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Chronic Diarrhoea Among HIV-infected Adult Patients in Nairobi, Kenya

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Objectives: Chronic diarrhoea and wasting are well recognized features of AIDS in Africa. However, because of resource constraints few comprehensive aetiological studies have been conducted in sub-Saharan Africa which have included a broad range of microbiological investigations. We undertook a prospective cross-sectional study of adult patients admitted to a government hospital in Nairobi, Kenya, to determine possible bacterial, mycobacterial, parasitic and viral causes of diarrhoea; to consider which may be treatable; and to relate microbiological findings to clinical outcome.

Methods: Stool specimens from 75 consecutive HIV-seropositive patients with chronic diarrhoea admitted to a Nairobi hospital were subjected to microbiological investigation and results were compared with clinical findings and outcome. Stool samples were cultured for bacteria and mycobacteria and underwent light and electron microscopy; lawns of *Escherichia coli* were probed for pathogenic types and aliquots were tested for the presence of *Clostridium difficile* cytotoxin. Blood cultures for mycobacteria and other bacterial pathogens were performed as clinically indicated.

Results: Thirty-nine (52%) patients yielded putative pathogens, the most common being *Cryptosporidium* sp. (17%), *Salmonella typhimurium* (13%), and *Mycobacterium tuberculosis* (13%). Of 41 patients investigated for pathogenic *Escherichia coli*, enteroaggregative *E. coli* and diffusely adherent *E. coli* were each found in four patients. Thirty-one (41%) patients died. Detection of cryptosporidium cysts was the single most significant predictor of death ($X^2 = 5.2$, $P<0.05$). Many patients did not improve (21; 28%) or self-discharged whilst still sick (5; 7%) but five (7%) were diagnosed ante mortem with tuberculosis and treated and a further 13 (17%) showed improvement by time of discharge.

Conclusions: HIV-infected patients with chronic diarrhoea in Nairobi have a poor outcome overall, and even with extensive investigation a putative pathogen was identified in only just over half the patients. The most important step is to exclude tuberculosis; and the most useful investigation appears to be Ziehl-Neelsen staining. Other potentially treatable Gram-negative bacterial pathogens, *S. typhimurium*, *Shigella* sp. and adherent *E. coli* were, however, common but require culture facilities which are not widely accessible for definitive identification. Further studies focussing on simple ways to identify sub-groups of patients with treatable infections are warranted.

Introduction

Chronic diarrhoea and wasting, slim disease is a well recognized feature of African AIDS.[1,2] In Nairobi it is a common cause of hospital admission in HIV-infected individuals, ranking fourth in cause of admission (after tuberculosis, acute pneumonia and enteric fever-like illness) and third as cause of death.[3] Community studies also suggest that it is also a common cause of death, particularly when associated with significant body wasting.

In Europe the aetiology of HIV-associated chronic diarrhoea has been comprehensively investigated[4] because of the routine use of intensive diagnostic investigations, access to well equipped microbiology laboratories and frequent post-mortem studies. Such services are not often routinely available in most government hospitals in sub-Saharan Africa; and despite the frequency of HIV-related chronic diarrhoea, the aetiology is far less well defined. Most investigations into the cause of chronic diarrhoea have limited themselves to small patient numbers,[5,6] to an intensive search for an individual pathogen[7–9] or have been narrowly based due to limited culture facilities, either ante-mortem or post-mortem.[6,10] In particular, it is not clear whether any treatable causes of chronic diarrhoea are frequently missed because of the lack of appropriate diagnostic facilities.

We undertook a 4-month study in Nairobi, Kenya, to determine possible bacterial, viral and parasitological

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causes of chronic diarrhoea and wasting using a broad range of investigations and related findings to patient outcome.

Subjects and Methods

Patients

From April to July 1992, consecutive patients reporting chronic diarrhoea (loose or watery stool for at least 4 weeks) were enrolled into a prospective clinical and microbiological study. All were adults (>16 years) admitted directly to the acute medical wards of the Kenyatta National Hospital (KNH), the main government hospital serving Nairobi. Patients referred from other hospitals were excluded. Recruitment occurred within 5 days of admission. All patients were examined, a brief history was taken and details were recorded on a standard clinical entry and follow-up form by a single observer (CM). Patients received HIV counselling and informed consent was obtained before recruitment and testing.

