

HELICOBACTER PYLORI IN AFRICA

Helicobacter pylori in Africa: Observations on an 'enigma within an enigma'

MARK KIDD, JAPIE A LOUW AND ISRAEL N MARKS

Gastrointestinal Clinic, Department of Medicine, University of Cape Town and Groote Schuur Hospital Observatory, Cape Town, South Africa

Abstract

Background: We conducted a retrospective literature review of all the data published on *Helicobacter pylori* in Africa in order to test whether the prevalence of diseases associated with this organism differs from that in developed nations.

Methods: Both sero-epidemiological ($n=8$) as well as prospective endoscopic studies in subjects with either dyspepsia or epigastric pain ($n=23$) and one retrospective study were available for analysis.

Results: Sero-epidemiology confirmed both the early age of acquisition in children (50% by 10 years) as well as the high prevalence of the organism (61%) in adult asymptomatic individuals. Endoscopic studies in dyspeptic individuals revealed the presence of the organism in 72%. Duodenal ulceration was noted in 26% of 3473 cases and in these, *H. pylori* was present in 90%. An association of gastric metaplasia with duodenal ulceration was identified in the one study in which it was investigated. Gastric ulceration occurred approximately four-fold less frequently (7% of 2286 cases) than duodenal ulceration and the organism was evident in 75% of the gastric ulceration cases. Findings of intestinal metaplasia (14%) and gastric cancer (3.4%) were not infrequent, but the paucity of accurate epidemiological data made it difficult to establish a correlation between the two.

Conclusion: It would appear that prospective endoscopic-based studies in African subjects may question the standard dogma of a low prevalence of *H. pylori*-associated diseases in Africa. Further research is clearly required.

© 1999 Blackwell Science Asia Pty Ltd

Key words: Africa, cancer, enigma, gastritis, *Helicobacter pylori*, ulceration.

INTRODUCTION

The disparity between the occurrence of *Helicobacter pylori* infection and the expression of clinically significant disease, 'the African enigma', has led some to postulate that this bacterium does not play a major role in the aetiology of upper gastrointestinal pathology in developing countries. Some have gone so far as to suggest that there is no established correlation between the organism and any pathology in Africa apart from gastritis,^{1,2} and, indeed, that infection with the organism in Africa may be protective against *inter alia* gastric cancer.³ The 'evidence' for these views is derived largely from sero-epidemiological studies in asymptomatic individuals combined with anecdotal evidence about

the prevalence of various disease entities.¹⁻⁵ The perceived lack of a pathogenic effect is rationalized by generalizations that major differences may exist in *H. pylori*-associated disease expression between developed and developing countries. Factors such as an earlier age of exposure, higher frequency of re-exposure, *H. pylori* strain variations, poorly defined environmental factors (e.g. diet), and different immunological responses are invoked to explain the differences in disease expression.^{1,6} Many of these, purely hypothetical, considerations can be questioned. It is now generally accepted, for instance, that infection with *H. pylori* occurs primarily in childhood in all populations.

On the basis of the adage that 'absence of evidence does not necessarily equate with an evidence of

absence', we have attempted to take a fresh look at the relationship between *H. pylori* infection and gastro-duodenal pathology in the African setting, using a retrospective literature survey of all the data (both serological and mucosal) published on the organism in Africa, as well as endoscopically controlled studies on gastro-duodenal pathology. Analysis of these data provide a current summary of the available data relating to the prevalence of the infection and the occurrence of gastro-duodenal disease in the African setting.

METHODS

A literature review was conducted by using a Medline search for the years 1981–97. The name of the country and *Helicobacter (Campylobacter) pylori* was used to generate search strings. An additional search of the primary literature, which revealed additional references, was also conducted. Manuscripts as well as abstracts and letters supplying endoscopic data were included in the final analysis if absolute numbers were provided. Duplicate communications were excluded. The literature was divided into sero-epidemiological studies and studies which involved upper gastrointestinal endoscopy with the aim of evaluating both *H. pylori* status and the presence of gastro-duodenal pathology with special reference to peptic ulcer disease and gastric cancer. All studies were included for completeness. The information derived from appropriate studies is grouped in tabular form for ease of reading. Tables 2–4 were constructed such that actual numbers are indicated where available, the percentages are bracketed and the prevalence of *H. pylori* (and percentage) is included. The inherent fallibility in determining incidence and prevalence rates, often from studies whose primary aims were different (some studies focused on peptic ulceration,^{7–9} while others focused on cancer^{10,11}), is acknowledged.

