so that they happen in other seasons besides these." (Greenhill, 1848). Rhazes drew an incomplete distinction between measles and smallpox. Confusion in diagnosis continued for eight hundred years until, in the seventeenth century, Thomas Sydenham finally delineated the two diseases.

Panum (1847) studied an epidemic in the Faroe Islands during 1846 and produced a monograph considered to be a classic among epidemiological descriptions of disease. Despite earlier observations and descriptions Koplik (1896) was the first to call attention to the diagnostic significance of the enanthem appearing on the buccal mucous membrane; these spots now bear his name.

Hektoen (1905) successfully transmitted the disease to two human volunteers by transferring the blood of measles patients to them.

Variation in severity of the disease occupies a fairly clear socio-geographical distribution which is determined to some extent by geographical factors; however, the pattern is being altered both passively and actively by man himself through the agency of social change and medical care, especially vaccination.

Endemic infection is interrupted by periodic epidemic fluctuation on a two to three year cycle with a peak seasonal incidence superimposed in the winter of years carrying epidemics. This periodicity is related to immune proportions of the entire community exposed to risk, a factor referred to as herd immunity. Brincker (1938) has shown that if, in the case of measles, herd immunity remains at or above 80.0 per centum the disease will continue to occur at a low level of endemicity but should it fall to 60.0 per centum or less epidemic fluctuation incidence may be expected, resulting, in turn, in a larger proportion of immune individuals to regenerate the cycle. This illustration accounts for both the periodicity of the disease and the predominance of young children affected in an epidemic.

3.2. Historical Review

Measles has constituted a serious health problem in the past in Libya; the incidence in children has been high and a considerable proportion of complicated cases occurs.

The second and last quarters of the year are usually the most affected periods.

Figure M.1. presents the pattern of morbidity throughout the period 1962-1977; these data are considered to be incomplete and no mortality data are available.

A compulsory vaccination programme was initiated in 1972.

3.3. Methods and Subjects

3.3.1. Methods

The opportunity arose, through the kind offices of Miss Kate Bellamy of the Standards Laboratory for Serological Reagents, Central Public Health Laboratory, London, for a small number of sera to be tested in a newly developed enzyme linked immunosorbent assay for measles immunity.

3.3.2. Subjects

Accordingly, nineteen sera were selected from the author's -70°C Libyan serum sample archive in Liverpool and forwarded to Miss Bellamy. These sera were selected from known six year old school children from Benghazi otherwise they were selected at random, two from eight schools and three from a ninth.

3.4. Results

The results are presented in Table M.1. and reveal that all nineteen test sera, 100.0 per centum, are measles immune.

3.5. Discussion

It is acknowledged that the number of test sera is small, the opportunity having arisen by chance.

Nevertheless, it is clear that all nineteen sera are immune and at a satisfactorily high level.

The likelihood that the measles immunisation programme initiated in Libya for children of nine months, has begun to exert its expected influence is indicated by Figure M.1. The classical cycle described in 3.1. is clearly demonstrated through the years 1959 - 1970 and a renewed cycle gathering momentum in 1971 and 1972 appears to have been retarded by 1973 and is flattening, possibly, on a low rising trend throughout 1974 - 1977.

The ELISA results suggest a probable high level of immunity in children upon entry to school at six years which should have been induced by the administration of vaccine.

The results clearly require an amplified effort in the future to obtain confirmation of the situation from a large scale random survey.

Serological techniques have been particularly useful in the study of measles epidemiology in the past because of the specificity of the measles immune response and the stability of the resulting antibody titres and there is the possibility that these can be employed rewardingly in the future.

3.6. Conclusion

The introduction of the administration of live measles vaccine in 1972 has resulted in a significant reduction in the incidence of measles; conversion rates between 90 - 95.0 per centum are frequently reported (Krugman, 1971).

It should be possible to eradicate measles, as was smallpox, by means of effective immunisation cover and active surveillance. Measles is much more easily transmitted than is smallpox and outbreaks have occurred in populations of which greater than 90.0 per centum were known to be immune (Shasby et al, 1977); thus, elimination from the community probably requires that a greater proportion than 95.0 per centum be immune (Yorke et al, 1979).

For such a programme to be successful in Libya it would be necessary to gather information as to birth rate, family size and the density and mobility of populations; this knowledge would enable the immunisation of all susceptible subjects before they contract measles naturally. Finally, the same containment strategy as that employed for the eradication of smallpox would be applied. Each case of measles would be carefully followed and all contacts vaccinated unless they have acceptable proof of previous vaccination.

Mass random surveys to establish more accurately the level of herd immunity, possibly employing the technique used by Miss Bellamy, would be a prerequisite.

figure M.1

MEASLES in LIBYA

1962/77 notified cases

per hundred thousand

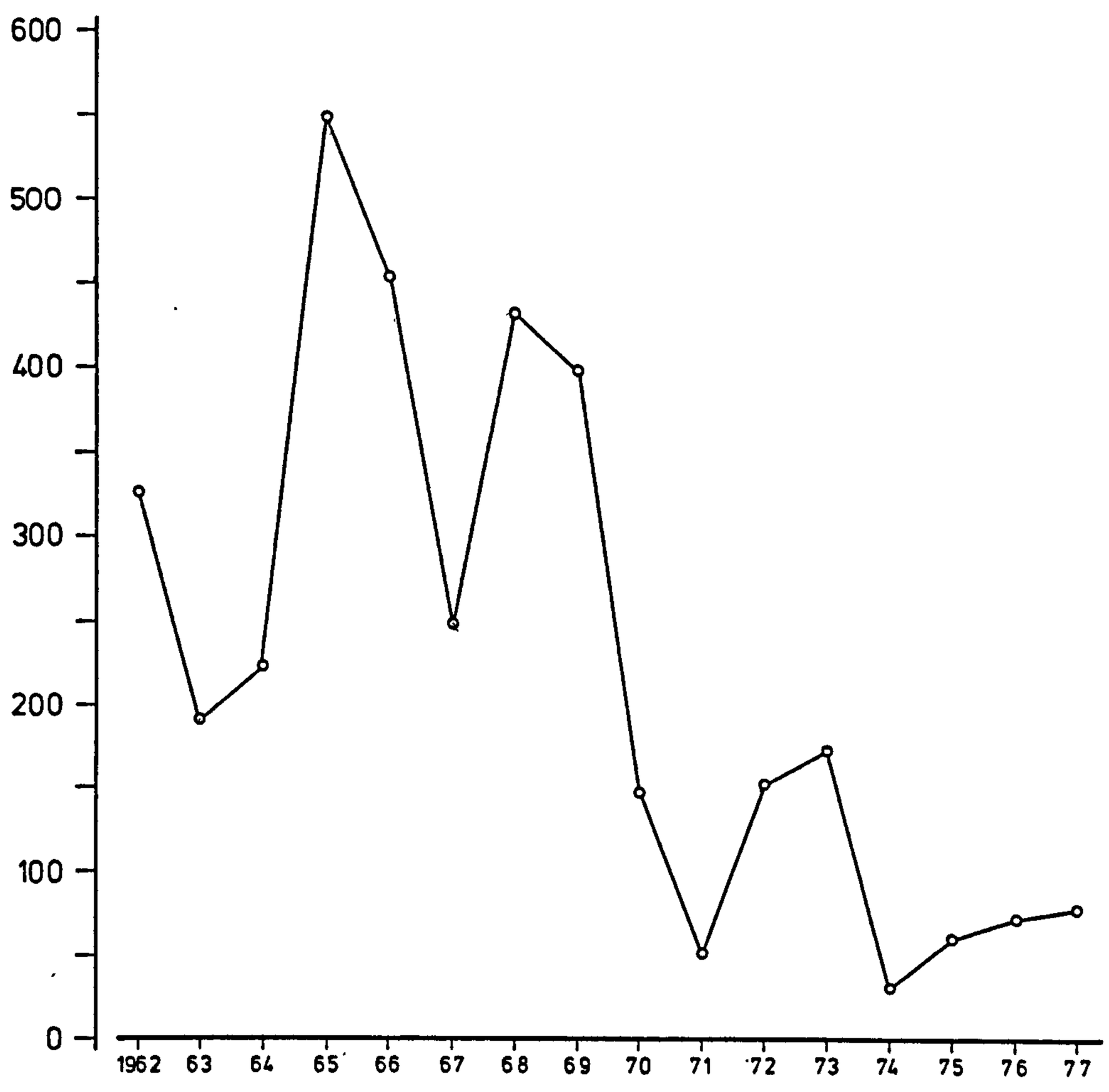


table M.1 Measles: Benghazi 6 years schoolchildren

ELISA RESULTS

Measles antigen: Standards Batch 1/78 used at a dilution of 1:50

Vero control antigen: Standards batch 1/78 used at a dilution of 1:50

Sera diluted 1:100 for the assay

Specimen No.	Absorbance at 405nm For Measles Antigen	Vero Control Antigen
4	2.14	.16
5	1.48	.10
44	.78	.24
49	1.68	.11
58	1.18	.10
66	1.95	.15
70	2.02	.14
102	1.32	.12
103	.81	.15
108	1.14	.13
115	1.38	.14
116	.75	.11
117	1.20	.12
151	1.27	.105
152	1.37	.12
172	1.23	.10
179	1.67	.10
180	1.34	.11
198	.96	.12

Specimen No.	Absorbance at 405nm For Measles Antigen	Vero Control Antigen	
Stds.1/75	2.36	.44	Positive control serum
Stds.1/70	.19	.15	Negative control serum

Standards 1/75 serum has a titre of 1:80 in the complement-fixation test

Sera giving an absorbance (at 405nm) greater than 0.2 are considered positive.

CHAPTER 4.0 : RUBELLA

4.1 Introduction

Rubella (German measles) is a mild viral disease common in children and young adults. Infection of a woman during pregnancy may, however, have a severe teratogenic effect on the foetus. Because of the mild, often subclinical, nature of the disease and the ease of confusion with other viral exanthems, a history of a rubella-like illness cannot be relied upon to indicate the immune status of an individual. Accordingly, screening for rubella antibodies as an indication of previous infection has become an important aspect of routine clinical virology. In most western countries pregnant women are screened during the early part of pregnancy so that those found to be lacking antibodies can be offered rubella vaccine in the immediate post-partum period.

Rubella was reported initially by German authors in the 18th century, but not until 1938 was its viral nature established by Japanese workers and its transmissibility demonstrated by the injection of throat washings. Before 1941, rubella was known as a mild disease of children and young adults, being characterised by lymphadenopathy and by an acute rash that lasts for about 3 days; it had been reported to be more severe in adult females since about half experienced some form of arthralgia or arthritis. Rubella is considered to be less infectious than measles and the risk of infection is greatest following household contact.

In 1962, rubella virus was isolated by two independent groups in the U.S.A. Attempts to develop vaccines started immediately following this initial isolation of the virus. At first, most attempts were directed towards the development of a killed vaccine, but they were all abandoned because it soon became clear that these killed preparations were not sufficiently immunogenic. All efforts were then oriented towards live vaccines, and this resulted in 1969 in the licensing of two vaccines, first the Cendehill (trade name Cendevax) in Switzerland and then the HPV-77 in the United States of America (trade name Meruvax).

Sero-epidemiological studies of rubella are of recent origin, dating from 1962 when the virus was isolated in tissue culture (Parkman et al, 1962; Weller and Neva, 1962) some 21 years after Sir Norman Gregg's remarkable discovery (1941) of the association of rubella in early pregnancy with characteristic congenital anomalies in the offspring. As a result of which observation, rubella was thrust from its position as a mild inconsequential disease of childhood to become a major medical problem.

Epidemiological studies in many countries established the age-specific and seasonal incidence of the disease more accurately, and prospective investigation showed that the risk of major foetal malformation is 20-30 per cent when rubella occurs in the first trimester of pregnancy.

The sero-epidemiological tests provide means of confirming clinical observations, identifying susceptibles and comparing the age-specific patterns of immunity in different population and sub-groups.

4.2 Historical Review

In Libya official statistics tell nothing, since countrywide data are limited by the fact that rubella was not made reportable nationally until 1979 and, most important, as with so many other diseases, the frank clinical cases represent only a fraction of the total number of infections.

4.3. Method and subjects

4.3.1. Single radial haemolysis test

Until recently the haemagglutination inhibition (HI) test was that most commonly used for the determination of rubella antibodies.

In 1973 Schild et al reported the successful combination of the principles of plate haemolysis and single radial immunodiffusion to produce the single radial haemolysis (SRH) test for the detection of viral antibodies and so proceeding to the development of a method for the determination of influenza antibody : subsequently, the SRH technique was applied to the measurement of rubella antibodies (Clarke et al, 1977; Appleton and Macrae, 1978; Russell et al, 1978).

The principle of the SRH test is that indicator erythrocytes are sensitised by coating with viral antigen and these are then suspended in a mixture of warm agarose and complement, which is poured into plates : following cooling, wells are cut into the solid gel. Test sera are filled into the wells diffusing thence into the agarose mixture; any specific antibody present combines with the antigen carried on the erythrocyte surfaces and this complex binds complement. During incubation at 37°C the bound complement is activated and lyses the erythrocytes, resulting in a clear circular area surrounding the well corresponding to the zone of diffusion of specific antibody.

Diffusion of antibody from the test wells follows kinetics identical with those governing single radial immunodiffusion (Mancini et al, 1965); hence the area of the zone of haemolysis is directly proportional to the log of the antibody concentration.

The SRH test is able to detect immunoglobulin G (IgG) but not IgM (Strannegard et al. 1978); nevertheless, this does not detract from its value in routine screening.

The SRH technique is considerably simpler to organise and employ than is the HI technique which requires complex manipulation in preparation and execution. The sensitivity of SRH exceeds that of HI and of certain enzyme immuno-assays (Morgan-Capner et al. 1979).

Accordingly, SRH is the method of choice for mass survey in developing countries and was employed in this study using commercially prepared plates and control sera.

4.3.2. Survey subjects

In order to determine the current status of rubella immunity in the school population in Libya, the following subjects were sampled by venepuncture and the subsequent separation and storage of serum; as described in 2.3 previously, with the exception that final storage in Liverpool was at -70°C.

4.3.2.1.

In Benghazi, a coastal town approximately 1200 kms due east of Tripoli, and its immediate environs 630 children aged 6 - 12 years were selected and bled during 1979 to constitute a random survey.

Also in this area 200 children of six years were bled in 1978 with the intention that they should be bled subsequently annually for a period of four years. Unfortunately, a drastic reorganisation of the school system early in 1979 made it possible to follow only 70 of the original cohort and these were bled in 1979, 1980 and 1981 at the ages of seven, eight and nine years respectively in order to observe serially their progress in terms of immunity to rubella virus.

4.3.2.2.

In Gharian, a rural town approximately 100 kms due south of Tripoli, approximately 200 children aged 6 - 13 years were selected and bled during 1979 to provide a random survey possibly in epidemiological contrast to that in Benghazi.

4.4. Results

4.4.1. Benghazi

The mass random serological survey undertaken among school children in Benghazi in 1979 (Table R.1. and Figure R.1.) indicated that more than half (58.8 per centum) of those of six years, the point at which they enter primary school, were immune and that this rate progressed on a rising trend to 78.3 per centum at the age of twelve.

The cohort of 70 children bled annually from 1978 to 1981 (Table R.2. and Figure R.2.) yielded a broadly similar result; the immune positive rate being 55.7, 61.4, 77.1 and 78.6 per centum at the age of six, seven, eight and nine respectively.

4.4.2. Gharian

The random survey in this location revealed a similar pattern of immunity; the positive rate being 61.1 per centum at six years proceeding to 89.3 at twelve years and 94.4 per centum at thirteen years. (Table R.3. and Figure R.3.)

4.5. Discussion

The foregoing results indicate broadly similar levels of immunity in the age range 6 - 9 years and where applicable to 12 years : except in the matter of unequal sampling the results do not appear to be unduly biased by sex.

Gharian is a town of 17,000 population in rural Tripolitania and Benghazi an urban complex comprising 297,000 people in coastal Cyrenaica. In the light of these facts it would appear that the results are not biased by geographical, climatological or sociological considerations.

It is clear that a proportion in excess of 55.0 per centum of the school population is immune upon entry to the primary educational system, at six years, and that this proportion progresses to between 70 - 80.0 per centum at nine years; there are indications that 80 - 90.0 per centum is reached at 12 or 13 years of age.

The indication of these surveys is that rubella is endemic in Libya, affecting children below six years and that subsequent local epidemics continue to erode the number of susceptible subjects, although not dramatically.

The low rate of susceptibility at school entry and its natural reduction suggests that mass rubella vaccination for school populations would be unnecessary. However, consideration of possible vaccination policies is in order.

4.5.1.

To vaccinate all children at school entry with the object of attempting to eliminate rubella virus from the community.

Where this has been tried it has not been completely successful for the following reasons : the difficulty of persuading parents to have their children, particularly boys, immunised against so mild a disease; the further vaccination is in time from the child bearing period of life the more likely it is that the vaccine induced immunity of some women will have waned; there is a considerable time lag before such a policy takes effect.

4.5.2.

To vaccinate all school girls in the age range 11 - 15 years.

This policy aims to protect those principally in need but does little to interfere with the natural circulation of wild virus; it can add somewhat to the natural immunity rate. It is difficult to ensure that all girls are immunised. Again, there is a time lag before all women of child bearing age become immune, either naturally or by vaccination. However, there is no need to screen subjects.

4.5.3.

Supplementary to the foregoing, 4.5.1. and 4.5.2., married women may be screened for immunity and the non-immune vaccinated. This procedure is conservative of vaccine but requires adequate laboratory services since inaccurate screening is pointless.

Inevitably, some vaccinated women become pregnant despite warnings to the contrary and because it is known that vaccine virus can cause foetal abnormality, as does the wild virus, those becoming pregnant within two months of vaccination are offered termination. If vaccine has only been given to the non-immune totally unnecessary termination can be avoided.

Some public health experts in the United States of America regard this policy, as used in Britain, as unrealistic.

4.5.4.

A further policy is to conduct the post-partum vaccination of women. This cannot obviate the problem of rubella infection during a first pregnancy otherwise it has much to recommend it. If vaccine is given within a few days following delivery there is little likelihood of conception within the potential danger period of two months : vaccine could be given with or without screening. In the United Kingdom screening is carried out when women attend their ante-natal clinic.

4.6 Conclusion

The vaccination policies given under 4.5.2. and 4.5.4. seem to be the most practical for conditions in Libya. Nevertheless, it is concluded that it is not a good use of resources, either human or financial, to employ any vaccination policy against rubella in Libya at the present time.