Samples of stool and blood for serology were collected from all study patients. Blood culture for mycobacteria and other bacterial pathogens was performed on patients according to clinical assessment. Because of resource constraints there was limited access to the general diagnostic microbiology service when the study was conducted, and few stool or blood samples were routinely cultured in the service laboratory. All culture work was therefore carried out in the Kenya Medical Research Institute (KEMRI) microbiology research laboratory. Relevant results were given by the study team to the clinicians caring for the patients in KNH as soon as they were available.

Patients were otherwise investigated and treated as was appropriate and in line with local policy, and followed daily or until death. The majority of patients (75%) were given cotrimoxazole with or without metronidazole on admission. CD4 counts are not routinely performed as a service investigation in KNH, and few families or patients were prepared to pay for them. The study had insufficient funds to carry out CD4 counts on all patients recruited. At the time of the study, sigmoidoscopy was not routinely carried out because of the limited capacity of the service, and no biopsies were taken. Post-mortems were occasionally requested, but usually only a few relatives consented. It was concluded that it would not be possible in this study to obtain biopsy or autopsy material in a consistent fashion, so this was not attempted. The study was approved by the Kenya Hospitals National Ethical Committee and the KEMRI research committee.

Bacterial culture

Unless otherwise stated, the investigations described were applied to all patients. All specimens were processed for culture on the day of collection using Oxoid (Unipath, Basingstoke, U.K.) media and incubated in air at 37 °C for 18 h, unless specifically stated. Identification of isolates was by standard bacteriological techniques and confirmation of identification, along with phage typing and serotyping, where appropriate, were carried out by the Public Health Laboratory Service (PHLS), U.K. Culture of stool samples for *Salmonella* spp. and *Shigella* spp. was carried out by direct inoculation onto xylose lysine desoxycholate agar (XLD), brilliant green agar (BG) and selenite F broth. After incubation the broth was subcultured onto both XLD and BG agars. Campylobacter blood-free medium, with cefoperazone selective supplement, was directly inoculated and incubated microaerophilically at 37 °C for 48 h before examination. Cefsulodin-irgasan-novobiocin (CIN) medium was used to culture *Yersinia* spp. after direct inoculation and after cold enrichment in phosphate buffered saline at 4 °C for 14 days. CIN plates were incubated at 30 °C for 24 h before examination. Direct inoculation onto thiosulphate citrate bile salt sucrose (TCBS) medium and enrichment in alkaline peptone water were used to culture *Vibrio* spp. *Aeromonas* spp. were cultured on Ryan's selective medium with 5 mg/l ampicillin added. Blood culture was carried out, for 18 patients, in brain-heart infusion broth incubated in CO_2 for up to 7 days.

Mycobacterial culture

Patients were investigated for mycobacterial infection not as a putative cause of diarrhoea *per se*, but because a role for tuberculosis has been implicated in slim disease.[9] Mycobacterial culture from stool was in selective Kirchner medium (10 ml), following decontamination with 5% sodium hydroxide for 15 min. Blood samples (2 ml) from 17 patients for mycobacterial culture were inoculated directly into Kirchner medium (10 ml) at collection. All samples were incubated at 37 °C for up to 6 weeks.

Microscopy

Phenol-auramine stained smears were examined directly by fluorescent microscopy for *Mycobacterium* spp. and *Cryptosporidium* sp. Modified Ziehl-Neelsen (ZN) staining was used to confirm equivocal results. Specimens were examined by light microscopy for ova, cysts and parasites directly and following formalin-ether concentration as wet preparations. The Uvitex 2B fluorescent method was

applied to examine for microsporidia in faecal smears from 36 patients. In addition, aliquots of faeces were preserved in 50% (vol/vol) formalin solution and transported to Oxford PHL, U.K. Grids were prepared and examined for enteric viruses under a Phillips 301 electron microscope following negative staining with 1% methylamine tungstate.