Statistical analysis

The Fisher test for comparing dichotomous samples was used to examine the relationship between *H. pylori* and gastric pathologies for each distinct country.

RESULTS

A total of eight sero-epidemiological studies with information about four countries were available for study. These studies evaluated immunoglobulin (Ig)G antibodies against *H. pylori* in either children or adults by using commercial or modified commercial ELISA kits. There were 24 endoscopically based studies comprising 14 countries available for analysis of associated pathology: 11 studies for referrals of either dyspepsia or epigastric pain lasting longer than 2 weeks, seven prospective studies investigating the relationship between the organism and the disease in a similar study group, one retrospective study and five studies of consecutive endoscopies for the organism in symptomatic subjects. One to two biopsies were available from the antrum in 23 cases and one biopsy was available from the fundus in two cases. Histology (Giemsa, Warthin–Starry stain) was available in 21 studies, the organism was cultured in seven and urease activity was measured in four studies.

Sero-epidemiology of *Helicobacter pylori*

We separated the sero-epidemiological studies into prevalences for different age groups in order to question some of the assumptions about the natural history of *H. pylori* infection. The early age of acquisition of *H. pylori* IgG antibodies in African children is demonstrated by seropositivity rates of 41% (seven of 17) in 0–1-year-old South Africans,¹² 13.5% in 3 months–2-year-old South African children from Bloemfontein¹³ and 57% (12/21) in Nigerian children of 6 months–2 years.¹⁴ Overall, antibodies were present in 317/635 (50%) of children under 10 years of age (Table 1). Analysis suggested that significantly more children were infected in Nigeria (82%)¹⁴ than in Algeria, Cote d'Ivoire or Natal, South Africa ($P < 0.05$). The prevalence of antibodies was lowest in children from the one South African study (42%).¹² Irrespective of these differences, the presence of serum antibodies was considerably higher than generally reported for children in developed nations (<5–10%). This review confirms both the early acquisition of antibodies against *H. pylori*

Table 1 Summary of *Helicobacter pylori* sero-epidemiology studies

Country	<i>n</i>	< 10 years	10–50 years	> 50 years	Reference
Algeria	200	ND	43/100 (43)	58/100 (58)	15
Algeria	218	21/42 (50)	153/176 (87)	ND	16
Cote d'Ivoire	274	64/116 (55)	113/147 (77)	9/11 (82)	16
Nigeria	212	14/17 (82)	148/181 (82)	30/31 (97)	14
Nigeria	43	39 (91)			43
Nigeria	420		160 (39)		17
South Africa	137	45/106 (42)	25/31 (81)	ND	12
South Africa	311	134 (43)			13
Total		317/635 (50)	642/1055 (61)	97/142 (68)	

ND, not determined. Figures in parentheses are percentages.

as well as the high prevalence of the infection in children in Africa. In total, 61% (642/1055) of asymptomatic individuals between the age of 10 and 50 years had antibodies. Of interest was the observation that two studies in Algeria and two in Nigeria demonstrated significantly different antibody results despite the similar age groups: 43 versus 87%,^{15,16} and 39 versus 82%, respectively.^{14,17} These discrepancies remain to be resolved but may be a reflection of the sensitivity and specificity of the serological kits used (a potential problem with all sero-epidemiological studies).¹⁶

Endoscopic prevalence of *Helicobacter pylori* in dyspeptic subjects

Helicobacter pylori was present in 72% of all dyspeptic subjects, with a range from 25 to 97%. The prevalence of *H. pylori* was high (60–97%) in 19 of the 21 studies cited. The prevalence in the remaining two studies, from Uganda and Sudan, was 25 and 39%, respectively.^{18,19} Despite this, this review confirms the high prevalence of the organism in the gastric mucosa in most dyspeptic populations in Africa.

Helicobacter pylori and gastritis

Helicobacter pylori is causal for chronic (antral, type B) gastritis throughout the world, including African countries. While the overall prevalence of gastritis was 60% and *H. pylori* 85% (Table 2), gastritis was present in 77% of samples positive for *H. pylori*. These data confirm that the organism is associated with gastritis in Africa. *Helicobacter pylori* was also found fairly often in the fundus (40–76%),^{10,20} but there were no reports detailing the presence or extent of *H. pylori*-associated fundic gastritis.