4.6.1. The following investigations are proposed for future study in Libya.

4.6.1.1. Periodic surveys of immunity levels in women attending ante-natal clinics.

4.6.1.2. An attempt to discover the frequency of the occurrence of rubella induced foetal abnormalities.

4.6.1.3. Relevant to the policy outlined in 4.5.4. to attempt to discover the frequency of conception within two months of parturition.

table R.1

RUBELLA IMMUNITY in BENGHAZI

random survey : school children

		6 years		7		8		9		10		11		12	
		m	f	m	f	m	f	m	f	m	f	m	f	m	f
SUBJECTS	number	190	67	93	19	62	15	81	11	8	4	4	7	33	27
	per centum	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
NEGATIVE		83	23	36	4	16	4	25	1	1	2	nil	2	7	6
		43.7	34.3	38.7	21.1	25.8	26.7	30.9	9.1	12.5	50.0	-	28.6	21.2	22.2
POSITIVE		107	44	57	15	46	11	56	10	7	2	4	5	26	21
		56.3	65.7	61.3	78.9	74.2	73.3	69.1	90.9	87.5	50.0	100.0	71.4	78.8	77.8

SUBJECTS	number	257		112		77		92		12		11		60	
	per centum	100.0		100.0		100.0		100.0		100.0		100.0		100.0	
NEGATIVE		106		40		20		26		3		2		13	
		41.2		35.7		26.0		28.3		25.0		18.2		21.7	
POSITIVE		151		72		57		66		9		9		47	
		58.8		64.3		74.0		71.7		75.0		81.8		78.3	

figure R.1

RUBELLA IMMUNITY in BENGHAZI

random survey : school children

per centum

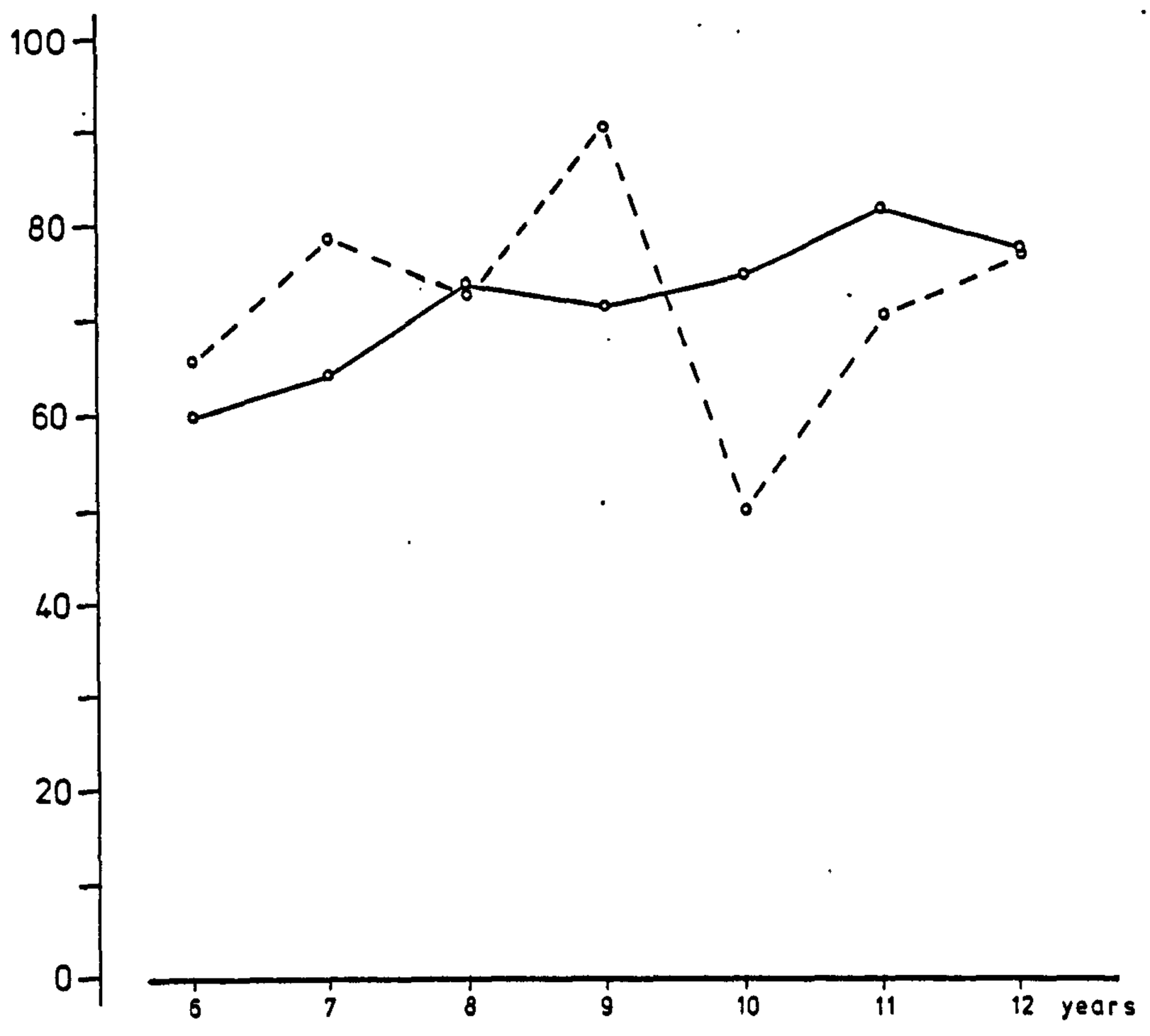


table R.2

RUBELLA IMMUNITY in BENGHAZI

serially sampled cohort

		6 years		7		8		9	
		m	f	m	f	m	f	m	f
SUBJECTS	number	61	9	61	9	61	9	61	9
	per centum	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
NEGATIVE		29	2	25	2	15	1	14	1
		47.5	22.2	41.0	22.2	24.6	11.1	22.9	11.1
POSITIVE		32	7	36	7	46	8	47	8
		52.5	77.8	59.0	77.8	75.4	88.9	77.1	88.9
SUBJECTS	number	70		70		70		70	
	per centum	100.0		100.0		100.0		100.0	
NEGATIVE		31		27		16		15	
		44.3		38.6		22.9		21.4	
POSITIVE		39		43		54		55	
		55.7		61.4		77.1		78.6	

figure R.2

RUBELLA IMMUNITY in BENGHAZI

serially sampled cohort

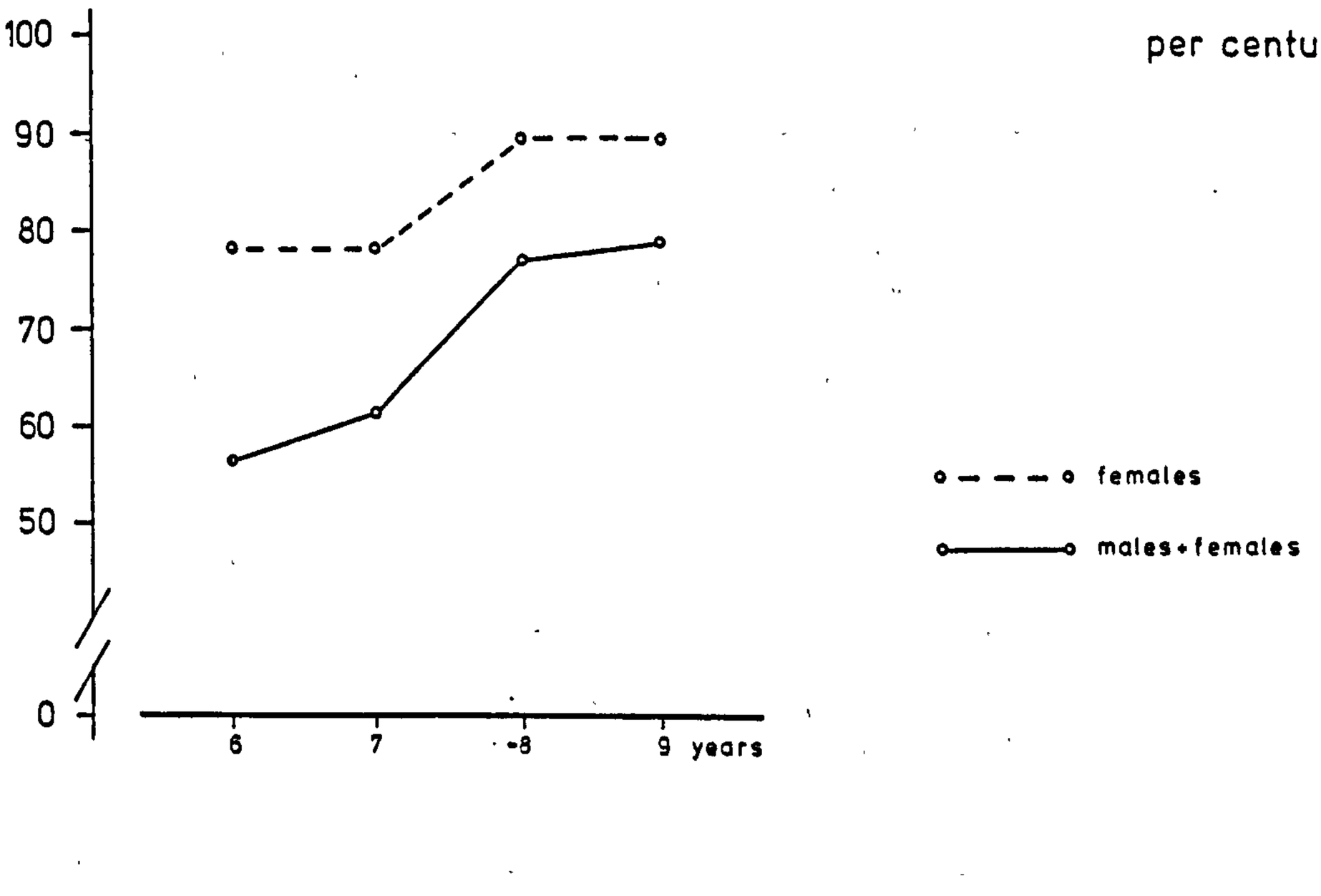


table R.3

RUBELLA IMMUNITY in GHARIAN random survey : school children

		6 years		7		8		9		10		11		12		13	
		m	f	m	f	m	f	m	f	m	f	m	f	m	f	m	f
SUBJECTS	number	10	8	13	6	13	10	15	14	27	2	12	12	15	13	13	5
	per centum	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
NEGATIVE		3	4	3	4	6	7	3	6	2	nil	2	1	1	2	1	nil
		30.0	50.0	23.1	66.7	46.1	70.0	20.0	42.9	7.4	-	16.7	8.3	6.7	15.4	7.7	-
POSITIVE		7	4	10	2	7	3	12	8	25	2	10	11	14	11	12	5
		70.0	50.0	76.9	33.3	53.9	30.0	80.0	57.1	92.6	100.0	83.3	91.7	93.3	84.6	92.3	100.0

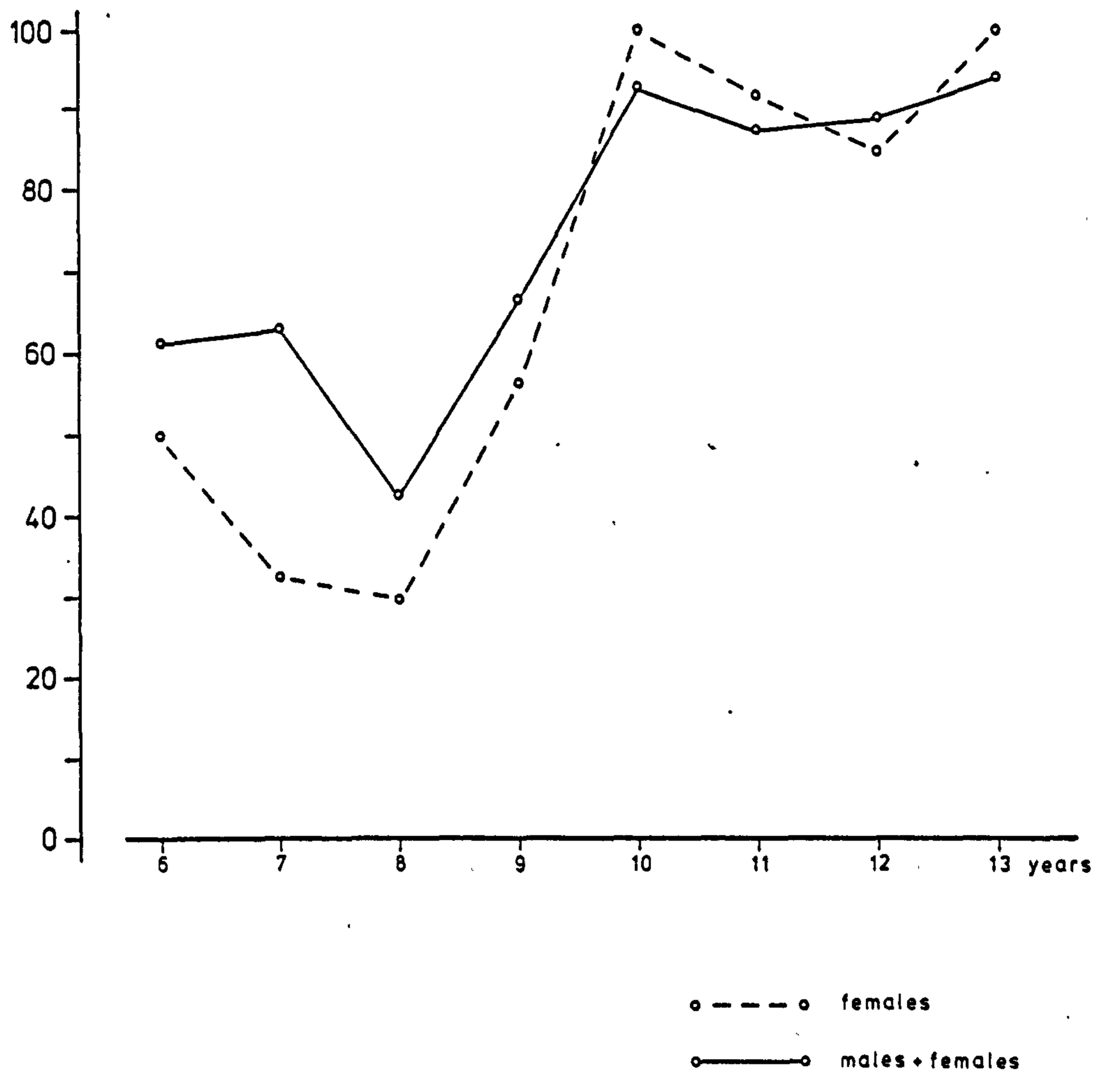
		6 years	7	8	9	10	11	12	13
SUBJECTS	number	18	19	23	29	29	24	28	18
	per centum	100.0	100.0	100.0	100.0	100.0	100.0	100.0	100.0
NEGATIVE		7	7	13	9	2	3	3	1
		38.9	36.8	56.5	31.0	6.9	12.5	10.7	5.6
POSITIVE		11	12	10	20	27	21	25	17
		61.1	63.2	43.5	69.0	93.1	87.5	89.3	94.4

figure R.3

RUBELLA IMMUNITY in GHARIAN

random survey: school children

per centum



CHAPTER 5.0 : MALARIA

5.1. Introduction

Malaria in Libya has always been of low, localised endemicity with the principal foci sited in the southern region (Fezzan). Thus, the prospect for eradication has always been good; such a programme was initiated by means of a pre-eradication survey in 1958. The programme was generally successful although a resumption of transmission occurred in 1964-1965, this being effectively controlled (Table Ma.1.).

The malarious areas of the southern region occurred in the few fertile valleys and a number of isolated oases scattered throughout some 600,000 square kilometers of otherwise arid desert.

The disease was endemic in the irrigated, fertile western coastal region (Tripolitania) but, due to low rainfall, the incidence remained low.

Little malaria was found in the more arid littoral of the eastern coastal region (Cyrenaica).

The principal plasmodium infecting man has been P.falciparum in the south and P.vivax in the north.

It has been estimated that in the seventeenth century 9.5 per thousand of the population were infected with malaria (approximately 6,000 persons). A calculation by the World Health Organisation suggested that 0.019 per centum of the national terrain was under threat in 1958, with 2.58 per centum of the population at risk. On the assumption that one third of these were actually infected the rate of infection in 1958 would approximate to that current in the seventeenth century : thus, no essential shift would appear to have occurred in three centuries.

At the present time, however, this stable situation is exposed to new influences; considerable spread of water bodies of all kinds relating to agricultural and housing development, container hazard in respect of the multiplicity of discarded tins, jars and bottles and an influx of immigrant

workers from many areas, to a greater or lesser degree malarious, Pakistan, India, Ghana, Gambia, Niger, Chad, Egypt, Turkey, Iraq, Tunisia, Algeria; many of these persons bearing potentially relapsing P.vivax infections and the occasional asymptomatic P.falciparum parasitaemia.

5.2. Historical Review

Little is recorded concerning the distribution of malaria during the Turkish occupation, which preceded the Italian occupation. Nachtigal (1879) recorded that all oases in Fezzan were highly malarious with the exception of Hofra el Shergia in the east, the southern Wadi Hekma and Bouanis oasis; he recorded also that Murzuk, then the capital city of Fezzan, suffered greatly from malaria as a result of the camel caravans arriving there from territories further south. Indeed, malaria was the principal reason for the transfer of capital city status and development from Murzuk to Sebha in 1962.

Soon after the arrival of the Italian occupying forces, in 1911, their physicians and biologists began to assess the prevalence of malaria and its vectors. Malaria was reported as being widespread in the Fezzan. In 1932 Lodato observed that in most cases a small proportion of women (7.0 - 9.0 per centum) were affected by malaria in contrast to that of children (96.0 per centum). Ricci (1934) found Kufra oasis to be free from malaria, with no anopheline mosquitoes being present; nevertheless, he recorded having treated a number of imported cases arriving from Egypt and the Sudan. Prior to 1935 several somewhat densely populated areas were discovered to be favourable to the development of anopheline mosquitoes. Two principal foci were defined and controlled by various means. Ain Zara at the southern edge of Tripoli city was originally an area of dunes containing swamps fed by ground water and by water from the Wadi Megenin during rain in autumn and winter. It was here that the caravan routes from the south terminated and where travellers assembled for the return journey; nowadays, the caravan trade has ceased and the area is desolate of traffic. Tajoura, to the east, in Cyrenaica, a similarly swampy area was successfully drained and the population given anti-malaria treatment.

West of Tripoli, small foci existed along the coast towards the Tunisian border, again in brackish marshland, in Zanzur, Zawia, Sabratha, Agelat and Zuara. Some 50 km. south of Misurata, itself 300 km. east of Tripoli, lies the marsh (sebkha) of Tauorga and here Ragazzi (1933) declared that one third of the population was infected prior to the inauguration of a land reclamation project.

Military operations in Libya in connection with the second World War interrupted all Italian activity and ultimately brought that occupation to an end.