Detection of pathogenic Escherichia coli

From stool samples from a random selection of 41 patients, lawns of presumptive *E. coli* were harvested and shipped to the Laboratory of Enteric Pathogens, Central Public Health Laboratories, U.K. on Columbia agar slopes for detection of pathogenic *E. coli* using DNA probes directed at the following groups: enteropathogenic *E. coli* (EPEC), enterotoxigenic *E. coli* (ETEC), verocytotoxin-producing *E. coli* (VTEC), enteroinvasive *E. coli* (EIEC), enteroaggregative *E. coli* (EAggEC) and diffusely adherent *E. coli* (DAEC).

Clostridium difficile *toxin*

Aliquots of faeces were stored at −70 °C and then transferred to Oxford PHL, U.K. for detection of *C. difficile* cytotoxin using MRC 5 human fibroblast cell lines.

HIV serology

HIV antibody testing was performed using Wellcozyme HIV-1 (Wellcome Diagnostics, Dartford, U.K.) and confirmed using Enzynergost HIV 1+2, (Behringwerk AG, Marburg, Germany).

Results

One hundred and sixteen adults fulfilled the entry criteria for the study. All patients gave their consent and were entered into the study. Of these, 21 (18%) were found to be HIV-seronegative, three (3%) had equivocal HIV serology and 17 (15%) either had inadequate clinical information recorded or inadequate samples collected to enable any useful analysis to be performed; all were excluded. Results are presented for the remaining 75 patients.

Clinical findings

All patients were considered to have clinical AIDS. CD4 counts were not available for the study patients. Details of clinical features and outcome of hospitalization are shown in Table I. One observer (CM) recruited all patients and 'marked weight loss' reflected the subjective impression of whether the patient was clinically wasted or not. Most patients were unable to state their pre-morbid weight. Thirty-seven (49%) patients reported fever and 18 (24%) were febrile on recruitment or during hospitalization.

Microbiology

The wide range of potential pathogens detected can be seen in Table II. *Clostridium difficile* toxin, *Vibrio* spp. and *Yersinia* spp. were not detected. Light microscopy failed to detect ova, cysts or parasites normally associated with diarrhoea, although the following were detected: *Chilomastix mesnili* (one), *Ascaris lumbricoides* (two), *Entamoeba coli* (two) and hookwork (two). No cases of *Isospora belli* were seen. No patient yielded ETEC, EPEC, EIEC or VTEC. One patient had both EAggEC and DAEC. The only *Salmonella* sp. isolated was *S. typhimurium*, of which the commonest phage type (PT) was PT 56 (40%). Four of 18 standard blood cultures (22%) were positive. One of 17 mycobacterial blood cultures was positive, yielding *Mycobacterium avium-intracellulare*. Fifteen patients had multiple pathogens isolated: most had just two, the commonest combinations being *S. typhimurium* with *Cryptosporidium* sp. ($n=5$). Potential pathogens (apart from HIV) were not found during the investigation of 36 (48%) patients.

Outcome

There was no significant difference in mortality rate between overall groups of patients yielding pathogens (17/39, 44%) and not yielding pathogens (14/36, 39%) (Table III). However, mortality was significantly associated with detection of *Cryptosporidium* cysts. The mortality rate in patients with cryptosporidium cysts was 9/13 (69%) compared with 22/62 (36%) for cryptosporidium-negative patients ($X^2=5.2$; $P<0.05$). Of the 44 patients who survived, 13 (17%) improved with bed rest, broad spectrum antibiotics and symptomatic therapy: five patients (7%) were diagnosed ante-mortem with tuberculosis and started on treatment; 21 patients (28%) failed to show any significant benefit from the hospital admission and were discharged home, and five patients (7%), all still sick, took their own discharge.

Discussion

In Africa, chronic diarrhoea is common in adult patients presenting to hospital and is often associated with HIV

Table I. Clinical features at recruitment and outcome of hospitalization.