The importance of gastritis as a precursor lesion has been recently demonstrated by observations of a strong relationship between gastric ulcer, gastric cancer and multifocal atrophic gastritis.²¹ Unfortunately, the paucity of histological details makes it almost impossible to analyse the sequelae of *H. pylori* and gastritis in the studies reviewed.

Helicobacter pylori and peptic ulcer disease

Ulcer disease in Africa has reflected either one of two polarities. In central Africa, it is apparently not uncommon for surgeons to manage perforated ulcer disease.⁴ In contrast, the first two cases of ulcer disease in black South African women were associated with the extremely rare Zollinger–Ellison syndrome.^{22,23} Dyspeptic symptoms, however, appear to be more consistently common in sub-Saharan Africa. In some regions they may account for up to 10% of all hospital admissions.²⁴ This review summates the published endoscopic and histological findings from subjects complaining of upper gastrointestinal symptomatology (dyspeptic

symptoms of 2 weeks–3 months duration: epigastric pain, nausea, vomiting, heartburn, postprandial pain and bloating) referred for endoscopy in 14 African countries. The bias inherent in this is acknowledged.

Duodenal ulceration

In this review, duodenal ulceration (DU) was evident in 26% of patients with dyspepsia and *H. pylori* was coevident in 90% (Tables 3,4). Traditional areas of high DU incidence (west coast of Africa, Nile–Congo watershed) often had a high prevalence of DU, of the order of 30–59%, among patients referred for endoscopy, with some exceptions. While only 9% of cases studied in the Cote-d'Ivoire were found to have DU, a similar percentage of patients with gastric ulcers were also seen in this country.²⁵ Of particular interest was the finding of a high prevalence of DU in southern Africa, traditionally considered to be a low-incidence area. In a prospective study from Zimbabwe, DU was noted in 516 of 1714 patients (30%) referred for endoscopy; the authors calculated a crude prevalence rate of 456/100 000.⁹ In South Africa, the prevalence of DU ranged from 12 to 30%.^{26–28}

All available studies to date suggest that duodenal disease is associated with *H. pylori* gastritis in almost every case in developed countries.^{21,29} It is postulated that gastric metaplasia (GM) in the duodenum colonized by *H. pylori* precedes the formation of duodenal ulcers in developed nations and that GM varies from 41 to 90% in these patients. We could only identify one study that investigated the relationship between GM and DU in the African setting. Forty-six of 64 patients (72%) with DU from Cape Town demonstrated the presence of GM,³⁰ suggesting a similar aetiopathogenetic mechanism for this disease process as in developed nations.

Gastric ulceration

The ratio of DU to gastric ulceration (GU) is 4:1 in developed nations. Data for GU prevalence in Africa are fragmentary: previous observations¹ have suggested a very high DU:GU ratio (in the order of 15–20:1) in African countries and in India.³¹ In one South African study, examining admissions of black patients to a large teaching hospital between 1979 and 1988, the ratio of DU to GU ranged between 5:1 and 9:1.³² In this review, albeit a collocation of studies whose main objective may not have been to determine GU prevalence, GU was identified in 7% of cases, while *H. pylori* infection was noted in 75% of them (Tables 3,4). There was a wide range in the DU:GU from 1:4 to 41:0, but on average was approximately 4:1. This spread is of interest and probably reflects the heterogeneity of the study objectives. The inherent bias in over-interpreting these results is, therefore, noted.

Helicobacter pylori and gastric cancer

Multifocal atrophic gastritis increases the risk of developing gastric carcinoma (GC) and a positive correlation