In 1943 the British Army Health Service carried out a malaria survey in Libya; the following entomological findings were recorded. Anopheles coustani, Tauorga and Wadi Torgut; An.maculipennis, Tajoura, Wadi Scian, Corradini area, Fonduk Nagasa, Wadi Ga'am and Sidi-Bushiala; A. algeriensis, Wadi Ramla.

After the second World War the medical service of the British Civil Administration produced a further survey report.

In coastal Tripolitania the principal malarial mosquito is A.maculipennis. This species is not found in Cyrenaica nor around the Saharan oases where the principal species are A.sergenti and A.multicolor. Anopheles sergenti will breed in fresh, vegetated waters and A.multicolor in brackish water.

Control has been attempted in endemic areas by the canalisation of swamps combined with the use of larvicides. Residual spraying was commenced in 1949.

In 1954 the health and sanitation division of the United States Operation Mission (USOM) initiated a malaria control programme. Residual insecticide spraying commenced in 1955 and continued into 1957 at which point an agreement between the United States Government and the Kingdom of Libya established a Malaria Eradication Programme to be administered under a Joint Services Organisation : subsequently in 1958, the World Health Organisation also reached agreement with the Kingdom of Libya

covering its participation in the said Malaria Eradication Programme.

In conjunction with the 1954 USOM programme (Goodwin and Paltrinier, 1959) the following anopheline species were defined during 1954-1959 - Anopheles multicolor (Camb.); A.sergenti (Theo.); A.superpictus (Grassi); A.algeriensis (Theo.); A.coustani tenebrosus (Dontiz); A.coustani ziemanni (Greunberg); A.marteri (Senevet and Prunelle); A.hyrcanus (Pallas); A. hispaniola (Theo.); A.maculipennis complex; A.labranchiae (Fall); A.sacharovi; A.gambiae (reported by Lodato 1935); A.broussesi (reported from El Berket 1933).

During this same period the following species were defined in Tauorga - 1954 - A.coustani, adult and larvae; A.labranchiae, adult. 1955 - A.coustani, adult; A.labranchiae - adult; A.algeriensis - adult. 1956 - A.coustani - adult; A.algeriensis - adult. 1957 - A.sacharovi - two larvae (1st instar), first report from Libya.

Pre-eradication parasite surveys undertaken in 1957 (USOM), 1958 and first six months of 1959 (WHO) indicated that only P.falciparum and P.vivax were found, the former being predominant, and that malaria occurred in each of the three regions or governorates; as follows, 25 villages in Fezzan, 4 villages in Tripolitania, 2 villages in Cyrenaica.

In 1960 a Malaria Eradication Programme was organised by the Kingdom of Libya and WHO for the following objectives -

1. To achieve complete eradication of malaria in the whole country by means of appropriate measures.
   a) Residual insecticide application, anti-larval measures and chemotherapy.
   b) Epidemiological surveillance in order to ensure total case detection.
2. To promote training of national personnel of various categories in malaria eradication techniques.
3. To develop within the National Health Service, a mechanism for active vigilance against the re-introduction of malaria following its initial eradication.

A malariometric survey relating to this programme indicated that in the southern region (Fezzan) the prevalence of P.falciparum stood at 75.0 per centum against P.vivax at 25.0 per centum.

Parasite surveys conducted in 1957, 1958, 1959 and 1960 following residual insecticide spraying were all negative.

It would appear, therefore, that transmission had been interrupted effectively, despite the outbreak of 1964-65. Table Ma.1. indicates confirmed cases through the period 1963-1973.

A circuit of Libya, by the author, in 1979 taking in widely separated towns across the former regions yielded the following information.

Kufra : cases of P.vivax only are seen. The majority occur as imported cases in foreign immigrants from Sudan and Chad. No separate figures reported as distinct from general hospital records.

Sebha : Majority of cases are P.vivax with occasional P.falciparum; most of these occur in foreign immigrants from Chad and Uganda. Detailed figures are held in the Endemic Disease Centre and, for 1978, are reported in Table Ma.2, to indicate the scale of surveillance and the occurrence of imported cases.

Low densities of A.multicolor and A.sergenti are reported - two rounds of DDT spraying per annum control these populations.

Ghat : No malaria in Libyan nationals; 1500 immigrant Indians yielded 12 cases P.vivax.

Ghadames : No malaria reported.

In September/October 1980 a small outbreak of malaria involving 18 patients occurred in Zuara, a coastal town approximately 120 km west of Tripoli and 70 km east of the Tunisian border. On the fifth of September two Tunisian immigrants were diagnosed as having P.vivax infection. During the ensuing 36 days a further 16 cases were diagnosed; these comprised 11 Libyans who had never left Libya, one Sudanese, one Indian and three more Tunisians. The outbreak was controlled and extinguished.

5.3. Methods and Subjects

5.3.1. Methods

The 1980 outbreak in Zuara suggested that although transmission is uncommon in Libya there is a risk of the recrudescence and, possibly, of the re-establishment of malaria arising directly from the large numbers of foreign immigrants, authorised or otherwise, currently arriving and staying in Libya for periods ranging from six weeks to one year.

It was decided to attempt to quantify this risk by means of the indirect fluorescent antibody test (IFA) as described by Bruce-Chwatt et al. (1972) : to this end Dr. C.C. Draper, Senior Lecturer, Ross Institute, School of Hygiene and Tropical Medicine, London, kindly provided guidance, laboratory facilities and antigens for this purpose.

Blood specimens were collected by the finger-prick/filter paper method (Bruce-Chwatt et al. 1973), transferred to Liverpool and stored at -20°C prior to elution and testing.

All serum samples were screened at a dilution of 1 : 16 against Plasmodium fieldi antigen. All positive samples were tested again, in a four fold titration, at 1 : 64 and 1 : 256 against P.fieldi and at 1 : 16, 1 : 64 and 1 : 256 against P.falciparum antigen; those positive at 1 : 256 were again tested with the relevant antigen, at 1 : 1024 and 1 : 4096 in order to determine their end-point.

5.3.2. Subjects

5.3.2.1. One hundred adult labourers, all from India, were sampled on a port construction site in Zuara, the location of the 1980 malaria outbreak, approximately 120 km west of Tripoli.

5.3.2.2. Eighty-one labourers, all from India, were sampled on a hospital construction site in Ghat, a small town approximately 1,000 km south south west of Tripoli, in the far south west corner of the Fezzan adjacent to the Algerian border.

Here also, one hundred and six native school boys, in the age range 6 - 10 years, were sampled, in view of the possibility that they might function as a control group.

5.3.2.3. One hundred and forty-nine mixed immigrants who could be described generally as non-Asian, although a few Pakistanis were included, were sampled in Derna, a coastal town 300 km east of Benghazi, in Cyrenaica. These subjects came from Turkey, Bulgaria, Algeria, Tunis, Niger and the Gambia.

5.3.2.4. With the exception of the native school boys, who had never left Libya nor even Ghat, none of the subjects detailed above had been in Libya for more than six months.

5.4. Results

All results are summarised in Table M.3.

5.4.1. Zuara : Indian immigrants.

Of the 100 subjects tested 47.0 per centum were positive at a dilution of 1 : 16 to P.fieldi antigen : of these 5.0 per centum reacted positively to P.falciparum at the same dilution.

Lest any of these reactions were false at the level of 1 : 16 those with a positive titre of $\geqslant$ 1 : 64 are shown separately. Thus, 19.0 per centum were positive to P.fieldi and 4.0 per centum to P.falciparum.

5.4.2. Ghat : Indian immigrants

These 81 subjects yielded a positive rate of 46.9 per centum at 1 : 16 to P.fieldi antigen; of these 2.5 per centum reacted at this dilution to P.falciparum. At dilutions $\geqslant$ 1 : 64 the positive rates were 12.4 and 2.5 per centum for P.fieldi and P.falciparum respectively.

5.4.3. Ghat : Native school boys

All 106 boys failed to react at 1 : 16 dilution in the P.fieldi primary screen.

5.4.4. Derna : Mixed non-Asian immigrants

Of the 149 subjects 10.7 per centum reacted to the primary P.fieldi screen : of these 3.4 and 2.0 per centum were positive to P.fieldi and P.falciparum respectively at $\geqslant$ 1 : 64.

5.5. Discussion

For the purpose of primary screening P.fieldi antigen was employed as a detector of unspecified malarial infection in the experimental sera, tested at a dilution of 1 : 16. Accordingly, all non-reacting sera were classed as malaria negative. All primary screen positives were further tested at 1 : 64 and 1 : 256 dilutions against both P.fieldi and P.falciparum and any of those reacting strongly at 1 : 256 was further tested at dilutions of 1 : 1024 and 1 : 4096 against the relevant antigen.

Those sera reacting strongly to P.falciparum and less strongly to P.fieldi are classed as P.falciparum positive. In the reverse case those reacting more strongly to P.fieldi are classed as non-falciparum positives. It would be possible to define the individual nature of those infections by the use of species specific antigens but in this context it is necessary only to distinguish between P.falciparum, a dangerous parasite, and other species, somewhat less directly dangerous but more menacing in epidemiological terms since their human carriers may relapse and initiate transmission.

The results presented in Table Ma.3. indicate that roughly half of immigrants from India, 47.0 and 46.9 per centum from Zuara and Ghat respectively, yield IFA positivity in the primary screen whilst those from a variety of other locations outside Libya yield a rate of only 10.7 per centum.

Those sera not exceeding a titre of 1 : 16 may be either false positives or, at best, weak positive indicating old infections. Therefore, those sera reacting at a titre of 1 : 64 or greater are considered as indicating recent and/or heavy infections, even, possibly, asymptomatic parasitaemia.

The native school boys, in the event, function as a control group : having been born after the eradication campaign of the early nineteen sixties and not having travelled outside Libya or even very far from Ghat they yield a negative rate of 100.0 per centum.

In all immigrant groups there appears to be a rate, averaging 3.0 per centum, of P.falciparum positive at 1 : 64 or greater.

Indian immigrants present a positive rate between 10.0 and 19.0 per centum of strong reactions, 1 : 64 or greater, in respect of species other than P.falciparum. This rate is the potential relapse rate.

Immigrants from locations other than India, including a few Pakistanis, yield a positive rate of 3.4 per centum to non-falciparum or potential relapsing species.

Thus, all immigrants present a risk of either relapsing or non-relapsing malaria of the order of 3.0 per centum to the Libyan community.

Indian immigrants, in particular, present a risk to the community of relapsing malaria, principally P.vivax, as high as 19.0 per centum.

Furthermore, the native community at risk would appear to have little or no immunity as a result of past efficacious eradication campaigns.

5.6. Conclusion

A high degree of malaria control has been achieved in Libya : to the point where autochthonous cases had become uncommon until 1980 when such cases occurred, for the first time in five years,in Zuara, in coastal Tripolitania. This outbreak indicated the possible danger of the resurgence and establishment of malaria in Libya, as has occurred recently in Turkey; in several countries in south east Asia and in some in Latin America following earlier effective control.

There are many areas in Libya with a receptive ecology where transmission might occur if active human cases were introduced. The principal threat lies in the large groups of immigrant labour coming from distant malarious areas and in the illegal immigrants from contiguous malarious countries; to a lesser degree, also, from inadequately

protected Libyans returning from periods in malarious areas abroad.

This study has indicated that approximately half of immigrant labourers from India have been exposed to malaria and that of these as many as 19.0 per centum have antibody levels indicating recent or very recent infection. In these persons parasitaemia is often difficult to detect microscopically and many are asymptomatic : additionally, the majority has been exposed to relapsing forms of the infection. Whilst it would appear that immigrants from other areas present a lesser threat in terms of numbers of potential relapsing cases it is clear that the immigrant labour force from malarious areas present a real danger; particularly in areas, like Ghat, where 100.0 per centum of school boys are non-immune.

It would be realistic to assume that vector populations will have recovered in some measure from the assault delivered upon them, twenty years ago, by the national malaria eradication programme : except in the Fezzan, there have been no recent anti-anopheline programmes conducted.

The principal vectors in Libya, responsible in the past for oasis malaria, are An.multicolor and An.sergenti; other vector species exist, however, and An.labranchiae could pose a particular threat in coastal Tripolitanian marshland.

There is a clear need for a thorough national survey of Anopheline species, in order to define their current distribution and density.

5.6.1. The control of malaria requires wide knowledge of its epidemiology and calls for continuous imaginative investigation and appraisal. The following recommendations are offered.

5.6.2. Human reservoir.

5.6.2.1. Libyan nationals. All Libyan nationals visiting malarious areas should take prophylactic drugs one week before departure, throughout their stay abroad and for four weeks following their return. Chloroquine 300 mgm base weekly is satisfactory for use in all but chloroquine resistant areas and in these Maloprim one tablet (100 mgm dapsone and 12.5 mgm pyrimethamine)

weekly will suffice.

5.6.2.2. Immigrant labourers in receptive areas.

All immigrant labour should be given presumptive treatment for malaria, as follows, immediately on arrival or at registration.

Day 1. Chloroquine 600 mgm as a single oral dose (4 tablets, each 150 mgm base)

Day 2. Primaquine 30 mgm as a single oral dose (4 tablets each 7.5 mgm base)

If any person develops fever, malaria should always be excluded; if found, treatment is essential.

5.6.2.3. Illegal immigrants.

By definition this group is difficult to identify and to manage but, where possible, malaria must be excluded should they develop fever and, if found, treatment shall be given.

5.6.3. Vector control

Elimination or reduction of anopheline vector populations may be achieved by one of two strategies.

5.6.3.1. Larval populations.

The control of larval populations requires the abolition of all unnecessary bodies of water and the insecticidal treatment of those which cannot be removed.

Of the various insecticides available temephos (Abate) would be the compound of choice in Libya : the dosage employed should provide a final concentration of one part temephos per million parts of water. During periods of anopheline activity the frequency of application should be weekly.

5.6.3.2. Adult populations.

The control of adult populations is based primarily upon house spraying programmes designed to leave a deposit of insecticide on the inner walls of dwelling places and animal shelters.

In the absence of DDT resistance, a dose of 2 g/sq.m. of DDT has proved effective against malaria

vectors in Libya. Since a single treatment remains effective for a period of six months DDT spraying would be the most efficient strategy.

The effectiveness of house spraying is proportional to the thoroughness of an individual treatment and to the proportion of houses treated in the target area.

House spraying was employed in the national malaria eradication programme and is still used in the Fezzan.

A high degree of cooperation is required from the general public, some of whom will object to the inevitable domestic disturbance caused by such operations.

5.6.4. Administration

A permanent central anti-malaria service composed of experienced malaria workers intimately acquainted with local conditions is required.

This group shall maintain close links with the community health services and other relevant groups outside the health sector who could contribute variously to the campaign; for example, agriculture, irrigation, economic development and education authorities.

table Ma.1

MALARIA in LIBYA

notified cases 1963/73

	Fezzan				Tripolitania				Cyrenaica				annual total
	f	v	m	mx	f	v	m	mx	f	v	m	mx	
1963	25	3											28
1964	251	19		1			1						272
1965	380	30	1	2			1						414
1966	35	39											74
1967	6	9											15
1968	17	20	3										40
1969		1											1
1970						1*							1
1971			1			10*							11
1972		10				23*				3*			36
1973		3				41*				5*			49

f P. falciparum
v P. vivax
m P. malariae
mx mixed

* imported cases

table Ma.2

MALARIA in SEBHA (Fezzan)

Endemic Disease Centre surveillance

1978

1978 month	slide total	positive f	v	total
Jan	1059	1	2	3
Feb	1035	·	·	·
Mar	1915	·	1	1
Apr	1155	·	3	3
May	1135	·	2	2
Jun	1174	·	7	7
Jly	2031	·	3	3
Aug	587	·	7	7
Sep	979	1	1	2
Oct	2496	·	12	12
Nov	1582	·	5	5
Dec	1059	·	1	1
	16,207	2	44	46

INDIA	5	All foreign cases P.vivax;
PAKISTAN	10*	except one P.falciparum*
MAURITANIA	4	from Pakistan
NIGER	2	and at least
CHAD	3*	one P.ovale*
SUDAN	2	from Chad
PALESTINE	1	
TURKEY	1	
FOREIGN IMMIGRANTS	28	
LIBYAN NATIONALS	18	

table Ma.3

MALARIA ANTIBODY SURVEY

selected immigrant groups : IFA

SUBJECT			ANTIBODY RESPONSE				
			⩾ 1:16			⩾ 1:64	
location	category	total number per centum	total number per centum	fieldi	falciparum	fieldi number per centum	falciparum
ZUARA	INDIAN IMMIGRANTS	100 100.0	47 47.0	42 42.0	5 5.0	19 19.0	4 4.0
GHAT	INDIAN IMMIGRANTS	81 100.0	38 46.9	36 44.4	2 2.5	10 12.4	2 2.5
GHAT	NATIVE SCHOOLBOYS	106 100.0	nil -	nil -	nil -	nil -	nil -
DERNA	NON-ASIAN IMMIGRANTS	149 100.0	16 10.7	13 8.7	3 2.0	5 3.4	3 2.0

CHAPTER 6.0 : LEISHMANIASIS

6.1. Introduction

Leishmaniasis occurs in many locations, in diverse clinical forms and epidemiological patterns. The causative organism belongs to the genus Leishmania of the family Trypanosomiidae and is adapted to man, canines and rodents. Man is infected by the bite of a phlebotomine sandfly carrying promastigotes of Leishmania in its proboscis, usually having fed previously upon an animal reservoir.

Four principal clinical forms exist, as follows -

6.1.1. Cutaneous leishmaniasis : occurs in the old world in scattered foci throughout the tropics and sub-tropics; caused by L.tropica.

6.1.2. Chiclero's ulcer : occurs throughout central and south America; caused by L.mexicana. Also called New World cutaneous leishmaniasis.

6.1.3. Espundia : occurs in south America, notably Brazil; caused by L.brasiliensis.

6.1.4. Visceral leishmaniasis : occurs in Mediterranean littoral, Middle East, India, East Africa, China and south America; caused by L.donovani. Also called kala-azar.

6.2. Historical Review

6.2.1. Human Cases

Several authors from the last days of the Turkish occupation and throughout the Italian occupation recorded cases of both cutaneous and visceral leishmaniasis. Tashim Ibrahim (1910), a Turkish military physician, reported two cases of visceral leishmaniasis from Tripoli; one, a seventeen year old boy, born in Homs, had lived in Tripoli since the age of six and the other, a Jewish boy of eleven years, had always done so : both cases were confirmed by the detection of amastigotes in spleen biopsy smears examined by Charles Nicolle of

the Institut Pasteur, Tunis.

The Italian authors were generally of the opinion that leishmaniasis in Libya was uncommon by comparison with Sicily and southern Italy.

Mazzolani (1933) diagnosed eleven cases of kala-azar Tripolitania, two of which were confirmed by bone marrow examination. Onorato (1931) diagnosed twelve cases in the same region.