	Males ($n=43$)	Females ($n=32$)	All ($n=75$)
Clinical features			
Age: mean (range)/years	34 (30–56)	30 (18–50)	32 (18–56)
Characteristics of diarrhoea			
Duration: mean (range)/weeks	14 (4–52)	15 (4–52)	14 (4–52)
Stool frequency: mean (range)	6 (4–12)	6 (3–9)	6 (3–12)
Reported symptoms			
Abdominal pain	18 (41%)	12 (38%)	30 (40%)
Fever	24 (71%)	13 (41%)	37 (49%)
Clinical signs			
Temperature >37.5 °C	10 (23%)	8 (25%)	18 (24%)
Marked weight loss	41 (95%)	30 (94%)	71 (95%)
Watery stool	25 (59%)	22 (69%)	47 (63%)
Semi-formed stool	18 (42%)	10 (31%)	28 (38%)
Oral candidosis	38 (88%)	25 (78%)	63 (84%)
Outcome of hospitalization			
Died	22 (51%)	9 (28%)	31 (41%)
Self-discharged	3 (7%)	2 (6%)	5 (7%)
No improvement	11 (26%)	10 (31%)	21 (28%)
Improvement	5 (12%)	8 (25%)	13 (17%)
Treated for TB	5 (12%)	0	5 (7%)

Table II. Putative aetiological agents of diarrhoea and/or wasting disease detected in study population.

Pathogen	Male ($n=43$)	Female ($n=32$)	All patients ($n=75$ (%))
Mycobacterium tuberculosis	6	4	10 (13)
*Mycobacterium avium**	0	1	1 (1)
Salmonella typhimurium†	5	7	12 (16)
Shigella spp.‡	2	1	3 (4)
*Escherichia coli**	0	1	1 (1)
Enteroaggregative *E. coli*	2/21	2/20	4/41 (10)
Diffusely adherent *E. coli*	2/21	2/20	4/41 (10)
Campylobacter coli	0	2	2 (3)
Aeromonas caviae§	0	1	1 (1)
Small round-structured virus	0	1	1 (1)
Coronavirus	0	1	1 (1)
Cryptosporidium sp.	8	5	13 (17)
Enterocytozoon bieneusi	0/21	1/15	1/36 (3)
One pathogen	11	13	24 (32)
Multiple pathogens	7	8	15 (20)

* Identified in blood culture but not stool.
† Isolated from stool and blood from one female patient and from blood but not stool from two male patients.
‡ *S. flexneri* serotype 2a, *S. flexneri* serotype 6, *S. sonnei.*
§ *A. caviae* serotype 03.

infection. In Zaire, for example, studies have shown 40–85% of patients with persistent diarrhoea to be HIV-seropositive.[2,11] In our study, 79% of 116 consecutive admissions investigated over a 12-week period tested were HIV-seropositive. Such figures are in keeping with the results of other studies in 1992 which suggested that about 800–850 HIV-positive patients would be admitted to KNH every 3 months[12]; and that about 10% of HIV-related admissions would present with chronic diarrhoea.[3]

The spectrum of pathogens recovered was largely in accordance with previous reports from Africa, but was in some respects at variance with the experience of HIV-related illness in Europe and America. Cryptosporidium

Table III. Mortality related to potential pathogens detected in 75 patients.

Pathogen	No. cases	No. of deaths	Mortality (%)
None detected	36	14	39
Any pathogen	39	17	44
Cryptosporidium sp. alone	7	5	71
Cryptosporidium + *Salmonella*	5	3	60
Cryptosporidium + *M. tuberculosis*	1	1	100
Salmonella typhimurium alone	7	4	57
M. tuberculosis alone	9	3	33
M. avium	1	1	100
Other pathogens	9	0	0

was the most commonly detected pathogen, being found in 17% of patients, compared with reported rates of 13% in Burundi,[13] 30% in Zaire[5] and 32% in Zambia.[14] Other protozoa associated with diarrhoeal illness were not detected in our study. We saw no cases of *Isospora belli*, a pathogen with marked variation in geographical distribution.[15] Nor, like other workers in Zambia, did we identify any cases of *Giardia lamblia* or *Entamoeba*.[16] A single patient yielded *Enterocytozoon*, the only microsporidian seen, and our low detection rate differed from other studies in Zimbabwe and Zambia.[9,17] Although simple staining methods on unconcentrated stool samples have been shown to be effective,[9,15,17] small numbers may be revealed only after prolonged examination of preparations from at least two stool samples, and it is possible that more meticulous analysis would have yielded greater numbers.