Table 2 Summary of *Helicobacter pylori* status and histology

Country	<i>n</i>	<i>H. pylori</i> +	Normal histology	Gastritis	Reference
Egypt	80	53 (66)	ND	ND	44
Cameroon	93	67 (72)	11 (12) 0 (0)	82 (88) 67 (82)	7
Cote d'Ivoire	277	253 (91)	12 (4) 7 (60)	247 (89) 247 (100)	25
Ghana	39	38 (97)	1 (3) 0 (0)	38 (97) 38 (100)	45
Nigeria	57	46 (81)	4 (7) 1 (25)	53 (93) 46 (87)	46
Nigeria	40	32 (75)	5 (13) 0 (0)	35 (87) 32 (91)	47
Rwanda	166	131 (79)	25 (15) 12 (48)	90 (54) 67 (74)	48
Uganda	56	14 (25)	21 (38) 0 (0)	25 (45) 14 (56)	18
Zaire	324	285 (88)	1 (0.3) 0 (0)	133 (41) 122 (92)	20
Ethiopia	207	127 (61)	5 (2) 0 (0)	202 (98) 128 (63)	49
Ethiopia	444	324 (73)	173 (39) 109 (63)	102 (23)	50
Kenya	187			150 (80) 128 (85)	51
Kenya	66	40 (61)	26 (39) 13 (50)	16 (24) 11 (69)	52
Sudan	100	39 (39)	31 (31) 5 (16)	15 (15) 12 (80)	19
Malawi	160	141 (88)	3 (2) 0 (0)	157 (98) 141 (90)	8
South Africa	176	129 (73)	38 (22) 13 (34)	107 (61) 84 (79)	10
South Africa	169	106 (63)			53
South Africa	224	183 (82)	30 (13) 3 (10)	194 (87) 180 (93)	26
South Africa	200	139 (70)	78 (39) 46 (59)	41 (21) 26 (63)	28
South Africa	51	37 (73)	7 (14) 5 (71)	12 (24) 9 (75)	27
South Africa	585	474 (81)	125 (21)	372 (63)	11
Zimbabwe	100	76 (76)			9
Total	3801	2734 (72)	596 (18)	2071 (60)	

+, Positive; ND, not determined. Figures in parentheses are percentages.

exists between the prevalence of intestinal metaplasia (IM) (particularly type III) and the incidence of GC.^{21,33} In spite of the difficulties in grading atrophy, there appears to be a good correlation between atrophic gastritis and IM. In the present review, atrophic gastritis was present in 28% of cases, while IM and GC were present in 14 and 3.4% of cases, respectively (Table 3). The presence of *H. pylori* varied between 69 and 78% in these samples (Table 4).

In the absence of accurate population statistics in the majority of African countries, the proportional fre-

quency of one tumour compared with that of all the others has been used as an indicator of tumour incidence.³⁴ Using this measure, the prevalence of GC has been noted in the past to be 2–3% of all malignancies in Nigeria, Sudan, Uganda and Zimbabwe.¹ In South Africa, in the latest publications available, GC, as a percentage of all cancers, ranges from 3.3 to 11.5% depending on ethnic grouping.³⁵ Non-standardized rates would seem to suggest incidences as low as 0.8 per 100 000,³ while age-standardized rates vary from 2.4 to 20 per 100 000.³⁵ In the present review, the overall

Table 3 Summary of gastric pathologies

Country	n	DU	GU	Atrophy	IM	Cancer	Reference
Cameroon	93	28 (30)	7 (8)			1 (1)	7
Cote d'Ivoire	277	26 (9)	23 (8)			6 (2)	25
Ghana	39	23 (59)	0 (0)				45
Nigeria	57	6 (11)	1 (2)			1 (2)	46
Rwanda	166	49 (30)	2 (1)	18 (14)		7 (4)	48
Uganda	56			25 (45)	7 (13)	1 (2)	18
Zaire	324	38 (12)	5 (1.5)		60 (22)	23 (7)	20
Kenya	66	14 (21)	6 (9)				52
Sudan	100	32 (32)	3 (3)			1 (1)	19
Malawi	160	41 (26)	0 (0)				8
South Africa	176			59 (34)		6 (3)	10
South Africa	224	67 (30)	21 (9)	2 (1)	5 (2)		26
South Africa	200	71 (36)	10 (5)				28
South Africa	51	6 (12)	24 (47)				27
South Africa	80			45 (56)	16 (20)		54
South Africa	84	44	40	59 (70)	18 (24)		36
South Africa	585		58 (10)	179 (31)		16 (3)	11
Zimbabwe	1714	516 (30)					9
Total	4452	917 (26.4)	160 (7)	387 (28)	106 (14)	62 (3.4)	

DU, duodenal ulcer; GU, gastric ulcer; IM, intestinal metaplasia. Figures in parentheses are percentages.