Patane (1928) reported having found only two cases in Cyrenaica during the period 1912 - 1925; one being a child in Tolmetta, near El Merj, and the other in Benghazi hospital, reported by a Dr. Costa, had come from Eritrea, presumably an adult colonial official.

Dar (1978) reported a case of visceral leishmaniasis from Libya which was confirmed microscopically in bone marrow aspirate and subsequently in culture; he also recorded this as the first autochthonous case in Libya. This latter claim was refuted as being erroneous by Dedet (1979).

In the first quarter of 1971, 40 cases of cutaneous leishmaniasis were registered in Gharian province, principally in Nalut, Tigi and El Gosh. In 1972, 60 cases were registered in Gharian province and 241 cases in Zawia province, mainly from Surman. In 1973, 239 cases in Gharian province and 925 in Zawia province were registered. Ashford et al. (1976) examined suspected cases and confirmed the cutaneous infection in 25 subjects, demonstrating the parasite microscopically or in culture.

Approximately 20.0 per centum of 300 Yugoslav immigrant labourers were found to be infected at Bir Ayad; presumably, as a result of their invasion of a previously uninhabited area for the purpose of land developments. Ashford and Gebreel found the situation much improved during 1980, particularly at Bir Ayad, as development projects achieved completion.

Figure L.1. presents the national incidence for the period 1971 - 1980.

6.2.2. Animal Reservoir

Dogs, jackals, hyaenas and rodents are said to be hosts to leishmaniasis.

Funaioli (1972) examined 117 dogs in Tripolitania, finding two infected, and 638 in Cyrenaica of which seven in El Merj were infected, one in Tolmetta and one in Benghazi.

Ashford et al. (1977) concentrated upon rodents in north west Libya. Amastigotes of L.tropica were found in ear smears from six of eight Psammomys obesus and in one of four Meriones libycus; these rodents were trapped in Bir Ayad wadi where permanent burrows exist. No parasites were discovered in P.obesus, Meriones spp. and Gerbillus spp. trapped on the flood plain, where less permanent burrows existed.

6.2.3. Suspected Vectors

Gabbi and Visentini (1910) identified P.papatasi as being common in Tripolitania and collected these in connection with an epidemic three-day fever. Patane (1928) identified P.papatasi in a scanty collection of Testi, made throughout 1912 - 1916 in Cyrenaica, and collected three females personally at Benghazi after much searching; he also collected six female P.perniciosus with difficulty at Benghazi. Nitzulescu and Nitzulescu (1933) collected P.langeroni in Cyrenaica.

Health Data publication 42 (Walter Reed Army Research Institute, 1968) states that cutaneous leishmaniasis, caused by Leishmania tropica, is endemic in Libya. The principal vector, probably,being P.papatasi, P.perniciosus and P.major may also be vectors. The report adds that the occasional cases of visceral leishmaniasis seen in Libya are probably imported.

Ashford et al. (1977) state that while no single species is ever abundant both P.papatasi and P.longicuspis occur in all habitats in north west Libya; the former being most common within houses and, far from dwellings, in rodent holes; the latter more commonly found in peridomestic habitats. They also record the collection and identification of P.sergenti, Sergentomyia minuta, S.fallax and S.clydei.

6.3. Methods and Subjects

6.3.1. Methods

It was decided to attempt to discover something of the situation concerning transmission in the area west of Gharian, in north west Tripolitania on or about the Jebel Nefusa escarpment (Map L.1.) by means of skin testing.

6.3.1.1. Two antigens were each prepared as follows. Promastigotes in culture were washed in normal, physiological saline three times by means of centrifugation. The parasites were resuspended in a solution of 0.5 per centum phenol in saline for injection (BP) to a final concentration of 10^6/ml and the suspension stored at $+4.0^{\circ}C$ until use.

One antigen, A561, derived from a Libyan parasite strain and the other, B304, from a Jordanian (West Bank) strain. A control antigen comprised only 0.5 per centum phenol in saline for injection (BP).

6.3.1.2. In field use each antigen was injected intradermally, in a dose of 0.5 ml, into the extensor surface of the right forearm.

6.3.1.3. Reaction wheal size was measured by means of a graduated flexible perspex disc, at forty-eight hours following inoculation of a single antigen.

6.3.2. Subjects

People were invited to attend at one of three locations for skin testing and to return forty-eight hours later for wheal assessment. (Map L.1.)

6.3.2.1. Gawasem

On a plateau 400 m above sea level in heavily farmed land, bearing grain and fruits. Here 267 subjects attended for skin testing, receiving antigen B.304, and a further group well in excess of 50 received control antigen.

6.3.2.2. Rabta

On the Jefara plain, below the escarpment, about 100 m above sea level, grain bearing land requiring irrigation for fruit production. Some 246 subjects attended, some receiving antigen A561 and others, approximately half, receiving antigen B.304. A further group, in excess of fifty, received control antigen.

6.3.2.3. Mizda

On the Jebel Nefusa 90 km south of Gharian, at approximately 700 m above sea level; all agriculture dependent upon irrigation. Some 79 subjects attended and received antigen A561. A further group, in excess of fifty, received control antigen.

6.4. Results

6.4.1. Numbers tested

It is a requirement of skin testing that experimental subjects should attend first to receive antigen injection and then attend again after forty-eight hours for wheal measurement.

Table L.1. presents the numbers of subjects inoculated and read, in respect of both parasite antigens; the control figures are not included.

Thus, 194 subjects were read in Gawasem, 214 in Rabta and 50 in Mizda.

6.4.2. Differential wheal measurement

Table L.2. presents the differential reaction, measured in millimetres of wheal diameter, to both parasite antigens and to the control : in the latter case, only 50 subjects in each location were recorded from an excess actually measured.

6.4.3. Positive reaction rates for each location are presented in Table L.3.

6.4.3.1. Positive reaction : Gawasem

The rate of positive reactions in young people up to 19 years of age was low, being 2.5 per centum; subjects in age group 20 – 39 years yielded 43.8 per centum, with this peak rate declining to 30.8 and 23.8 per centum in 40 – 59 years age group and in those older than 59 years, respectively.

6.4.3.2. Positive reaction : Rabta

The positive rate in this location indicated a rising trend on a steady level, being 21.4, 45.9, 63.3, 66.0 and 66.7 per centum in age groups 0-9, 10-19, 20-39, 40-59 and greater than 59 years, respectively.

6.4.3.3. Positive reaction : Mizda

The positive rate here also exhibited a rising trend on a lower level than that of Rabta being nil, 5.0, 16.7 and 22.2 per centum for age groups 0-9, 10-19, 20-39 and 40-59 years respectively.

6.5. Discussion

Since the subjects of this study attended the skin testing sessions by general invitation they may be said to have been self selected rather than randomly sampled. These groups are also biased against those living or working at a distance from the inoculation assembly point; farmers and nomads, for example. Indeed, adult males and adolescents of either sex were few and for this reason Table L.3. presents no sex analysis. Age definition was difficult in subjects over 30 years of age.

Of these self selected subjects from Gawasem, Rabta and Mizda (Table L.1.) 72.7, 87.0 and 63.3 per centum, respectively, of those receiving antigen initially returned for the wheal size measurement sessions, so reducing the original sample. It is assumed that the higher return rate in Rabta was due to a heightened awareness of the danger of infection since nine cases had been reported in 1980/1981.

Table L.2. presenting the differential reaction to the two parasite antigens and the control antigen indicates that antigen B.304 gave larger numbers of small diameter reactions in the range 1 - 4 mm than did its fellow A561 : this effect may indicate poor antigenicity. It may be that this factor distorted the positive rate for Gawasem subjects, who received this antigen exclusively.

It was not possible thoroughly to examine all positive reactors; some of these had scars which they related to a leishmaniasis-like disease whilst others had leishmaniasis-like scars which they could not relate to any particular condition. Many positive reactors had no scars of any sort.

The positive results for Gawasem would appear to suggest that transmission virtually ceased in that area, approximately twenty years ago; a situation difficult to account for since life continues in this area much the same as it has done since 1950. It may be that the poor subject sample is further distorted by the poor antigen used there. Certainly,

fewer people live in dwellings incorporating individual underground caves and the annual spraying regime conducted throughout the past ten years is very efficiently executed in this particular area.

In Rabta there would appear to be a high rate of transmission generally.

In Mizda there appears to be a relatively low rate of transmission which may increase in future following housing and other development projects there which leads to human invasion of previously uninhabited areas as has occurred at Bir Ayad in the recent past.

6.6. Conclusion

6.6.1. Cutaneous leishmaniasis remains endemic in the north west of Tripolitania.

6.6.1.1. Transmission appears to be at a low rate in Gawasem area but skin testing requires to be repeated there on better population samples and employing a better antigen than B.304 in order to clear confusion.

6.6.1.2. In Rabta transmission appears to be more intense than previously suspected, despite the fact that all houses are said to be sprayed : it must be assumed that local spray teams are not operating efficiently.

6.6.1.3. The findings in Mizda area, where leishmaniasis was not expected, suggests that transmission occurs over a wider area than hitherto suspected. It is possible that transmission will intensify as a result of development work in this area.

6.6.2. The following recommendations are urged.

6.6.2.1. Repetition of skin testing in Gawasem employing better antigen.

6.6.2.2. Skin testing to be mounted in other related areas in order to determine more closely the current extent of transmission.

6.6.2.3. The improvement of population sampling for activities defined in 6.6.2.1. and 6.6.2.2.

6.6.2.4. The improvement of case diagnosis and notification.

6.6.2.5. The improvement of local spray team efficiency; training, equipment checks, transport.

6.6.3. Further field research recommendations.

6.6.3.1. A survey of phlebotomine sandflies to determine species distribution and density in the Jebel Nefusa escarpment area.

6.6.3.2. A survey of rodents to determine species distribution and density in the Jebel Nefusa escarpment area.

figure L.1

CUTANEOUS LEISHMANIASIS in LIBYA

case notifications 1971/79

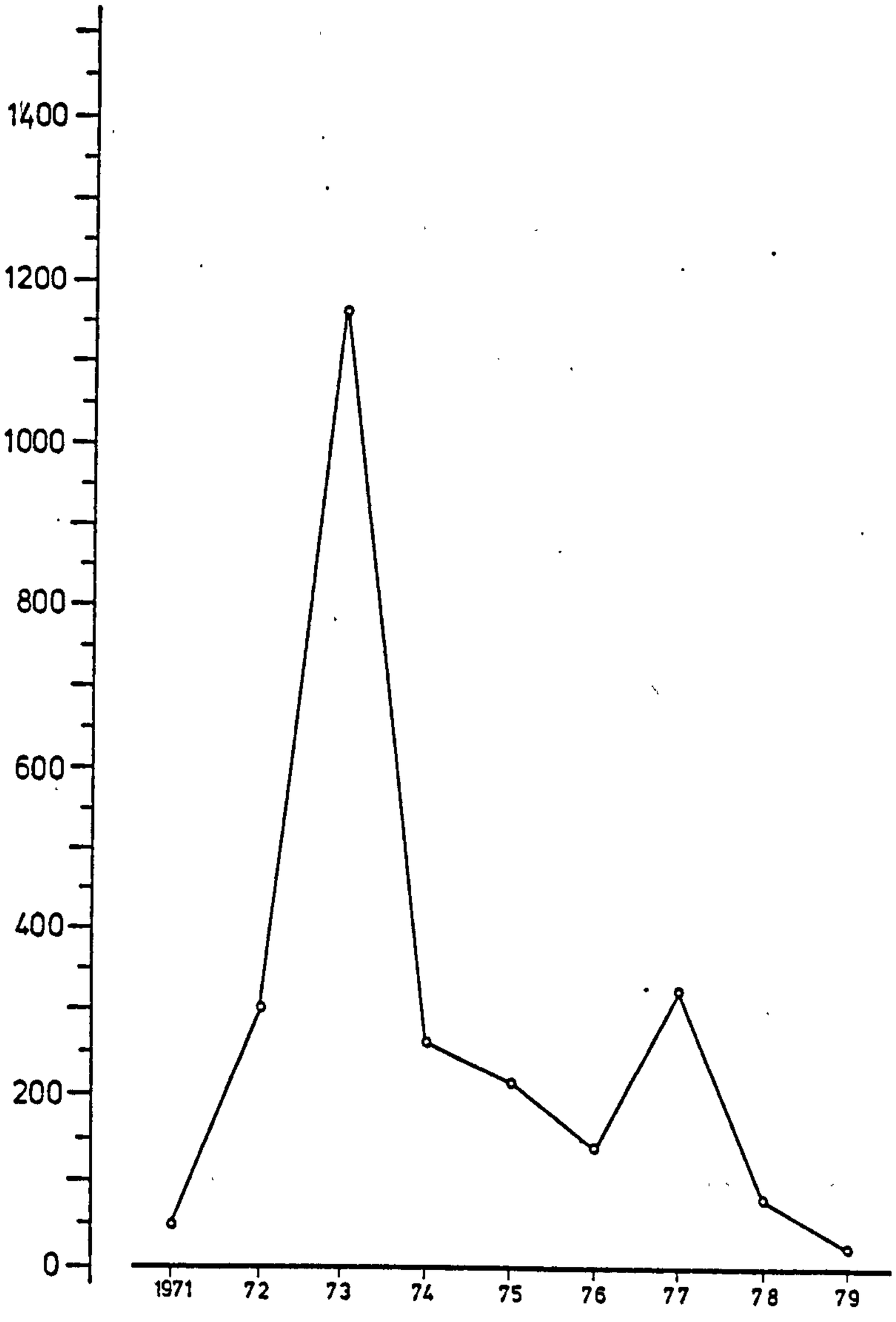


table L.1

LEISHMANIASIS in north west TRIPOLITANIA

skin test survey

location	inoculated number	inoculated per centum	assessed number	assessed per centum
GAWASEM	267	100.0	194	72.7
RABTA	246	100.0	214	87.0
MIZDA	79	100.0	50	63.3

table L.2

LEISHMANIASIS : skin test survey

wheal assessment

ANTIGEN	REACTION : wheal diameter / mm. nil	1	2	3	4	5	6	7	8	9	10	>10	total
A.561	137	5	5	9	11	9	20	10	10	4	7	17	244
B.304	115	13	20	15	17	8	10	3	2	3	6	2	214
CONTROL	136	6	6	1	1	nil	nil	nil	nil	nil	nil	nil	150

table L.3

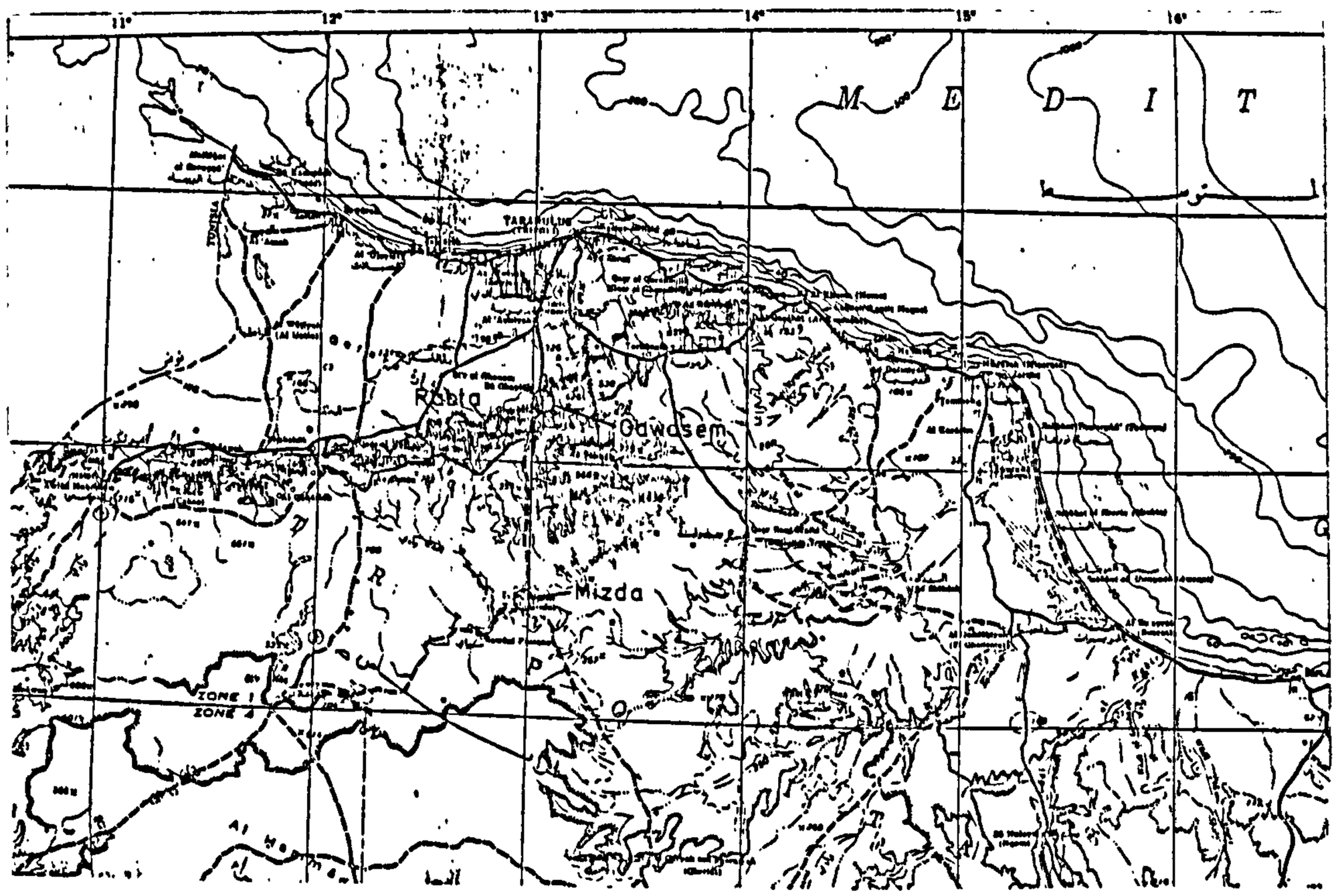
LEISHMANIASIS : skin test survey

age grouped : positive rates

LOCATION		0-9 yr	10-19	20-39	40-59	> 59	total
GAWASEM	NUMBER ASSESSED	38	80	16	39	21	194
	POSITIVE per centum	2.6	2.5	43.8	30.8	23.8	
RABTA	NUMBER ASSESSED	42	61	49	47	15	214
	POSITIVE per centum	21.4	45.9	63.3	66.0	66.7	
MIZDA	NUMBER ASSESSED	15	20	6	9		50
	POSITIVE per centum	nil	5.0	16.7	22.2		

map L.1

NORTH WEST TRIPOLITANIA - Gawasem, Rabta, Mizda



GAWASEM plateau

a panoramic view of sandstone hills

GAWASEM village

a disused dwelling : cave entrance at right

CHAPTER 7.0 : ECHINOCOCCOSIS

7.1. Introduction

"When the liver is filled with water and bursts into the epiploon, in this case the belly fills with water and the patient dies" Hippocrates, BC 460-379; aphorism 55, Section VII.