When profound weight loss is a feature of HIV-related illness in Africa it is often referred to as slim disease.[1] In our study chronic diarrhoea was the primary entry criterion, but as this is inextricably linked with wasting in many patients it was considered important to seek evidence of mycobacterial infection as a cause of wasting and *M. tuberculosis* was isolated from the faeces of 10 (13%) patients. Although these patients presented complaining of chronic diarrhoea, subsequent clinical evaluation identified five of these patients as likely to be suffering from pulmonary tuberculosis and appropriate therapy was started. These five patients survived, providing further evidence that initially unrecognized tuberculosis may be a significant and treatable contributing factor to the wasting seen in slim disease.[10] Nevertheless, in a further five patients who were stool culture positive for *M. tuberculosis*, tuberculosis was not diagnosed as a result of routine clinical procedures. Wasting may be the only noticable feature in a significant number of patients with tuberculosis; or it may be an agonal infection. Only one patient yielded *Mycobacterium avium-intracellulare*, which was grown from a blood culture. Unlike Europe and America, atypical mycobacterial infection is rarely seen in Nairobi.[12]

Salmonella typhimurium was the leading bacterial pathogen in this study and was isolated from 12 patients, two of them from blood culture but not from stool. It is unclear how such acute disseminated salmonellosis, and the single case of *E. coli* bacteraemia, relate to chronic diarrhoea. These may be secondary infections in debilitated patients with marked immunosuppression. In a previous study, non-typhi salmonellae were found to be the most common cause of HIV-related bacteraemia in hospital admissions in Nairobi.[18]

Detection of EAggEC or DAEC from 9/41 (22%) patients was an interesting finding. One patient yielded both of these forms of pathogenic *E. coli*. A significant association between colonization with adherent *E. coli* and chronic diarrhoea and wasting in AIDS patients has been demonstrated by Kotler *et al.*,[19] who found such strains in 17% of study patients in the USA. Adherent *E. coli* have also been described from HIV-positive patients with chronic diarrhoea in Zambia.[20]

Despite use of a broad range of microbiological investigations, there was failure to detect a pathogen in almost half the patients. It is likely that analysis of multiple stool samples taken at separate times might have increased yields, as might invasive procedures such as duodenal aspiration and rectal biopsy.[4] It is possible that novel agents remain to be characterized and associated with chronic diarrhoea and wasting in HIV patients, and HIV itself may be the cause of chronic diarrhoea in some patients.[21] Whether any such additional investigations would identify more treatable infections remains to be seen.

How then may these results contribute to the care of HIV-infected patients with chronic diarrhoea in areas with limited diagnostic and microbiological facilities? The study results clearly show that seropositive patients presenting with chronic diarrhoea have a poor outcome irrespective of whether a potential pathogen is isolated

or not. Careful diagnostic evaluation, in particular looking for pulmonary tuberculosis, should nevertheless be undertaken. Sputum (or stool) ZN microscopy for mycobacteria should be feasible almost everywhere and some patients with active tuberculosis will respond well to therapy. Stool microscopy using modified ZN staining can also identify cryptosporidium cysts, the presence of which is associated with a very limited prognosis. For such patients in the absence of effective therapy, it may be better to aim for symptomatic therapy and early discharge home as soon as the cysts are identified.

What of the potentially treatable Gram-negative enterobacterial pathogens identified, which were cultured from over 20% of study participants? Furthermore, as many as 20% of patients may be colonized with adherent *E. coli*, which may also play a role in pathogenesis and may respond to antibiotic treatment. To identify such infections requires access to a microbiology laboratory routinely performing culture and sensitivity testing. Unfortunately, few hospitals in sub-Saharan Africa can at present afford to provide such a service routinely because of severe resource constraints. Clinical trials focussing on these patients may be able to define more clearly signs and symptoms which predict bacterial infection without necessarily needing access to culture facilities, and thus more effectively identify a sub-group of patients with chronic diarrhoea for whom hospital admission and intensive antimicrobial therapy may be justified.