Table 4 Summary of *Helicobacter pylori* status

Country	n	DU	GU	Atrophy	IM	Cancer	Reference
Cameroon	93	22 (79)	4 (57)				7
Cote d'Ivoire	277	26 (100)	21 (91)				25
Ghana	39	23 (100)	0 (0)				45
Nigeria	57	6 (100)	1 (100)			0 (0)	46
Rwanda	166	49 (100)	2 (100)	15 (83)		3 (43)	48
Uganda	56			14 (56)	0 (0)	0 (0)	18
Zaire	324	38 (100)	3 (60)		48 (80)	17 (74)	20
Kenya	66	8 (57)	2 (33)				52
Sudan	100	18 (56)	0 (0)			1 (100)	19
Malawi	160	39 (95)	0 (0)				8
South Africa	176			46 (78)		6 (100)	10
South Africa	224	65 (97)	13 (62)	0 (0)	3 (60)		26
South Africa	200	58 (82)	9 (90)				28
South Africa	51	6 (100)	17 (71)				27
South Africa	80			35 (78)	10 (63)		54
South Africa	84	43 (98)	35 (88)	52 (88)	16 (88)		36
Zimbabwe	50	45 (90)					9
Total		446 (90)	107 (75)	162 (78)	77 (78)	27 (69)	

DU, duodenal ulcer; GU, gastric ulcer; IM, intestinal metaplasia. Figures in parentheses are percentages.

prevalence of GC in subjects with dyspepsia and epigastric pain was 3.4%: in western Africa it ranged from 1 to 2%, in central Africa between 2 and 7% and in South Africa it was 3%. The data suggest that both GC and its precursor lesions are not rare in African patients with dyspepsia, but the caveat of over-interpretation should be obvious.

Helicobacter pylori and intervention

The best test of a cause and effect relationship between an organism and any pathology is to evaluate the effect of eradication on disease symptomatology or recurrence. In one study in South Africa, eradication therapy in 27 patients resulted in a duodenal ulcer relapse of

five patients (19%) over a 2-year period.³⁶ Of the two instances of re-infection in this group, one was associated with DU relapse. Of the 21 patients with 'healed' duodenal ulcers who were infected with the organism, 15 relapsed. The effect of eradication on the natural history of GU disease has been less well documented. However, in a similar study at the same institution, eradication therapy in 24 patients resulted in a GU relapse of two (8%), while 50% (eight of 16) of the non-eradicated group relapsed over the 12-month study period.³⁷ It appears that eradication of the organism is an effective long-term treatment strategy, at least for peptic ulcer disease. Re-infection is low in Africa, despite the high prevalence of the organism.^{36,37} Although clearly limited, these data support the practice of *H. pylori* eradication in *H. pylori*-associated peptic ulcer disease (PUD) in the African setting.

DISCUSSION

The relationship between *H. pylori* infection and gastric pathology in Africa is controversial and many authors have suggested that the organism either has no relationship to pathology or that it has a protective effect. This state of affairs is clearly at odds with that in developed countries, despite the recent publication of differing views.³⁸

The difficulty with definitively ascribing a pathogenic role to *H. pylori* in the African setting is aggravated by the paucity of appropriate studies directly investigating this. In addition, a review of the literature reveals that the several assumptions regarding peptic ulcer incidence in sub-Saharan Africa have been based on clinical findings, X-ray evidence, surgical experience and necroscopy examinations reported 20–30 years ago.^{4,5} In spite of these difficulties, a review of the prospective, endoscopically based studies in the *H. pylori* era, albeit in subjects who have been selected by varying criteria which may represent a selection bias, is somewhat at odds with current perceptions. Indeed, it would appear that the organism's association with gastritis in Africa is as strong as in the rest of the world and the available data generated in the endoscopy era suggest that the infection is strongly associated with PUD, while PUD itself may not be as rare as is commonly perceived. It is of interest that the data under review show a predominance of DU disease. In this context, the observations of Hansson *et al.* regarding the potential for DU disease to protect against the development of gastric cancer may be relevant.²¹ Clearly, prospective studies need to be performed. It should be noted that the dogma underpinning the 'African enigma' (i.e. a relative paucity of upper gastrointestinal disease in the African setting) has been questioned before. Cook stated as early as the 1980s that 'the belief strongly held earlier in this century that peptic ulcer was rare in Africans, in Africa, is now therefore firmly demolished'.³⁹