Echinococcosis is a cyclozoonotic infection of man and certain other mammals caused by the adult and larval stages of the genus Echinococcus (family Taeniidae).

This cestode infection presents an important public health problem found, in varying degrees, on every continent. Despite the attention which echinococcosis, or hydatidosis, has received from parasitologists, veterinary surgeons, physicians and public health workers there remain important gaps in the knowledge of this infection which continue to hamper efforts directed to its treatment, prevention and control.

The nature of the infection renders its initiation and development inapparent for a number of years. No especially effective drug treatment exists and the surgical removal of cysts, once defined, carries serious risk of complication.

The sheep provides the principal meat eaten by Libyans and bears strong cultural weight being slaughtered ceremonially at the time of religious intervals and at social celebrations such as marriages. In urban areas sheep are nurtured in domestic compounds and even inside houses and these are slaughtered in situ as need occurs; in such areas some house dogs are kept as pets or guards but many wild dogs enter towns, from the desert on the fringe, and feed on rubbish heaps, at municipal abattoirs and from individual garbage cans.

The Moslem tradition has it from the hadith, or sayings of the Prophet Mohammed, some seven statements to the effect that the dog is unclean. Accordingly, as children grow up and begin to read and otherwise learn they begin to behave culturally as Moslems and abhor the dog but prior to this, from infancy, they may caress or hand feed

domestic dogs incurring considerable risk of infection early in life. In rural areas where traditional life continues no dog enters a tent but will lie at a distance when not actively functioning as a flock guard or marshal; nonetheless, ritual sheep slaughter occurs at a higher rate than in towns, since butchers meat is not available, and animal waste is eaten by the dogs. It is of interest in this connection to note the observation from Lebanon (Schwabe and Abou-Daoud,1961) that little difference in the incidence of dog bite occurred between Christian and Moslem children up to the age of ten years; thereafter, the incidence in Christians was twice that in Moslems. It was considered that this index of dog contact was reflected in the rate at which echinococcosis affected the religious components of the population.

Other sources of meat, cattle, goats and camels are infected as well as sheep (Table E.1.).

It has been suggested that the gibli, the dust laden wind from the south, may play an important part in the dissemination of ova since it blows towards the principal centres of population (Fossati, 1970).

7.2. Historical Review

Echinococcosis is endemic and enzootic in Libya but there is a paucity of reliable epidemiological data.

Casoni (1911) conducted development work upon his well known, and still extant, skin test in Tripoli. Medulla (1931) stated that infections are common in camels and other domestic animals. Cicogna (1961) recorded that dogs are much infected with echinococcus, these tapeworms being found in approximately 60.0 per centum of herder's dogs examined and 10.0 per centum of town dogs, whilst the larvae were found in 40.0 per centum of sheep, 70.0 per centum of cattle and 20.0 per centum of pigs; and that 57 human cases were treated in the government hospital in Tripoli, throughout 1951 - 1961.

Fossati (1970) presented data, collected throughout the preceding ten years, in respect of thoracic hydatidosis : of 147 surgical cases 116 were located in the lung, 10 in the pleura, 8 in the mediastinum, 4 the heart, 4 in the ribs, 3 the diaphragm and 2 in muscle. He comments also upon 19 cases of thoracic complication caused by cysts in the liver. In 1978, Dar and Taguri published a retrospective survey of surgical case records in respect of echinococcosis in Benghazi hospitals throughout 1971 - 1976; the age/decade analysis is presented graphically in Figure E.1. These cases comprised 83 males and 97 females.

No epidemiological surveys have been conducted in Libya amongst the general population. Indeed, this is not easy to undertake since no particularly reliable means is available for the purpose.

7.3. Methods and Subjects

7.3.1. Methods

The Casoni test is known to produce a considerable number of false positive results (Kagan, 1968; Varela-Diaz and Coltorti, 1974).

A review of certain serological techniques (Bout et al. 1976; Felgner, 1978; Matossian et al. 1979) led to the decision to adopt an enzyme linked immunosorbent assay (ELISA) employed for diagnostic purposes by Professor M. Clarkson, Professor of Veterinary Preventive Medicine, Liverpool University. Professor Clarkson kindly supplied antigen for this purpose.

7.3.1.1. The ELISA was based upon the original method of Engvall and Perlman (1972), incorporating the microplate modification of Voller et al. (1976a) and the further modifications of Bullock and Walls (1977). The antigen was a simple hydatid cyst fluid obtained from a horse and employed at a dilution of 1 : 200. Test sera were diluted to 1 : 200. Goat antiserum to human immunoglobulin IgG and labelled with horseradish peroxidase was employed at 1 : 200. Reaction of the enzyme substrate, orthophenylenediamine (OPD), was stopped

by means of 3M sodium hydroxide. The test was conducted in 96 well microplates using 300 µl volumes. The ELISA reaction was based upon a fixed time of 50 minutes and read visually.

7.3.1.2. In order to refine this ELISA for use with a spectrophotometer optimal reagent dilutions were determined by the chequer board technique described by Voller et al. (1976 b). Reagent consumption was improved, as follows : antigen dilution 1 : 5000; rabbit antiserum to human IgG conjugated with horseradish peroxidase 1 : 10,000 : test sera diluted to 1 : 300 and the OPD reaction stopped with 25 µl 2N sulphuric acid. The test was conducted in 96 well Linbro/Titertek polystyrene plates in 150 µl volumes. The ELISA reactions were read by spectrophotometer at 490 nm.

The sensitivity of the test was balanced by means of ten sera derived from English born, adult Caucasian subjects thought not to have been exposed to Echinococcus sp., and so presumed to be antibody negative, and ten sera derived from Kenya born, adult Turkana known to be immediate post-operative cases of echinococcosis and so presumed to be antibody positive. Subsequent replicate testing confirmed these assumptions of antibody value.

7.3.1.3. All experimental testing was undertaken using one Turkana positive antiserum as a reference standard in pair with one English Caucasian negative antiserum and two positive antisera from Libya, of somewhat lesser value than the positive reference as positive control reactions. Reaction was controlled by the reference positive value ignoring time.

7.3.1.4. All test sera were withdrawn from experimental subjects and processed as described in 2.3 and stored, thereafter, in 100 µl aliquots at - 70°C.

7.3.2. Subjects

A small rural town, El Abiar, with a population approximating to 9,000 and situated some 50 kms east north east of Benghazi was selected as the study area. The town is surrounded by rocky desert inhabited by Bedouin tribesmen traditionally tending sheep.

For the purpose of an initial survey the following subjects were bled in the field, during the period 1979/1980.

7.3.2.1. El Abiar township

Approximately 200 hundred subjects were bled within the township, of which some 150 were schoolchildren between six and twelve years of age. The remainder being secondary school children and adults.

7.3.2.2. El Abiar environs

A number of Bedouin encampments within a radius of 30 kms were visited and fifty subjects were bled, as available. These proved to be six children below six years, twenty-one between six and twelve years, one of thirteen years along with twenty-two adults.

7.4. Results

The results of ELISA test described in 7.3.1.2 and 7.3.1.3. are presented in Table E.2.

7.4.1. El Abiar township

The positive rate, calculated overall, proved to be 8.38 per centum. The related rates for sub-groups being 6.87, 12.5

and 16.67 per centum for school children of six to twelve years, thirteen to sixteen, and adults, over sixteen years, respectively.

7.4.2. El Abiar environs

The overall positive rate was 12.0 per centum. The sub-group rates being nil for children below six years, with 9.52 and 18.18 per centum for children of six to twelve years and adults, respectively. The single child of thirteen years proved to be negative.

7.5. Discussion

Table E.1. illustrates the fact that the incidence of echinococcosis in man depends directly on the incidence in animals. The infection rate is high in indigenous camels, goats and cattle, and, although sheep yield a lower rate, 3.0 per centum, this figure may relate to the fact that those slaughtered for food tend to be young rather than old animals; however, the sheep in Libya is in intimate contact with a high proportion of the population and exists in numbers at least double that of the human population. The sheep is probably the most important of the intermediate hosts as its Echinococcus cysts are fertile and so infective to man and to dogs; the latter having easy access to offal and other slaughter waste as well as to naturally dying animals : jackals and foxes also have easy access on sheep ranges.

Nothing is known of the fertility of cysts in other intermediate hosts slaughtered for food. Table E.1. indicates that the infection rate in animals imported for slaughter as food is lower than that in local animals, except in the case of camels; usually, these are killed within ten days of arrival. Imported camels have a higher rate of infection than local camels, 47.0 per centum : this is to be expected in the light of figures from areas bordering Libya. The infection rate in Morocco is quoted by Briouga (1974) as being 100.0 per centum in 1964 : other figures being 40.0 per centum in Algeria in 1968/69 and 30.0 per centum in Tunisia in 1978. It is estimated (Mann, 1978) that of 1.3 million camels in eastern Africa 90.0 per centum are infected.

The most obvious source of infection is in sheep dogs in rural areas and stray dogs in urban and semi-urban areas. Faecal contamination of pasture by dogs is bound to occur continuously. Although cysts are very

common in camels and cattle, the fertility of these is in doubt : even if they were fertile it is much less likely that dogs would have much access to these animals apart from the increasing number of camel deaths on the highway as a result of collision with motor vehicles, particularly after dark.

In urban areas disposal of offal and condemned carcasses is usually inadequate. In Benghazi, in particular, disposal is conducted principally at the municipal refuse dump, at Qwarsha, about 10 kms south of the town; the intention is to dispose by incineration but this is commonly incomplete and many stray dogs feed here as do others from nearby villages. In El Abiar, the slaughter house has an inadequate disposal system; again with its groups of stray dogs, as well as children taking offal from it.

Whether the gibli is responsible for the dissemination of ova leading to pulmonary infection by the respiratory route is not known but certainly any ova so disseminated could enter domestic water storage tanks or contaminate directly any exposed foodstuffs, so increasing the risk of infection by ingestion. Dar and Taguri (1978) showed that there were 53.3 per centum of liver cases as against 30.6 of lung cases in a particular group. According to Sherlock (1981) most ova are trapped in the hepatic sinusoids and that 70.0 per centum of eventual cysts occur in the liver; a few ova pass through the liver and the right side of the heart to be held up in the pulmonary capillary bed to give rise to pulmonary cysts.

Table E.2. indicates positive rates of 8.38 per centum in the township area and 12.00 per centum in the rural area. The difference between these values is not statistically significant ($P => 0.05$).

Nevertheless, despite the uneven sampling, there appears to be a parallel rising trend of infection with age between these two samples on the basis of the age groups selected : 6 - 12 years, primary school children; 13 - 16 years, secondary school children and adults over 16 years of age.

Thus, although there is no difference between the township and rural areas, where the principal environmental variation is one of housing construction and density the fact remains that on this evidence echinococcosis

is endemic in the community at a rate approximating to 10.0 per centum.

Table E.2. further indicates that infection occurs in children of six years and this may be explained by their ignorance of hygienic principles, their plantigrade habits at an earlier age, their proximity to dogs and the continual placing of objects, frequently dirty, into their mouths. The symptoms and signs of unilocular echinococcosis are not usually manifest for five to twenty years following initial infection (Ferro, 1946); it is noteworthy, in this connection, that the case analysis in Figure E.1. indicates the peak rate at 21 - 30 years of age.

7.6. Conclusions

7.6.1. General

In Libya traditional animal husbandry and the practice of domestic slaughter of animals contribute to the maintenance of the Echinococcus cycle. Evidence in other countries suggest that changes in traditional practice may affect transmission dramatically and there is need for the study of cultural habits to define points which might be pertinent in the favourable alteration of the incidence of echinococcosis.

7.6.2. Economic considerations

The cost of this disease in animals is high and in heavily affected areas may have a significant influence on the national economy; in this sense it must be understood that echinococcosis control may be more than an investment in health.

The cost of the disease in man should be determined by the price of surgical treatment plus hospital costs over approximately two months per patient and the pressure upon the hospital service. The patient also loses about four months from his work with consequential loss of productivity. Some mortality and varying degrees of permanent disability ensue.

7.6.3. Control

An echinococcosis control programme in Libya requires political commitment and decisions : of fundamental importance is the establishment of a long term surveillance programme as an indication of progress. Experience in other countries suggests four important functions for a control authority (Gemmell, 1978). The first concerns operational funding and its planned expansion over many years; the second concerns the selection of personnel and their training in health education and other relevant matters; the third, requiring collaboration with other authorities, involves the collection and evaluation of baseline and subsequent surveillance data; the fourth concerns the direction of continuing education.

The measures to be taken in echinococcosis control arise from the life cycle of Echinococcus.

In the majority of cases the dog is the final host of the parasite, man, sheep, goats, cattle and camels being intermediate hosts. .Stray dogs are the principal source of environmental contamination. Accordingly, all such dogs must be eliminated. The most feasible and economic means being euthanasia : special weapons are available employing either tranquilizing or euthanizing darts.

Domestic pet dogs may become infected and pass the infection to the family, particularly to the young children. These dogs must be examined regularly and treated as necessary. The limitation of arecoline hydrobromide as a treatment for adult Echinococcus in dogs has been recognised for some time : of the newer anthelmintics praziquantel (Droncit) is reported to be markedly active against both adult and larval infections of E.granulosus (Thakur, 1978)

In highly endemic areas, like Libya, the treatment of dogs, even with praziquantel, is nullified by prompt reinfection where the control programme is inefficient.

It would be of particular importance to prevent dogs from gaining access to offal and animal waste at municipal abattoirs, village slaughter houses and on farms.

Health education should be aimed at the general public, with special emphasis on schools, by means of leaflets and the powerful instruments of radio and television.

7.6.4. Recommendations for future survey in Libya

7.6.4.1. To determine the prevalence of infection and distribution of echinococcosis among animals and human and the relationship between them.

7.6.4.2. To ascertain whether animal/human echinococcosis is caused by an especially virulent strain or sub-species of E.granulosus.

7.6.4.3. To discover whether an unknown reservoir, other than dogs, exists such as hyaenas, foxes or jackals.

7.6.4.4. To study the occurrence of dust borne, or aerogenic, infection as related to the gibli and to define whether this causes pulmonary echinococcosis as a result of the respiratory system being a primary portal of entry.

7.6.4.5. To study the role of water borne infection; in water holes, pools and storage tanks.

7.6.4.6. To carry out surveys in all alleged endemic areas, sheep and camel breeding areas, using ELISA for both humans and animals.

7.6.4.7. To conduct a clinical trial of mebendazole which has proved effective in mice (Heath and Chevis,1974). If this should prove as effective in man, then the danger of secondary infection following surgery may be avoided : the drug might possibly kill primary cysts and obviate surgery in many cases.

table E.1

ECHINOCOCCOSIS in ANIMALS

BENGHAZI SLAUGHTERHOUSE

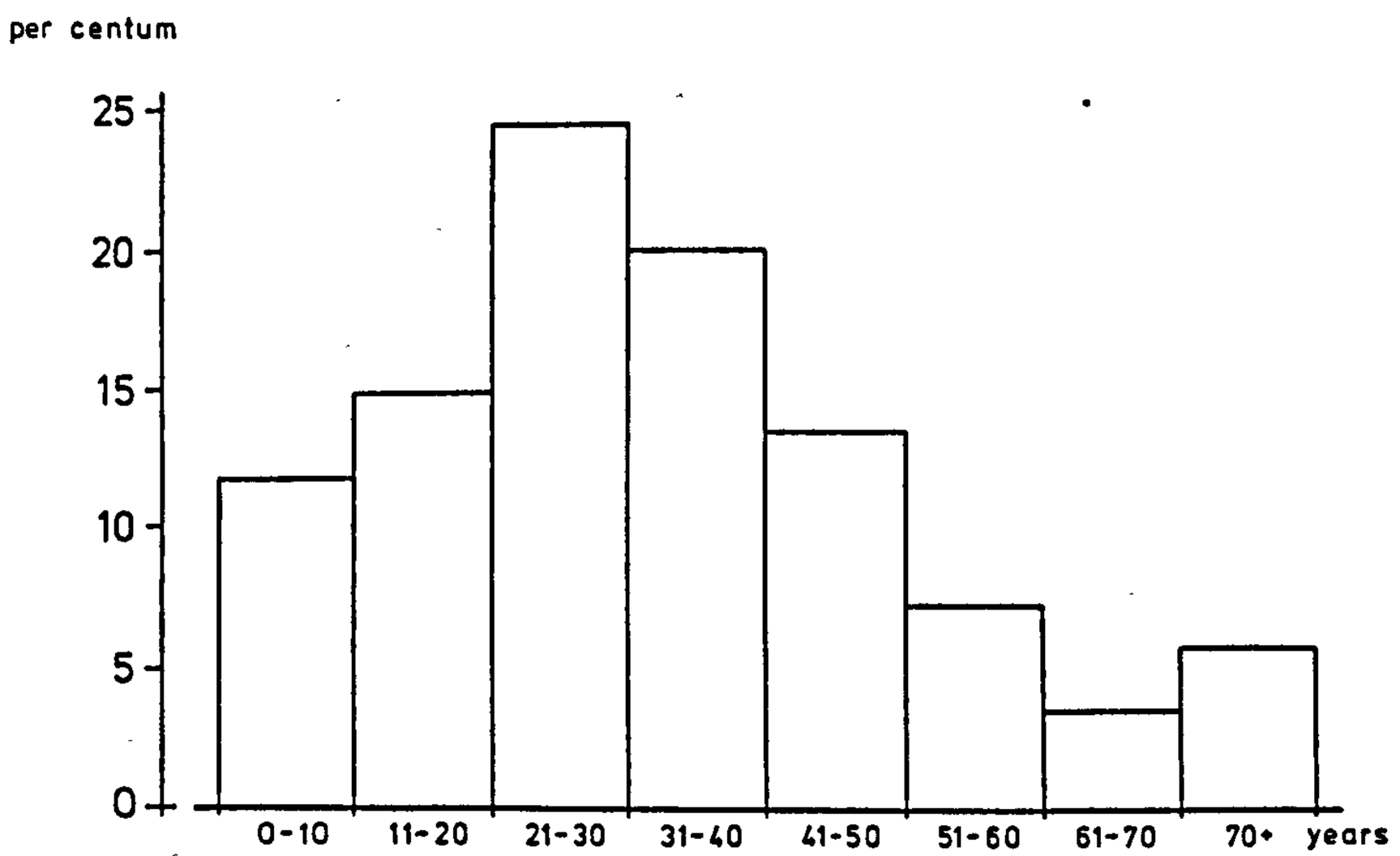
per centum

	SHEEP		CATTLE		GOATS		CAMELS	
	IMPORT	LOCAL	IMPORT	LOCAL	IMPORT	LOCAL	IMPORT	LOCAL
1975	0.64	3.08	0.75	8.98		nil	14.9	1.48
1976	0.37	1.82	3.46	10.60		5.45	47.0	17.6
1977	1.34	3.34	5.0	13.90		18.2		29.1

figure E.1

ECHINOCOCCOSIS in SURGICAL CASES 1971/76

BENGHAZI HOSPITALS



source: DAR & TAGURI 1978

table E.2 ECHINOCOCCOSIS in EL ABIAR
random survey: Elisa positivity

TOWNSHIP		< 6	6	7	8	9	10	11	12	13	14	15	16	>16
NEGATIVE	male		22	1	1	17	6	2	26	4	nil	nil	nil	7
	female		18	4	nil	7	2	6	10	6	4	3	4	3
	sub-total		40	5	1	24	8	8	36	10	4	3	4	10
POSITIVE	male		3	nil	nil	1	nil	nil	nil	nil	nil	nil	1	nil
	female		2	nil	nil	nil	nil	1	2	nil	nil	1	1	2
	sub-total		5			1		1	2			1	2	2
TOTAL	167		45	5	1	25	8	9	38	10	4	4	6	12
positive rate per centum	8.38		11.11	nil	nil	4.0	nil	11.11	5.26	nil	nil	25.0	33.3	16.67

AGE GROUPS

< 6	6-12	13-16	> 16
	9	3	2
	131	24	12
	6.87	12.50	16.67

RURAL AREA														
NEGATIVE	male	3	2	1	3	nil	1	2	2	nil				5
	female	3	3	nil	nil	2	2	nil	1	1				13
	sub-total	6	5	1	3	2	3	2	3	1				18
POSITIVE	male	nil	nil	nil	nil	nil	nil	nil	nil	nil				3
	female	nil	nil	nil	1	nil	nil	nil	1	nil				1
	sub-total				1				1					4
TOTAL	50	6	5	1	4	2	3	2	4	1				22
positive rate per centum	12.00	nil	nil	nil	25.0	nil	nil	nil	25.0	nil				18.18

nil	2	nil	4
6	21	1	22
nil	9.52	nil	18.18

El ABIAR rural area :

a traditional Bedouin encampment

El ABIAR rural area :

a modern Bedouin encampment

BENGHAZI rubbish dump

inadequately incinerated sheep carcasses

BENGHAZI environs

Echinococcus in stray dog

CHAPTER 8.0 : SCHISTOSOMIASIS

8.1. Introduction

Schistosomiasis is endemic in the southern region of Libya (Fezzan) where, for example, a prevalence of 86.0 per centum has been recorded in the Wadi el Shati.