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References

1 Serwada D, Sewankambo NK, Carswell JW *et al.* Slim disease: a new disease in Uganda and its association with HTLV-III infection. *Lancet* 1985; **2**: 849–852.
2 Colebunders R, Francis H, Mann JM *et al.* Persistent diarrhoea, strongly associated with HIV infection in Kinshasa, Zaire. *Am J Gastroenterol* 1987; **82**: 859–864.
3 Gilks CF, Otieno LS, Brindle RJ *et al.* The presentation and outcome of HIV-related disease in Nairobi. *Q J Med* 1992; **297**: 25–27.
4. Smith PD. Gastrointestinal infections in AIDS. *Ann Intern Med* 1992; **116**: 63–77.
5 Colebunders R, Lusakumuni K, Nelson AM *et al.* Persistent diarrhoea in Zairian AIDS patients: an endoscopic and histological study. *Gut* 1988; **29**: 1687–1691.
6 Sewankambo N, Mugerwa RD, Goodgame R *et al.* Enteropathic AIDS in Uganda. An endoscopic, histological and microbiological study. *AIDS* 1986; **1**: 9–13.
7 Thea DM, Glass R, Grohmann GS *et al.* Prevalence of enteric viruses among hospital patients with AIDS in Kinshasa, Zaire. *Trans R Soc Trop Med Hyg* 1993; **87**: 263–266.
8 Conlon CP, Banda HM, Luo NP, Namaambo MK, Perera CU, Sikweze J. Faecal mycobacteria and their relationship to HIV-related enteritis in Lusaka, Zambia. *AIDS* 1989; **3**: 539–541.
9 van Gool T, Luderhoff E, Nathoo KJ, Kiire CF, Dankert J, Mason PR. High prevalence of *Enterocytozoon bieneusi* infections among HIV-positive individuals with persistent diarrhoea in Harare, Zimbabwe. *Trans Roy Soc Trop Med Hyg* 1995; **89**: 478–480.
10 Lucas SB, De Cock KM, Hounnou A *et al.* Contribution of tuberculosis to slim disease in Africa. *Br Med J* 1994; **308**: 1531–1533.
11 Henry MC, De Clercq D, Lokombe B *et al.* Parasitological observations of chronic diarrhoea in suspected AIDS adult patients in Kinshasa, Zaire. *Trans Roy Soc Trop Med Hyg* 1986; **80**: 309–310.
12 Gilks CF, Brindle RJ, Mwachari C *et al.* Disseminated Mycobacterium avium infection among HIV-infected patients in Kenya. *J Acquir Immun Defic Syndr and Human Retrovirol* 1995; **8**: 195–198.
13 Kadende P, Nkurunziza T, Flock J *et al.* Infectious diarrhoea in African acquired immunodepression syndrome (AIDS). A prospective survey of 100 patients studied in Bujumbura (Burundi). *Med Trop (Madrid)* 1989; **49**: 129–133.
14 Conlon CP, Pinching AJ, Perera CU, Moody A, Luo NP, Lucas SB. HIV-related enteropathy in Zambia: a clinical, microbiological and histological study. *Am J Trop Med Hyg* 1990; **42**: 83–88.
15 Wuhib T, Silva TMJ, Newman RD *et al.* Cryptosporidial and Microsporidial Infections in HIV-Infected patients in Northeastern Brazil. *J Infect Dis* 1994; **170**: 494–497.
16 Hunter G, Bagshawe AF, Baboo KS, Luke R, Prociv P. Intestinal parasites in Zambian patients with AIDS. *Trans Roy Soc Trop Med Hyg* 1992; **86**: 543–545.
17 Drobniewski F, Kelly P, Carew A *et al.* Human Microsporidiosis in African AIDS patients with chronic diarrhoea. *J Infect Dis* 1995; **171**: 515–516.
18 Gilks CF, Brindle RJ, Otieno LS *et al.* Life-threatening bacteraemia in HIV seropositive adults admitted to hospital in Nairobi, Kenya. *Lancet* 1990; **336**: 545–549.
19 Kotler DP, Giang TT, Thiim M, Nataro JP, Sordillo EM, Orenstein JM. Chronic bacterial enteropathy in patients with AIDS. *J Infect Dis* 1995; **171**: 552–558.
20 Mathewson JJ, Dong Jiang Z, Zumla A *et al.* HEp-2 cell-adherent *E. coli* in patients with Human Immunodefiency Virus-associated diarrhoea. *J Infect Dis* 1995; **171**: 1636–1639.
21 Ullrich R, Zeitz M, Heise W, L'age M, Hoffken G, Riecken EO. Small intestinal structure and function in patients infected with Human Immunodeficiency Virus (HIV): evidence for HIV-induced enteropathy. *Ann Intern Med* 1989; **111**: 15–21.