In recent years, several biological studies have suggested that *H. pylori* may influence some of the mechanisms of gastric carcinogenesis. Evidence for a link between the organism and gastric cancer has been pro-

vided by findings that the prevalence of infection is high in populations with a high incidence of gastric cancer; others indicate that infected individuals have an increased risk (two–12 fold) of developing gastric cancer. It should be noted, however, that none of these data were generated in sub-Saharan African countries.⁴⁰ However, a recent publication reviewing evidence for *H. pylori* as a cofactor in gastric cancer stresses the paucity of hard evidence in this field.⁴¹ The authors are of the view that gastric cancer is due to a series of complex and correlated variables rather than to a single event, but concede that *H. pylori* probably plays an important role. There is no argument that in developed nations, atrophic gastritis increases the risk of developing GC and a positive correlation does exist between the prevalence of type III IM and the incidence of GC.³³ In *H. pylori*-positive patients in developed countries, the prevalence of IM ranges between 17 and 30%.³³ This review reveals that IM was present in 2–24% in the five series reported. The prevalence of *H. pylori* was 78% in these samples. These values are similar to those in developed nations and considerably higher than those quoted for India.⁶ Unfortunately, neither gastritis nor IM were adequately graded in these African studies and it is difficult to establish the possible potential risks of these predisposing conditions. The findings of a relatively high prevalence of GC (1–7%) in these samples suggest that prospective studies are clearly needed before any firm conclusions about a mechanistic role for *H. pylori* in GC in Africa can be drawn.

The basis of the 'African enigma', a perceived low prevalence of *H. pylori*-associated diseases in the setting of a high *H. pylori* carrier rate, may possibly be another expression of Africa's poor medical infrastructure, as evidenced by the 'health for all indicators' of the World Health Organization's 1996 Report.⁴² This report also identifies a further factor that may influence the expression of disease. It is clear that the average life expectancy in sub-Saharan Africa is much lower than in industrialized countries; the 1995 life expectancy in sub-Saharan Africa was 53 years (range 40–71). It is tempting to speculate whether an enigma exists at all or whether this phenomenon results from the difficulty inherent in determining the prevalence of a disease with a low mortality in the African setting. Our current review of available published endoscopic data suggest that well conducted, prospective collection of endoscopic data are clearly needed in order to resolve this position. The enigma may be in need of more science.

ACKNOWLEDGEMENT

M Kidd is a recipient of the AS Little Fellowship.

REFERENCES

- 1 Holcombe C. *Helicobacter pylori*: The African enigma. *Gut* 1992; **33**: 429–31.
- 2 Segal I, Ally R, Sitas F, Walker A. *Helicobacter pylori*: The African enigma. *Gut* 1998; **43**: 300.