Foci of infection exist in the coastal northern region (Tripolitania), principally in Tauorga, 50 km south of Misurata, and in the coastal eastern region (Cyrenaica) principally in the environs of Derna.

Generally the disease runs a mild course with a low output of ova.

The schistosome species involved are Schistosoma haematobium, which is predominant, and S.mansoni.

The molluscan intermediate host in respect of S.haematobium is Bulinus truncatus (B.contortus formerly); other possible host species have been identified but not fully proven in this role. The intermediate host in respect of S.mansoni being Biomphalaria alexandrina; other possible host species have been identified but not proven in this role.

8.2. Historical review

Ghigi (1913- 1914) reported finding Bulinus species in the Derna valley during a study of Libyan fauna. Traversa and Macotta (1916) recorded a case of bilharzia in Sicily as having been imported in a soldier from Derna. Mazzone (1917) reported a similar case in an Italian soldier serving in Derna. Fulci (1918) reported five cases of bilharzia imported to Italy in soldiers returning from service in Derna. Patane (1924) reported two indigenous cases of S.haematobium infection in Derna (both of these from the family of the author of this thesis); he also identified Bulinus contortus found at Ras el Ain in that area. In 1929 Zavattari demonstrated the occurrence of S.haematobium infection in Derna; he also identified B.contortus and stated that the endemic zone was confined to Derna town and the Derna valley. Medulla (1931) again reported the occurrence of bilharzia in Derna.

In the Fezzan, Durand (1926) established that both bilharzia and B.contortus occurred in Janet, 85 km south west of Ghat. Zavattari (1932) reported S.haematobium infection in Ghat but found no B.contortus. Lodato (1932) described cases of urinary schistosomiasis in Ubari, as well as the presence of B.contortus. Andolfato and Fedeli (1934) described similar cases in Murzuk; Giordano (1935) in Ghat and Impallomeni (1937) in Brak. Casati et al (1938) were the first to undertake a mass survey and examined 1195 subjects thus revealing S.haematobium infection in Tousca, Germa, Traghen and Mehruga. Another large scale survey by Nastasi (1939) discovered bilharzia in Sebha, Ubari, Shati and, again, in Murzuk and Ghat : he was the first to record the presence in Ghat of Biomphalaria species. Boscardi (1943) identified Bulinus (physopsis) africanus in Ghat and also observed the ova of S.mansoni in some persons. Vermeil (1951, 1952), (Vermeil et al. 1952) collected B.contortus from the slopes of the Tassili mountains to the east of Ghat and from wells in the environs of Ghat, especially El Berket, Feueat and Auenat. Berry (1964) reported the discovery of a species of Bulinus in both Sebha and Brak, which he thought might prove to be either a new species of within the variation range of B.truncatus. Yasuraoka (1966) and Halawani (1966) both reported S.haematobium infection from Sebha, Shati, Ubari and Murzuk. Dursoir (1967) reported cases of bilharzia from Gragra, El Berket, Mahrouga, Gedid (Sebha) and Traghen; he identified Bulinus species in Sebha and Murzuk.

In Tripolitania, Zavattari (1929) observed B.contortus in small water courses near Dersh and Tgutta, also in the Rumia spring near Jefren and in Forga near Jado. He found no snails in Ain-Zara close to Tripoli; as a result, presumably, of earlier attempts at drainage in pursuit of antimalaria measures. Goodwin (1957) was the first to report the occurrence of S.mansoni infection in Tauorga; here 126 stool specimens fixed in MIF preservative, yielded 8 positive for ova; a related snail collection was identified by Berry as Biomphalaria of a possibly new species and he later collected the same type from the principal well pool. Shortly afterwards, Halawani (1966) and Yasuraoka (1966) confirmed that this species was actually Biomphalaria alexandrina. Halawani also conducted a human case survey, finding 31.0 per centum positive from a group of 63 stool samples derived from persons living close to the spring pool.

During the period 1955-1963 six indigenous cases of S.haematobium infection were recorded by the Preventive Health Service in Derna. Berry (1964) identified B.truncatus in Dabbusiah spring, 50 km west of Derna. Hamami (1965) verified the endemicity of S.haematobium by means of 20 cases in school children who had never left the town. He also collected many specimens of B.truncatus from the Dabbusiah spring. Halawani (1966) reported 16 urine specimens as positive from 240 collected from schoolboys in Derna; 56 stool specimens from the same group proved negative for S.mansoni. He was able only to collect B.truncatus from water pools near the Dabbusiah spring, but not from the spring itself.

The Health Data Report of the Walter Reed Army Institute of Research (1968) includes the following information. In the latest WHO report available, no cases of schistosomiasis are listed as occurring in Libya in 1963. In another source, 345 cases are reported for that year (4 from Tripolitania, 13 from Cyrenaica, 328 from the Fezzan). The actual number of cases occurring, especially in the Fezzan where the disease is endemic, is probably many times more than that reported. It has been estimated that over 80 per cent of the inhabitants in some parts of the Fezzan are infected : other areas of the Fezzan are free of the disease. It is highly probable that infections contracted in Libya are all due to Schistosoma haematobium and that infections with S.mansoni are contracted elsewhere. It has been reported that S.haematobium infection is a relatively mild disease among the Libyans living in endemic areas, but a much more serious disease among the inhabitants who move from non-endemic areas to the endemic areas.

The report also carries the following concerning vectors -

The fresh-water snail Bulinus contortus is probably the principal intermediate host for S.haematobium. This snail is found in open wells, artesian wells and irrigation ditches. It cannot survive in brackish waters. In areas of the Fezzan where wells are protected to prevent invasion by snails or where waters are brackish, both the snail and the disease are absent. Other Bulinus species occur which may be intermediate hosts for S.haematobium. Several Biomphalaria species are found in Libya.

These are suspected of being intermediate hosts for S.mansoni, but infected snails have not been found in the country.

El-Gindy (1969) undertook a survey in 96 schools of the Fezzan in an attempt to define foci of S.haematobium; of these 58 had been surveyed by the end of the academic year 1970 comprising 9,600 pupils of whom 672 proved positive for ova (7.0 per centum). This survey revealed less than 5.0 per centum haematuria in positive cases and that less than 1.0 per centum had an ova load of 300 per urine sample, although these were varied in volume and the volumes not specified. El-Gindy also surveyed Ghat collecting 233 stool samples from sites where Biomphalaria snails yielded cercariae; Biomphalaria alexandrina was found in shallow water in Ghat and Biomphalaria pfeifferi was found in large numbers in a spring pool in El-Berket. Snails were found in all types of sweet water bodies but not in water of high salinity.

[illegible] the school at Tauorga; 1458 school children yielded 262 ova positive stools (18.0 per centum). A further survey of the general population, ranging in age from 1 to 86 years and comprising 2723 persons, yielded 643 ova positive (24.0 per centum). Data analysis of age and sex indicated that males and females suffered equal exposure with a peak prevalence in the second decade of life. Those persons residing nearest the spring pool suffered a higher rate of infection than those living at a distance.

8.3. Methods and Subjects

8.3.1. Methods

It was decided to attempt to assess, by serological methods, the prevalence of S.mansoni in marshland surrounding a natural spring pool in Tauorga, 50 kms south of Misurata, itself some 300 kms east south east of Tripoli.

8.3.1.1. This area constitutes the only focus of S.mansoni infection in Libya and the parasitological data derived from normal surveillance microscopy is poor, for a number of reasons. First, considerable difficulty is experienced by the surveillance team in obtaining samples of stool from the inhabitants; a matter of cultural resistance. Second, the individual intensity of infection

is thought to be low which may lead to false negative reporting; especially since only the simple smear technique is employed. Third, laboratory equipment is sparse and in poor condition, which increases the possibility of false negative reporting. Fourth, transport facilities are unreliable which further increases the difficulty of surveillance, since the field team operates from Misurata.

8.3.1.2. Reasonably effective surveillance of schistosomiasis incidence is required in the light of a molluscicíding programme introduced in 1976 and intended to free the principal water body from infection since it is now channelled for the irrigation of a nearby agricultural development project. A barrier fence, intended as an additional protective measure, was erected to enclose the pool in 1979/1980.

8.3.1.3. It was decided to employ the finger prick collection of blood onto filter paper, as mentioned previously in 5.3.1. (Bruce-Chwatt et al: 1973); this it was felt would be more acceptable to both school children and field team staff than the collection of stools.

8.3.1.4. The ELISA as described by McClaren et al. (1978) was selected as the method of choice for the experiment. Soluble egg antigen (SEA) was made available, most generously, by Dr. Moira McClaren, Research Fellow, Ross Institute, School of Hygiene and Tropical Medicine, London.

A number of modifications to that method was introduced, as follows -

i. The test was conducted in 96 well Linbro/ Titertek polystyrene plates, using 150 µl volume of each reagent.

ii. Antiserum to human immunoglobulin G, prepared in a rabbit, was labelled with horseradish peroxidase.

iii. Orthophenylenediamine (OPD) was used as the enzyme substrate and enzyme hydrolysis was stopped by means of 25 µl 2N sulphuric acid.

iv. Colour reactions were read spectrophotometrically at 490 nm.

8.3.2. Subjects

8.3.2.1. All children, approximately 1700, in Tauorga schools were bled by finger prick onto filter paper during October and November 1979.

Simple qualitative stool/ova data were made available for these children.

8.3.2.2. It was planned to repeat both finger prick blood and stool sampling, in the same months, during 1980 and 1981 for both the original 1979 group and for each new intake of six years old children in each of those years.

At this point the author is sad to relate that Dr. Ahmed Sami Abdul Razak, the medical officer in charge of the surveillance field team, unfortunately died during 1980, as a consequence of a road accident.

The loss of Dr.Ahmed so disrupted the work and organisation of the team that neither useful samples nor data were collected in 1980.

8.3.2.3. The fact that Dr.Ahmed was not replaced and that surveillance laboratory technical staff were constantly changed meant that only with difficulty was the

available proportion of the original 1979 school population blood sampled again in 1981. In addition, all those children who had entered Tauorga schools during 1980 and 1981 were blood sampled.

No stool samples had been collected in 1980 nor could be in 1981; therefore, no stool/ova data were generated for this 1981 school population survey.

Furthermore, of the original 1979 school groups (Table S.1.) coded as TD, TE, TF, TG, TH, TM, TMH, TS and TSH, neither group TH nor TM could be sampled before the summer vacation of 1981 prevented access to them : accordingly, these two groups were not available for comparison with the 1979 population sample.

In these circumstances 1605 double finger prick samples were collected in mid-1981 : these comprising the 1981 cohort of the original 1979 sample population and the 1981 sample population.

8.3.2.4. All blood samples taken onto filter paper in this study were thoroughly air dried and stored at +4.0C for approximately ten days prior to being conveyed by hand of the author to Liverpool where they were stored permanently at -70°C until testing.

8.4. Results

8.4.1. Table S.1 presents the result of ELISA in respect of the 1979 sample population compared with the qualitative stool/ova results for that year. The table is arranged to define the correlation between the two methods in respect of the 1664 school children sampled for both purposes, grouped by schools. The age groups quoted are nominal, employed for the classification of schools as primary, intermediate and secondary.

8.4.1.1. The summary figures indicate that 115 subjects were positive for S.mansoni ova and that 556 subjects were ELISA positive : these figures represent prevalence rates of 6.9 and 33.4 per centum.

8.4.1.2. The correlation figures, where stool and ELISA results agree, are revealed as 91, a positive rate of 5.5 per centum, and 1084, a negative rate of 65.2 per centum.

8.4.1.3. The non-correlation figures, where stool and ELISA results differ, are revealed as 24 where stool examination is positive and ELISA negative, and 465 where stool examination is negative and ELISA positive.

8.4.1.4. Thus, the correlation rate for both tests is 70.7 per centum and the non-correlation rate 29.3 per centum.

8.4.1.5. cont'd

These results suggest that ELISA is considerably more sensitive than the stool examination as practised in Tauorga, for although ELISA may detect antibody in persons recently cured of infection it is known that no official chemotherapeutic campaign is carried out in the area. It is reasonable also to expect microscopy to be less sensitive in an area of low grade infection, particularly in early low grade infection.

In respect of specificity McClaren (1978) defined the specificity of the soluble S.mansoni egg antigen, as used here, as being 95.0 per centum in the case of S.mansoni subjects and, in cross reaction with S.haematobium, of the order of 83.0 per centum in Egyptian children, for example : these two categories yielded mean extinction values of 0.96 and 0.53, at E490, respectively. Cross reaction in respect of bird schistosomes, bancroftian filariasis and other helminths yielded extinction values in the range 0.31 - 0.41 E490. Neither S.haematobium nor W.bancrofti occurs in Tauorga. Nothing is known of avian schistosomes or, indeed, of other helminths in this area but Figure S.1. indicates that extinction values for this series were predominantly in excess of 0.40 E400 except in young children. Thus, it may be presumed that this experiment achieved a specificity in respect of S.mansoni of the order of 95.0 per centum.

8.4.2.2. The ELISA positive rates being 5.0 per centum at six years, rising to peaks of approximately 60.0 per centum at both 12 and 15 years.

8.4.2.3. The mean E_{490} values range from 0.33 at six years and 0.37 at seven years, thereafter ranging from 0.41 to 0.51 per centum.

8.4.3. Table S.2. presents the sex analysis, by school groups, for all three sample groups in respect of ELISA.

8.4.3.1. The 1979 sample population is designated A and corresponds to the data presented in Table S.1., except that groups TH and TM are omitted since they are not available for further comparison with subsequent samples. A represents, therefore, the original sample.

8.4.3.2. Those children available in 1981, deriving from the original sample A, are designated B.

8.4.3.3. Those children entering the relevant schools after 1979, and so not part of sample A nor of its cohort B, are designated C.

8.4.3.4. In order to avoid unnecessary reference to this mass of data the essential data is consolidated in Table S.4.

8.4.4. The administrative difficulties referred to in 8.3.2.2. and 8.3.2.3. caused a single step two year wastage in respect of the repeat sampling of the 1979 population (A), aggravated in the case of TE, a boys secondary school, where a large loss arose from the dispersal of the older subjects in the A population since the original age range, nominally 12 - 15 but actually nearer 13 - 16 years became effectively 15 - 18 years in 1981.

8.4.4.1. These factors altered considerably the population size available in 1981. Additionally, there is a natural variation between population A and its cohort B where some A positives become B negatives and vice versa. Accordingly, Table S.3, and its continuation S.3a, presents, first, a diagrammatic scheme for this comparison, followed by the comparative data for each school group arranged in that scheme.

8.4.4.2. The comparative data for A and B and the results of their group significance tests are consolidated in Table S.4.

8.4.5. Table S.4. presents the comparison of prevalence rates for each school group, as determined by ELISA, in each sampling, A, B and C; with the corrected variation as between 1979 population A and its cohort B, and between 1979 population A and 1981 population C.

8.4.5.1. The cohort B prevalence changes were calculated by means of X% - Y%; see Table S.3. scheme.

8.4.5.2. The significance tests for groups TD, TE, TG, TS, and TSH employed McNemar's paired test and for groups TF and TMH exact probability was calculated; see Table S.3.

8.4.5.3. In respect of TD, for example, it will be seen that the prevalence rate of 5.1 per centum in the 1979 sample population A of 138 subjects became 19.5 in the 1981 cohort B of 77 subjects, giving an apparent increase of 14.4 per centum.

The corrected increase A : B arising from Table S.3, is 11.7 per centum and is statistically significant ($P = <0.05$).

The variation in prevalence as between sample population A and sample population C constitutes a reduction A : C of 1.7 per centum, which is not statistically significant.

8.4.5.4. This series of prevalence variations is considered below.

8.5. Discussion

The intention of this study was to evaluate a sensitive and specific serological test for the purpose of community screening, in respect of S.mansoni infections of low intensity, in order to replace stool collection and examination with all the attendant difficulties : clearly, the collection, labelling and processing of approximately 1700 stool specimens is a formidable task, requiring resources not adequate currently in Libya, compared with the execution of the same number of finger pricks, with the blood collected onto filter paper; the latter process being much more acceptable to the subjects concerned.