- 3 van der Merwe C. *Helicobacter pylori* and gastric cancer. *Eur. J. Gastroenterol. Hepatol.* 1995; **7**: 589–90.
- 4 Tovey F, Tunstall M. Duodenal ulcer in black populations in Africa south of the Sahara. *Gut* 1975; **16**: 564–76.
- 5 Tovey F. Geographical aspects of peptic ulcer surgery. *World J. Surg.* 1977; **1**: 47–53.
- 6 Gill H, Desai H. *Helicobacter pylori* and gastroduodenal ulcers in India: Lessons from epidemiology. *J. Clin. Gastroenterol.* 1993; **16**: 6–9.
- 7 Palmer D, Watson K, Allen M. *Helicobacter pylori* infection and peptic ulcer disease in Cameroon, West Africa. *J. Clin. Gastroenterol.* 1994; **18**: 162–4.
- 8 Harries A, Stewart M, Deegan K *et al.* *Helicobacter pylori* in Malawi, Central Africa. *J. Infect.* 1992; **24**: 269–76.
- 9 Gangaidzo I, Kiire C, Mason P, Sitima J, Gwanzura L. Prospective endoscopic study of duodenal ulcers in Zimbabwean blacks. *Central Afr. J. Med.* 1992; **38**: 397–402.
- 10 Jaskiewicz K, Louwrens H, Woodroof C, van Wyk M, Price S. The association of *Campylobacter pylori* with mucosal pathological changes in a population at risk for gastric cancer. *S. Afr. Med. J.* 1989; **75**: 417–19.
- 11 Jaskiewicz K, Louwrens H. Chronic atrophic gastritis in a population at risk for gastric carcinoma. *Anticancer Res.* 1991; **11**: 835–9.
- 12 Sathar M, Simjee A, Wittenberg D *et al.* Seroprevalence of *Helicobacter pylori* infection in Natal/Kwazulu, South Africa. *Eur. J. Gastroenterol. Hepatol.* 1994; **6**: 37–41.
- 13 Pelser H, Househam K, Joubert G *et al.* Prevalence of *Helicobacter pylori* antibodies in children in Bloemfontein, South Africa. *J. Pediatr. Gastroenterol. Nutr.* 1997; **24**: 135–9.
- 14 Holcombe C, Omotara B, Eldridge J, Jones D. *H. pylori*, the most common bacterial infection in Africa: A random serological study. *Am. J. Gastroenterol.* 1992; **87**: 28–30.
- 15 EUROGAST. Epidemiology of, and risk factors for, *Helicobacter pylori* infection among 3194 asymptomatic subjects in 17 populations. *Gut* 1993; **34**: 1672–6.
- 16 Megraud F, Brassens-Rabbe M-P, Denis F, Belbourni A, Hoa D. Seroepidemiology of *Campylobacter pylori* infection in various populations. *J. Clin. Microbiol.* 1989; **27**: 1870–3.
- 17 Olusanya O. Immunological response to *H. pylori* among Nigerians. *Trop. Geograph. Med.* 1991; **43**: 28–32.
- 18 Wabinga H. Frequency of *Helicobacter pylori* in gastroscopic biopsy of Ugandan Africans. *East Afr. Med. J.* 1996; **71**: 691–3.
- 19 Azim Mirghani Y, Ahmed S, Ahmed M *et al.* Detection of *Helicobacter pylori* in endoscopic biopsies in Sudan. *Trop. Doctor* 1994; **24**: 161–3.
- 20 Glupczynski Y, Bordeaux L, De Prez C *et al.* Prevalence of *Helicobacter pylori* in rural Kivu, eastern Zaire: A prospective endoscopic study. *Eur. J. Gastroenterol. Hepatol.* 1991; **3**: 449–55.
- 21 Hansson L-E, Nyren O, Hsing A *et al.* The risk of stomach cancer in patients with gastric or duodenal ulcer disease. *N. Engl. J. Med.* 1996; **335**: 242–9.
- 22 Marks I, Selzer C, Louw J, Bank S. Zollinger–Ellison Syndrome in a Bantu woman, with isolation of a gastrin-like substance from the primary and secondary tumors. *Gastroenterology* 1961; **41**: 77–86.
- 23 Bank S, Marks I, Sealy R, Silber W, Louw J. Malignant Zollinger–Ellison Syndrome in a Bantu woman with a prolonged remission after gastric irradiation. *Gut* 1965; **6**: 279–85.
- 24 Lester F, Tsega E. The pattern of adult medical admissions in Addis Ababa, Ethiopia. *East Afr. Med. J.* 1976; **53**: 620–34.
- 25 Diomande M, Flejou J, Potet F *et al.* Gastrite chronique et infection a *Helicobacter pylori* en Cote-d'Ivoire. Etude d'une serie de 277 patients symptomatiques. *Gastroenterol. Clin. Biol.* 1991; **15**: 711–16.
- 26 Miller N, Naran A, Simjee A *et al.* Incidence of *Campylobacter pylori* in patients with upper gastro-intestinal symptoms. *S. Afr. Med. J.* 1988; **74**: 563–6.
- 27 Wright J, Lastovica A, Emms M, Penfold S. *Campylobacter pyloridis* and the gastric mucosa. *S. Afr. Med. J.* 1987; **72**: 78–9.
- 28 Crewe-Brown H, Lucasson J, Greenhalgh J, Du Plessis D, van der Merwe C, Te Winkel W. Gastric *Campylobacter*-like organisms and peptic ulceration. *S. Afr. Med. J.* 1985; **68**: 517.
- 29 Van der Hulst R, Tytgat G. *Helicobacter pylori* and peptic ulcer disease. *Scand. J. Gastroenterol.* 1996; **31** (Suppl. 220): 32–7.
- 30 Louw J, Jaskiewicz K, Lucke W, Adams G, Winter T, Marks I. *Helicobacter pylori* in the antrum and duodenum of duodenal ulcer subjects. *S. Afr. Med. J.* 1994; **84**: 437.
- 31 Khuroo M, Mahajan K, Zargar S, Javid D, Munshi S. Prevalence of peptic ulcer in India: An endoscopic and epidemiologic study in urban Kashmir. *Gut* 1989; **30**: 930–4.
- 32 van der Merwe C, Te Winkel T. Ten-year observation of peptic ulceration at Ga-Rankuwa Hospital, Pretoria: 1979–88. *S. Afr. Med. J.* 1990; **78**: 196–9.
- 33 Valle J, Sipponen P, Pajares J. Geographical variations in *Helicobacter pylori* gastritis and gastric cancer. *Curr. Opin. Gastroenterol.* 1997; **13**: 35–9.
- 34 Burkitt D, Cook P. Cancer in Africa. *Br. Med. Bull.* 1971; **27**: 14–20.
- 35 Sitas F. Histologically diagnosed cancers in South Africa, 1988. *S. Afr. Med. J.* 1994; **84**: 344–8.
- 36 Louw J, Lucke W, Jaskiewicz K, Lastovica A, Winter T, Marks I. *Helicobacter pylori* eradication in the African setting, with special reference to reinfection and duodenal ulcer recurrence. *Gut* 1995; **36**: 544–7.
- 37 Louw J, Cariem A, Winter T, Osler W, Lucke W, Marks I. The natural history of non-NSAID gastric ulcer disease following *H. pylori* eradication: A 12 month follow-up study. *S. Afr. Med. J.* 1996; **86**: 1118.
- 38 Spiro H. About this issue. *J. Clin. Gastroenterol.* 1998; **26**: 1–2.
- 39 Cook G. *Tropical Gastroenterology*. Oxford: Oxford University Press, 1980.
- 40 EUROGAST. An international association between *Helicobacter pylori* infection and gastric cancer. The EURO-GAST Study Group. *Lancet* 1993; **341**: 1359–62.
- 41 Cheli R, Crespi M, Testino G, Citarda F. Editorial: Gastric cancer and *Helicobacter pylori*: Biologic and epidemiologic inconsistencies. *J. Clin. Gastroenterol.* 1998; **26**: 3–6.
- 42 World Health Organization. *The World Health Report, 1996*. World Health Organization
- 43 Holcombe C, Tsimiri S, Eldridge J, Jones D. Prevalence of antibody to *Helicobacter pylori* in children in Northern Nigeria. *Trans. R. Soc. Trop. Med. Hygiene* 1993; **87**: 19–21.

- 44 Omar M, el-Ansary M, Mostafa I *et al.* *Helicobacter pylori* among Egyptian patients with chronic liver diseases. A comparative study. *Ĵ. Egypt Soc. Parasitol.* 1997; **27**: 563–70.
- 45 Wyatt J, de Caestecker J, Rathbone B, Heatley R. *Campylobacter pyloridis* in tropical Africa. *Gut* 1987; **28**: A1409–10.
- 46 Holcombe C, Lucas S, Umar H, Abba A. *Helicobacter* (= *Campylobacter*) *pylori* in Africa. *Trans. R. Soc. Trop. Med. Hygiene* 1990; **84**: 294–6.
- 47 Holcombe C, Kaluba J, Lucas S. *Helicobacter pylori* infection and gastritis in healthy Nigerians. *Eur. Ĵ. Epidemiol.* 1994; **10**: 223–5.
- 48 Rouvroy D, Bogaerts J, Nsengiumwa O, Omar M, Versailles L, Haot J. *Campylobacter pylori*, gastritis and peptic ulcer disease in central Africa. *BMĴ* 1987; **295**: 1174.
- 49 Tsega E, Gebre W, Manley P, Afsaw T. *Helicobacter pylori*, gastritis and non ulcer dyspepsia in Ethiopian patients. *Ethiopian Med. Ĵ.* 1996; **34**: 65–71.
- 50 Tedla Z. *Helicobacter pylori* infection in patients with upper gastrointestinal symptoms in Arba Minch Hospital: Southwestern Ethiopia. *Ethiopian Med. Ĵ.* 1992; **30**: 43–9.
- 51 Lachlan G, Gilmour H, Jass J. *Campylobacter* in central Africa. *BMĴ* 1988; **296**: 66.
- 52 Lule G, Sang F, Ogutu E. *Helicobacter pylori* in peptic ulcer disease in Kenya. *East Afr. Med. Ĵ.* 1991; **68**: 324–7.
- 53 Louw J, Jaskiewicz K, Girdwood A *et al.* *Helicobacter pylori* prevalence in non ulcer dyspepsia: Ethnic and socio-economic differences. *S. Afr. Med. Ĵ.* 1993; **83**: 169–71.
- 54 Grundling HdK. *Helicobacter* in chronic gastritis. *S. Afr. Med. Ĵ.* 1992; **82**: 48.