8.5.1. Table S.1. indicates that a positive rate for S.mansoni infection in school children of 33.4 per centum was detected by ELISA, whereas a rate of 6.9 per centum was derived from qualitative stool smear examination. Furthermore, the correlation between these two methods totalled 70.7 per centum and the non-correlation rate was 29.3 per centum. The latter rate comprises ELISA failure, in the face of positive ova findings, of 1.4 per centum and 27.9 per centum of stool examination failure where ELISA antibody findings are positive. The first component is small enough to ignore but the second component must be considered. Two possible causes exist in this respect : either the ELISA positives are false or the stool negatives are false.

McClaren et al (1978) showed that specificity to S.mansoni antibody is high in respect of the soluble egg antigen they employed, of the order of 95.0 per centum, with cross reaction to S.haematobium antibody of the order of 83.0 per centum in Egyptian children : these categories gave mean E_{400} values of 0.96 and 0.53, respectively. Other subjects affected by bird schistosomes, bancroftian filariasis and certain other helminths yielded mean E_{400} values in the range 0.31 - 0.41. Earlier unpublished surveys in Tauorga have excluded the transmission of S.haematobium in the area and filariasis does not occur. Nothing is known of bird schistosomes nor of other helminths affecting indigenous humans in Tauorga, or elsewhere in

Libya. Nevertheless, Figure S.1. indicates that mean E_{490} values in this study are generally well in excess of 0.40 : it is acknowledged that no precise study of the relationship between E_{400} values in respect of the alkaline phosphatase ELISA reaction and E_{490} values in respect of the horseradish peroxidase ELISA reaction has been undertaken but parallel readings in the author's laboratory suggest reasonable compatibility

It would seem reasonable to suggest that the balance of probability for non-correlation lies with false negative stool reporting.

8.5.2. The presence of specific antibody, as detected here, will be either the result of an active infection, recent or well established, or occur at some point during recovery from such an infection, and it is useful to distinguish between these states. Salih et al (1978) attempted this in the course of a clinical trial employing hycanthone treatment of S.mansoni infection, in Sudanese subjects, where a rise in antibody titre was detected by a worm antigen ELISA system approximately six weeks following treatment. This was considered to be the result of antigen released from dead or dying worms. McClaren et al (1978) studied two chimpanzees, infected with S.mansoni, and detected a slight rise in antibody titre, following hycanthone treatment, when employing a worm antigen in ELISA but not when employing an egg antigen.

It may be presumed that no such effect was detected in this study which employed egg antigen : moreover, no official chemotherapeutic campaign is carried out in Tauorga.

8.5.3. Molluscicide (Bayluscide) is applied by means of twice yearly perimeter spraying of the Tauorga spring pool (see Map S.1.) and of the principal open outflow channel which carries water westwards to a pump house whence water is discharged by enclosed pipes either southwards to a minor agricultural area or further westward into an extensive open

reservoir, which impounds water for volume measurement prior to gravitational discharge into an open channel irrigation system serving the principal agricultural area to the north-west.

Molluscicide treatment began in 1976 and is monitored by means of snail search and examination by a resident Egyptian malacologist of considerable experience; as necessary, focal spraying is carried out in addition to the routine applications.

A perimeter fence enclosing the spring pool was completed in 1978 : it is furnished at two points with large double gates which have never been closed since their installation; no barrier guards the outflow channel where it pierces the wall and many of the iron bars forming the fence upon the wall have been removed by inhabitants who wish to gain access to the pool at points convenient to their house or school.

Thus, molluscicide treatment is efficient and the barrier fence useless.

8.5.4. Table S.2. shows fully, including sex analysis, the positive ELISA rates for those school groups sampled in 1979 (A) capable of further comparison with their 1981 cohort (B) and a further sample in 1981 (C) : no statistical significance attended the sex analysis.

8.5.5. Table S.4. consolidates these data, irrespective of sex, and may be considered together with Map S.1. against the foregoing descriptive background.

8.5.5.1. Clearly, TS carries the highest positive rate for A, 76.1 per centum, and this is not surprising since this school is within one kilometre of the principal spring pool and the open outflow channel to the pump house. Many of these children will have been infected prior to molluscicide operations. The cohort B shows no deterioration of the previous rate, in fact,

a slight decrease is detected but of little significance. However, the 1981 sample population C, including children taken in to the school during 1980 and 1981, shows a marked decrease in prevalence, 26.1 per centum ($P = < 0.001$). This improvement in the situation may be attributed to a combination of efficient molluscicide treatment of the water bodies relevant to the school and related housing and to the emphatic health education of the teaching staff by the author and the keen, and continuing, interest shown by the headmaster, who is a native of Tauorga. The barrier can have played no part.

8.5.5.2. Group TE carries the next highest A rate and this has some relation to the fact that it is the only secondary school in the area and, accordingly, its pupils are older than other schools and are drawn from all schools in Tauorga; its physical relation to water bodies is less important. Despite the wastage loss by age of many after the A sample the prevalence in B and C appears to be stable in these older children.

8.5.5.3. TSH has an A rate remaining stable at B but indicating improvement at C in a decrease of 9.7 per centum ($P = < 0.01$). This school contains children originally from the Tauorga natural drainage area with their families rehoused on the principal agricultural development area and since remaining out of contact with water bodies of any magnitude or permanence.

8.5.5.4. TD, TF and TMH remain stable, broadly speaking, at a low prevalence throughout A, B and C samples. TF and TMH are in discrete and distant parts of the natural drainage system and are not affected by molluscicidings, presumably. It is possible that the increase of some significance in cohort B of TD is due to some older boys swimming in the reservoir nearby and perhaps setting up some transmission in this gift of a swimming pool of great attraction where no molluscicidings takes place since it is below the pump-house.

8.5.5.5. TG, another case of subjects rehoused within the past five years, previously had a positive A rate of 27.7 per centum and indicated a decrease in cohort B of 43.0 per centum ($P = <0.01$) and a decrease in C of 27.0 per centum ($P = <0.001$). This school is furthest from possibly dangerous water and this, in conjunction with the adequate water facilities in the new housing, could account for the reduction between A and C samples, but no reason can be advanced for the marked decrease between A and B. This requires investigation.

8.5.6. Whilst some groups indicate broadly stable prevalence and others markedly decreased prevalence there is no increase in any group as between 1979 A and 1981 C.

8.6. Conclusion

8.6.1. The ELISA is an adequate test, when employing a soluble egg antigen, for the community screening of low intensity S.mansoni infections.

Such screening is sufficiently sensitive to enable serial monitoring of community prevalence in order to determine the effect of control measures.

8.6.2. The ELISA has indicated a beneficial effect of molluscicide treatment bearing upon an entire community in Tauorga.

8.6.3. Barrier fences, intended to prevent human access to water, are an inefficient means of protecting communities from schistosomiasis unless properly designed, operated and maintained.

8.6.4. Barrier fences constitute an affront to the local community and their cost would be better employed in furnishing communal laundry and shower units, employing a safe supply of water, for the washing of clothes affords an important occasion for social intercourse, especially to Moslem women.

8.6.5. It is recommended that annual ELISA screening of the school population in Tauorga should be undertaken.

8.6.5.1. Subjects detected as ELISA positive should be assessed by a suitable ova concentration technique in order to determine the relationship between ELISA positive and ova positive status.

8.6.5.2. All positive subjects should be given a single dose oral drug (e.g.oxamniquine) in order to reduce transmission levels.

8.6.5.3. Treated subjects should be carefully studied in order to determine the immunological response to chemotherapy.

figure S.1

SCHISTOSOMIASIS in TAUORGA SCHOOL CHILDREN

age analysis: 1979 sample population

OVA POSITIVE, ELISA POSITIVE & mean E_{490} values

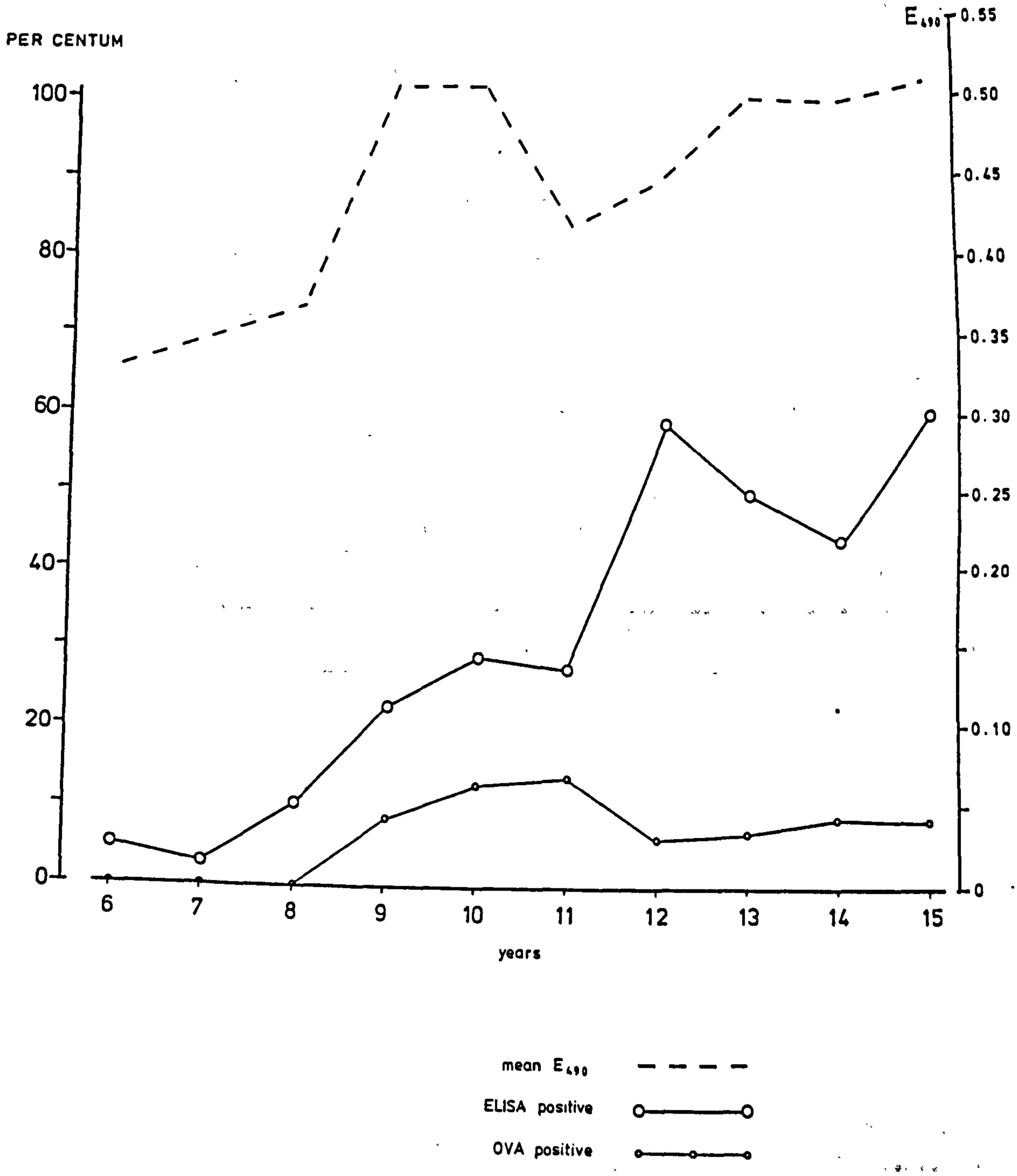


table S.1

SCHISTOSOMIASIS in TAUORGA : S.mansoni in children

1979: positive Ova & Elisa compared

GROUP CODE	AGE RANGE	TOTAL	Stool Elisa + -	Stool Elisa + +	Stool Elisa - -	Stool Elisa - +
		number per centum	number per centum	number per centum	number per centum	number per centum
TD	6-12	138 100.0	nil nil	nil nil	131 94.9	7 5.1
TE	12-15	397 100.0	12 3.0	20 5.0	193 48.6	172 43.4
TF	6-12	125 100.0	nil nil	nil nil	115 92.0	10 8.0
TG	6-12	274 100.0	nil nil	1 0.4	197 71.9	76 27.7
TH	10-12	53 100.0	nil nil	1 1.9	38 71.7	14 26.4
TM	11-16	211 100.0	2 1.0	nil nil	92 43.6	117 55.4
TMH	6-12	122 100.0	nil nil	nil nil	120 98.4	2 1.6
TS	9-13	134 100.0	9 6.7	65 48.5	23 17.2	37 27.6
TSH	6-12	210 100.0	1 0.5	4 1.9	175 83.3	30 14.3
	totals	1664 100.0	24 1.4	91 5.5	1084 65.2	465 27.9

CORRELATION 70.7

NON-CORRELATION 29.3

TOTAL SUBJECTS 1664

OVA positive 115 = 6.9 per centum
ELISA positive 556 = 33.4 per centum

table S.2

SCHISTOSOMIASIS in TAUORGA SCHOOL CHILDREN

three samples measured by Elisa

GROUP CODE	AGE RANGE	subject group	A original 1979 sample population			B 1981 available cohort of population 1979 A			C 1981 new sample population		
			+ ve number per centum	− ve n p c	total n p c	+ ve number per centum	− ve n p c	total n p c	+ ve number per centum	− ve n p c	total n p c
TD	6-12	total	7 5.1	131 94.9	138 100.0	15 19.5	62 80.5	77 100.0	8 3.4	228 96.6	236 100.0
		male	5 4.6	103 95.4	108 100.0	11 16.2	57 83.8	68 100.0	2 1.6	120 98.4	122 100.0
		female	2 6.7	28 93.3	30 100.0	4 94.4	5 55.6	9 100.0	6 5.3	108 94.7	114 100.0
TE	12-15	total	192 48.4	205 51.6	397 100.0	12 37.5	20 62.5	32 100.0	28 37.8	46 62.2	74 100.0
		male	192 48.4	205 51.6	397 100.0	12 37.5	20 62.5	32 100.0	28 37.8	46 62.2	74 100 0
		female									
TF	6-12	total	10 8.0	115 92.0	125 100.0	1 1.2	83 98.8	84 100.0	3 7.0	39 93.0	42 100.0
		male	6 9.0	61 91.0	67 100.0	nil -	46 100.0	46 100.0	2 6.1	31 93.9	33 100.0
		female	4 6.9	54 93.1	58 100.0	1 2.6	37 97.4	38 100.0	1 11.1	8 88.9	9 100.0
TG	6-12	total	76 27.7	198 72.3	274 100.0	23 11.3	180 88.7	203 100.0	1 0.7	143 99.3	144 100.0
		male	47 29.2	114 70.8	161 100.0	21 13.8	131 86.2	152 100.0	1 1.3	78 98.7	79 100.0
		female	29 25.7	84 74.3	113 100.0	2 3.9	49 96.1	51 100.0	nil -	65 100.0	65 100.0
TMH	6-12	total	2 1.6	120 98.4	122 100.0	4 4.6	84 95.4	88 100.0	nil -	27 100.0	27 100.0
		male	1 1.2	84 98.8	85 100.0	3 5.0	57 95.0	60 100.0	nil -	13 100.0	13 100.0
		female	1 2.7	36 97.7	37 100.0	1 3.6	27 96.4	28 100.0	nil -	14 100.0	14 100.0
TS	9-13	total	102 76.1	32 23.9	134 100.0	81 69.8	35 30.2	116 100.0	104 50.0	104 50.0	208 100.0
		male	76 88.4	10 11.6	86 100.0	64 83.1	13 16.9	77 100.0	54 50.9	52 49.1	106 100.0
		female	26 54.2	22 45.8	48 100.0	17 43.6	22 56.4	39 100.0	50 49.0	52 51.0	102 100.0
TSH	6-12	total	34 16.2	176 83.8	210 100.0	14 10.3	122 89.7	136 100.0	9 6.5	129 93.5	138 100.0
		male	23 19.2	97 80.8	120 100.0	12 14.8	69 85.2	81 100.0	5 6.7	70 93.3	75 100.0
		female	11 12.2	79 87.8	90 100.0	2 3.6	53 96.4	55 100.0	4 6.4	59 93.6	63 100.0

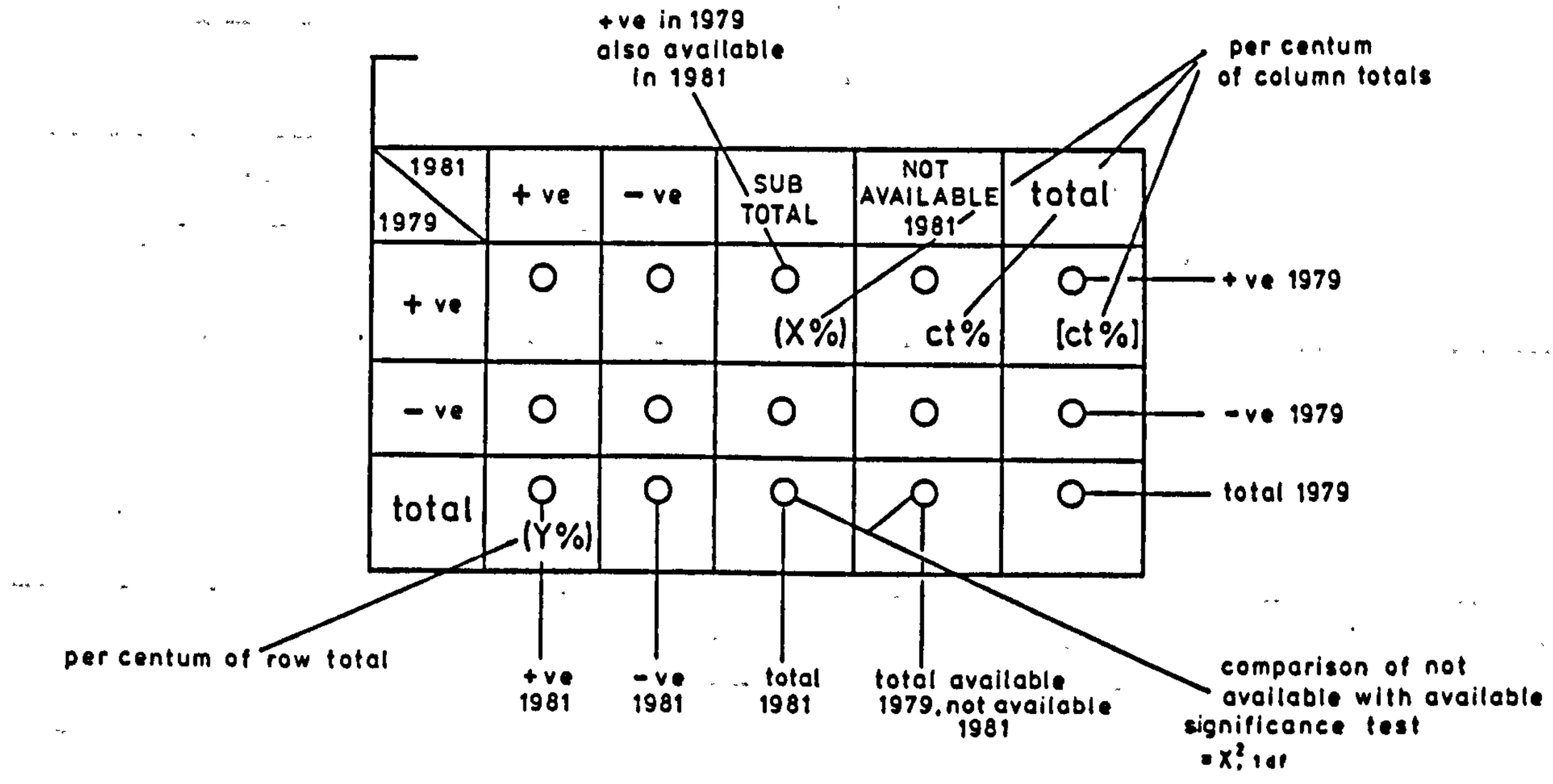
table S.3

SCHISTOSOMIASIS in TAUORGA SCHOOL CHILDREN

calculation of differential prevalence:

1979 sample population & 1981 cohort

scheme for comparison



1981 cohort prevalence change = X% - Y%

significance test for groups TD TE TG TS TSH employed McNEMAR's paired test.
for groups TF & TMH exact probability

GROUP RESULTS CONTINUED in TABLE S.3a →

results consolidated in table S.4

TD

1981 / 1979	+ ve	− ve	SUB TOTAL	NOT AVAILABLE 1981	total
+ ve	5	1	6 (7.8%)	1 1.8%	7 [5.1%]
− ve	10	61	71	50	131
total	15 (19.5%)	62	77	51	138

table S.3a

continuation of table S.3

1979 sample population & 1981 cohort

TE

1981 / 1979	+ve	-ve	SUB TOTAL	NOT AVAILABLE 1981	total
+ ve	8	4	12 (37.5%)	180 49.3%	192 [48.4%]
- ve	4	16	20	185	205
total	12 (37.5%)	20	32	365	397

TF

1981 / 1979	+ve	-ve	SUB TOTAL	NOT AVAILABLE 1981	total
+ ve	1	5	6 (7.1%)	4 9.8%	10 [8.0%]
- ve	nil	78	78	37	115
total	1 (1.2%)	83	84	41	125

TG

1981 / 1979	+ve	-ve	SUB TOTAL	NOT AVAILABLE 1981	total
+ ve	12	40	52 (25.6%)	24 32.8%	76 [27.7%]
- ve	11	139	150	47	197
total	23 (11.3%)	179	202	71	273

TMH

1981 / 1979	+ve	-ve	SUB TOTAL	NOT AVAILABLE 1981	total
+ ve	1	1	2 (2.3%)	nil -	2 [1.6%]
- ve	3	83	86.	34	120
total	4 (4.5%)	84	88	34	122

TS

1981 / 1979	+ve	-ve.	SUB TOTAL	NOT AVAILABLE 1981	total
+ ve	64	22	86 (74.1%)	16 88.9%	102 [76.1%]
- ve	17	13	30	2	32
total	81 (69.8%)	35	116	18	134

TSH

1981 / 1979	+ve	-ve	SUB TOTAL	NOT AVAILABLE 1981	total
+.ve	4	10	14 (10.3%)	20 27.0%	34 [16.2%]
- ve	10	112	122	54	176
total	14 (10.3%)	122	136	74	210

table S.4

SCHISTOSOMIASIS in TAUORGA SCHOOL CHILDREN

statistical significance of differential prevalence determined by Elisa

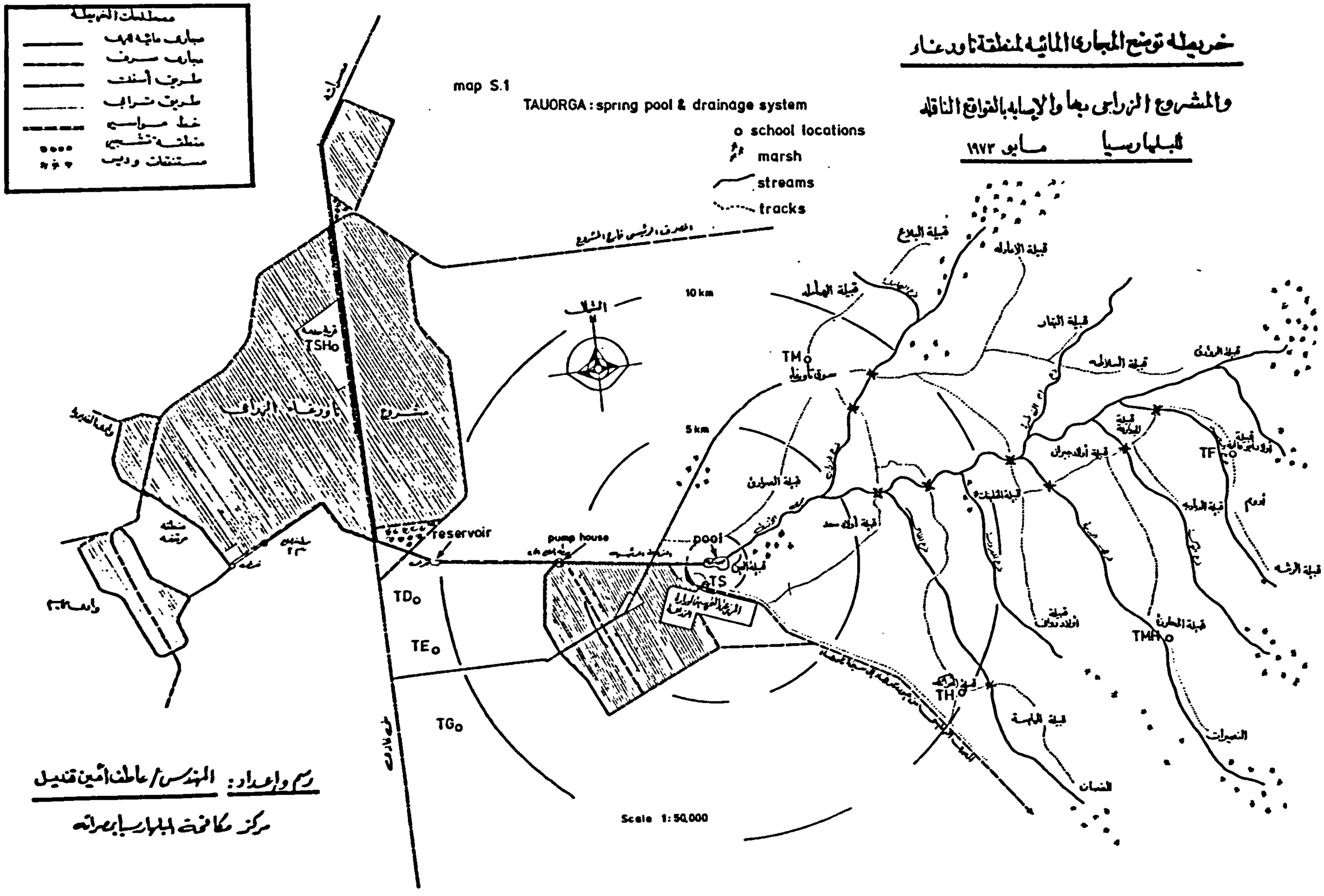
REFER TO table S.3 FOR DETAILS

GROUP CODE	A 1979 sample population TOTAL number	A 1979 sample population POSITIVE number per centum	B 1981 cohort of 1979 TOTAL number	B 1981 cohort of 1979 POSITIVE number per centum	A:B per centum variation & significance	C 1981 sample population TOTAL number	C 1981 sample population POSITIVE number per centum	A:C per centum variation & significance
T D	138	7 5.1	77	15 19.5	+ 11.7 $z = 2.4$ $P = <0.05$	236	8 3.4	- 1.7 n.s.
T E	397	192 48.4	32	12 37.5	nil n.s.	74	28 37.8	-10.6 n.s.
T F	125	10 8.0	84	1 1.2	- 5.9 $z = 1.8$ $P = >0.05$	42	3 7.0	- 1.0 n.s.
T G	274	76 27.7	203	23 11.3	-43.0 $z = 3.9$ $P = <0.01$	144	1 0.7	-27.0 $\chi^2 = 45.9$ 1DF $P = < 0.001$
TMH	122	2 1.6	88	4 4.6	+ 2.2 $z = 0.5$ $P = >0.05$	27	nil -	- 1.6 n.s.
T S	134	102 76.1	116	81 69.8	- 4.3 $z = 0.6$ $P = >0.05$	208	104 50.0	-26.1 $\chi^2 = 23.2$ 1DF $P = < 0.001$
TSH	210	34 16.2	136	14 10.3	nil n.s.	138	9 6.5	- 9.7 $\chi^2 = 7.2$ 1DF $P = < 0.01$

خريطه توضح المجارى المائيه لمنطقة تاورغاء

والمشروع الزراعى بها والإصابه بالمواقع الناقله

للبلهارسيا مايو ١٩٧٣



رسم واعداد: المهندس/ عاطف أمين قنديل

مركز مكافحة البلهارسيا بمصراته

TAUORGA Spring pool :

the largest body of water in Libya

TAUORGA Spring pool :

margin showing yellow Bayluscide staining

TAUORGA Spring pool :

principal natural outflow

TAUORGA Spring pool :

a typical natural drainage stream

TAUORGA Spring pool :

natural freshwater seepage pool

TAUORGA Spring pool :

people need access to water and will achieve it

by any means

CHAPTER 9.0 : CONCLUSION

9.1. Despite the tremendous socio-economic development which has occurred in Libya during the past ten years, the health status of the community has not been monitored in any systematic way.

Many of the health measures that have been taken have been based on inadequate local data and undertaken simply on general principles. Although, therefore, most of the decisions were likely to be correct, there is a need, first, to attempt to assess the value of those measures in order to advise their continuation, modification or termination; second, it is clear that with the influx of large numbers of immigrant labour, deriving from places as distant and diverse as the Philippines and Korea to Tunisia, that the introduction of imported disease to receptive areas of Libya was possible and probable; third, it is necessary to acquire epidemiological information in order to assist in the prevention or control of such imported disease.

The principal objective of this thesis has been to address these requirements, if only in a small way.

The findings have shown the following -

9.1.1. That certain health measures already introduced have been effective.

9.1.2. That other measures require modification.

9.1.3. That new methods of surveillance need to be introduced in certain respects.

9.2. Viral hepatitis : HAV

HAV is shown to be a common virus in Libya, infecting small children below 3 years of age; as a consequence all persons from 7 years upwards remain immune.

9.2.1. There is a need to determine the epidemiological basis for the outbreaks among young children.

9.2.2. The use of immune serum globulin is to be terminated since its use in adults is pointless in the face of their immunity.

9.2.3. An HAV vaccine will be of no value in Libya since infection occurs so early in life, viraemia is of short duration and not particularly severe, and there is no evidence to date of the development of a carrier state.

9.3. Viral hepatitis : HBV

HBV is shown to be uncommon in young children, affecting school children somewhat more so and adults more frequently again : dramatic outbreaks do not occur since only roughly half of the adult population is immune. However, the risk of infection is high in hospitals as a result of blood transfusion or renal dialysis and during surgery : the risk applies equally to patients and staff.

9.3.1. There is a need for a close study of HBsAg carrier state in Libya; since these subjects have been found elsewhere to suffer a high incidence of HBsAg positive chronic liver disease and hepato-cellular carcinoma.

9.3.2. Infants born to HBsAg positive mothers are at risk of HBV infection and becoming chronic carriers; such children tend to suffer a high incidence of fatal hepatoma in early adulthood.

9.3.3. An HBV vaccine will be of great value for high risk groups - surgeons, gynaecologists, renal haemodialysis staff, infants of HBsAg mothers and of HBeAg mothers and mothers infected with HBV in the late stages of their pregnancy.

9.4. Viral hepatitis : non-A, non-B viruses.

In the light of past fulminating outbreaks of doubtful aetiology amongst pregnant women in Libya and the discovery, during this study, of non-A non-B cases in young children in Gharian work is continuing

to elicit some knowledge of these infections.

9.5. Measles

It has been shown that the introduction in 1972 of live measles vaccination has resulted in a considerable reduction in the incidence of measles in Libya; the conversion rate will be more than 90.0 per centum.

9.5.1. A potential problem may arise from a few children remaining unvaccinated each year, and only small numbers acquiring immunity through natural infection, where the total number susceptible will gradually build toward the original pre-vaccination programme levels.

9.5.2. For a successful programme in Libya it will be necessary to gather information concerning birth rate, family size and the density and mobility of the population; this knowledge will enable the immunization of susceptible subjects before they might contract measles naturally. Cases would be followed and all contacts vaccinated unless they can provide acceptable proof of previous vaccination.

9.5.3. Mass random surveys, employing the requisite ELISA system, would define more accurately the level of herd immunity.

9.6. Rubella

Rubella is shown to be endemic in Libya, affecting children below 6 years of age and local epidemics continue to erode the number of susceptible subjects, although not dramatically.

9.6.1. The low rate of susceptibility, approximately 40.0 per centum, at the point of school entry and its natural reduction thereafter suggests that mass rubella vaccination of school populations would be unnecessary.

9.6.2. Consideration of possible vaccination policies indicates that the best policy for Libya would be to undertake post-partum vaccination of women.

9.6.2.1. This cannot obviate the problem of rubella infection during a first pregnancy but has much to commend it otherwise : for, if vaccination is carried out within a few days of delivery, the likelihood of conception within the potential danger period of two months is small.

9.6.2.2. Vaccine could be administered with or without screening.

9.6.3. It is not considered to be a good use of resources, human or financial, to initiate any form of vaccination policy at present.

9.6.4. The following studies are proposed for the future.

9.6.4.1. Periodic surveys of immunity levels in women attending ante-natal clinics.

9.6.4.2. Collection of data concerning the actual occurrence of cases where foetal abnormalities are related to rubella.

9.7. Malaria

A high degree of malaria control has been achieved in Libya in the recent past; to the point where autochthonous cases had become uncommon. A recent outbreak indicated the possible danger of the resurgence and re-establishment of malaria in Libya.

9.7.1. There are many areas with a receptive ecology where transmission may well occur if active human cases were introduced. The principal threat lies in the large groups of immigrant labour arriving from malarious countries, both near and far, and to a lesser degree from illegal immigrants from malarious countries contiguous with Libya, and also from inadequately protected Libyans returning from abroad.

9.7.2. This study, based upon immunofluorescent antibody testing, indicated that approximately half of Indian immigrants had been exposed to malaria whilst as many as 19.0 per centum possessed antibody levels indicating recent or very recent infection with relapsing malaria.

9.7.2.1. Immigrants from areas other than India indicated recent or very recent infection of the order of 5.0 per centum with relapsing malaria.

9.7.2.2. Native schoolboys were shown to be 100.0 per centum non-immune to malaria.

9.7.3. It may be assumed that vector populations will have recovered to some extent from the assault made upon them during past campaigns aimed at their control but there have been no recent anti-anopheline campaigns in Libya.

9.7.3.1. There is a clear need for a thorough nationwide survey of anopheline species in order to define their distribution and density.

9.7.4. Recommendations are given in respect of malaria prophylaxis in respect of Libyan nationals travelling abroad to malarious areas and for the presumptive treatment of immigrant labour.

9.7.5. The reduction or elimination of anopheline mosquitoes can be achieved by means of the control of larval populations in water bodies and improvement of container hazard : adult populations may be controlled by house spraying of insecticide.

9.7.5.1. Strong administrative control of these operations is essential. This requires a permanent, central anti-malaria service coordinating well with related authorities.

9.8. Leishmaniasis

Cutaneous leishmaniasis remains endemic in the north west of Tripolitania.

9.8.1. Transmission, as defined by skin testing, appears to be at a low level.

9.8.2. The skin testing requires repetition since one of the two antigens employed elicited poor responses.

9.8.3. When suitable antigen is available a larger number of sites within the endemic area should be visited and better population samples organised than those reported herein. The increased number of testing sites should assist in a better definition of the intensity of infection and the area in which it occurs.

9.8.4. Improvement in diagnosis and case notification is required.

9.8.5. Local spray team efficiency, equipment, training, transport all require improvement.

9.8.6. A survey of phlebotomine sandflies in order to determine species distribution and density should be mounted in the endemic area.

9.8.7. A survey of rodents in order to determine species distribution and density is required in the endemic area.

9.9. Echinococcosis

In Libya traditional animal husbandry and the practice of domestic slaughter of food animals contribute to the maintenance of the Echinococcus cycle.

The cost of this disease is high and may significantly affect the national economy.

9.9.1. This study, employing an ELISA system, indicates a positive rate for echinococcosis of the order of 10.0 per centum in children and young adults from the environs of Benghazi; no difference being apparent between rural and urban dwellers.

9.9.2. There is a need to determine the prevalence of infection in both animals and humans and to determine the relationship between them in respect of infection.

9.9.2.1. Surveys are required in all alleged endemic areas and in sheep and camel breeding areas.

9.9.2.2. It is necessary to determine the importance of foxes, hyaenas and jackals in transmission amongst other animals.

9.9.3. It is recommended to conduct a clinical trial to determine the value of mebendazole in treatment.

9.10. Schistosomiasis

9.10.1. This study, employing an ELISA system, detected a positive rate for S.mansoni infections of 33.4 per centum in Tauorga school children whilst qualitative stool examination detected 6.9 per centum.

9.10.1.1. Subsequent sampling of the school population indicated that a molluscicíding programme concerning the major water body in the area had prevented any increase in prevalence overall and appeared to have achieved decrease in prevalence in particular locations.

9.10.1.2. New housing, piped water, sanitary disposal of wastes and health education also affected the situation favourably.

9.10.2. It is recommended that annual ELISA surveys be undertaken to define the general situation in respect of schistosomiasis and the role of other beneficial influences.

9.10.2.1. It is intended to conduct stool/ova concentration in respect of all ELISA positives in order to determine the relationship between ELISA antibody positive status and the presence of S.mansoni ova.

9.10.2.2. Antibody positive subjects will be treated with a suitable single dose drug and monitored for variations in ova and antibody output.

9.11. Specimen collection

Whatever the test involved, no good laboratory work can be conducted upon a bad subject specimen.

The author wishes to emphasize that the collection of specimens, including blood by venepuncture, is essentially a simple matter given the correct equipment.

None of the field work underlying this study employed more than three persons, one being a driver/registrar.

The accompanying illustrations indicate the simplicity of equipment involved.

BLOOD COLLECTION by finger prick

Dr. Sami Abdul Razak in Tauorga

BLOOD COLLECTION by venepuncture

Dr. Ashour Gebreel in Gawasem

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