Nations Development Programme is planning to introduce regional offices and Unicef is strengthening its own regional structure. On a practical level, staff say that having regional offices reduces the time and money spent travelling to and from Geneva. Recently the independence of the offices has had the added benefit of insulating regional staff from the growing discontent in Geneva. WHO claims that the decentralisation allows fast, flexible, and relevant responses to the health needs of member states.

But the regions give only the illusion of decentralisation, while duplicating activities in headquarters and delaying resources and information getting to the point of need. WHO will be fully effective only if the regions are made properly accountable, both politically and financially, and if more of their responsibility is

devolved to country level. In the next article I will examine the role of the country offices and look at whether they are equipped to take on such additional responsibility.

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Controversies in Management

Eradication of *Helicobacter pylori* should be pivotal in managing peptic ulceration

Eradication largely prevents relapse

C J Hawkey

This is the thirteenth in a series of articles examining some of the difficult decisions that arise in medicine

Like tuberculosis, peptic ulcer was once a disease of unknown cause. Both were managed by empirical or symptomatic treatments which included (for tuberculosis) the wearing of gold, being touched by King Charles II, and use of cough suppressants,¹ and (for peptic ulcer) venesection, rhubarb infusions, nutrient enemas, and drugs which suppress acid.² With recognition of their infectious aetiology and the use of effective antibiotics, both can now be cured.^{3,4} Not all patients are cured (often because of poor compliance), but those who are cured rarely experience recurrence.

Reasons for eradicating *H pylori*

Deliberate ingestion of *H pylori* leads to a persistent active antral gastritis,⁴ which longitudinal studies have shown to increase the risk of duodenal ulcer about 30 times and the risk of gastric ulcer eight times.⁵ The prevalence of *H pylori* in patients with symptomatic duodenal ulcer (about 95%) and in patients with gastric ulcer (70-80%) is much higher than in the general population,⁴ and 37% of asymptomatic Italian blood donors who were positive for *H pylori* had duodenal ulceration, erosive duodenitis, or active gastric ulcers.⁶

Eradication of *H pylori* with one week antibiotic regimens heals duodenal ulcers as rapidly as reported for omeprazole.⁷ More importantly, many controlled trials have established that relapse of gastric and duodenal ulcer after eradication is rare, with annual relapse rates of 0-3%^{8,9} compared with 60-90% untreated or 10-30% with continued treatment with H₂ receptor antagonists.^{10,11} This is because eradicating *H pylori* eliminates the cause of the ulcer diathesis. The associated antral active gastritis resolves rapidly and chronic gastritis over several months.¹⁰ The complications of ulcer are prevented.¹¹ Such considerations have persuaded the United States National Institutes of Health to recommend that treatment to eradicate *H pylori* is offered to all patients who have a duodenal ulcer.

Invalid reasons for not eradicating

Reliability—*H pylori* is eradicated more effectively than *Mycobacterium tuberculosis*. A recent meta-analysis found an average 87% eradication with standard tetracycline based triple therapy.⁹ For the numerically challenged prescriber who advances the number of tablets to be taken as a reason not to eradicate, equally effective one week regimens are now emerging.⁹ Imperfections of existing regimens and the prospect of future improvement have not prevented prescribers from treating tuberculosis with antibiotics, nor should they stop treatment of *H pylori*.

Toxicity—Up to one third of patients have experienced antibiotic related side effects, but these are usually mild. However, data are accumulating that H₂ antagonists and proton pump inhibitors used for maintenance treatment are less benign than once thought, with increased enteric infections¹² and accelerated gastric atrophy¹³ among the side effects.

Cost—The cost of a single course of two week standard triple therapy is about £15.00. The addition of two weeks of amoxicillin to omeprazole costs £4.67. Compared with life long treatment with H₂ receptor antagonists or proton pump inhibitors these costs are minimal.

Validity of treatment—In the Nottingham catchment area (about 630 000 people) roughly a quarter of a million courses of antibiotics are prescribed annually, many for conditions such as sore throats or urinary tract infections. In this context, using antibiotics for peptic ulcer, which has been estimated to have a 4% annual incidence of complications and from which over 4000 patients a year die in the United Kingdom, does not seem unjustified.

Too soon to change—Conservatism in medical practice can be defensible, and there are legitimate concerns—for example, the hazards of indiscriminate use are considerable; benefits may be obtained at the price of other unwanted and hazardous actions; in the old and unfit it may be better to use existing treatments; the relapse (recrudescence) rate is not fully determined. All of these are sentiments uttered, not about treatment

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for *H pylori*, but about cimetidine at an analogous stage of its development.^{14,15} For *H pylori* such conservatism is less defensible than it was in the 1970s for cimetidine since the drugs used for eradication are well known and established.

It took Koch eight months to establish the tubercle bacillus as the cause of tuberculosis,³ and by all accounts his colleagues and rivals were rapidly convinced of his case. It is difficult to explain why, faced with a far greater body of data, today's doctors show greater resistance to the evidence for, and therapeutic implications of, the infectious aetiology of peptic ulceration. True, Koch was able to transmit tuberculosis to guinea pigs whereas a satisfactory animal model for *H pylori* is still lacking. Conversely, the case for eradicating *H pylori* rests directly on many therapeutic trials, a compelling line of evidence to which Koch was not able to turn. The reason for the resistance is surely that prescribers have got used to the comfort of being able to suppress but not cure peptic ulceration with acid suppressing drugs. However, if history had been reversed so that *H pylori* and its associated diseases had already been treated with antibiotics, alongside streptococcal sore throats, tuberculous pneumonia, or urinary infections, we would rightly have greeted the advent of acid suppressing drugs as no more than a useful symptomatic adjunct to curative treatment, alongside gargles, cough suppressants, and potassium citrate.

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Helicobacter pylori is not the causative agent

C O Record

A pathogenic role for helicobacter in the stomach has been proposed for the past 10 years, but despite about a thousand publications a year on this subject, treatment to eradicate helicobacter remains controversial. Several questions need to be considered.

Does *Helicobacter pylori* cause peptic ulcers?

In the 19th century there was much controversy concerning the role of micro-organisms and the causation of disease. These discussions resulted in the formulation of Koch's postulates. The first is that the infectious agent occurs in every case of the disease and under circumstances that can account for the pathological changes and clinical course of the disease.

About 95% of patients with symptomatic duodenal ulcer are colonised with *H pylori*, 50% of those with perforated duodenal, and 17% of those with bleeding duodenal ulcers.¹⁻³ About 77% of patients with gastric ulcer are colonised.⁴ Thus not all patients are infected while those with the severest disease resulting in complications exhibit a lower colonisation rate than patients presenting with uncomplicated dyspepsia.

By extension of this first postulate the organism should not occur in other disease as a fortuitous and non-pathogenic parasite. Epidemiological studies in Europe have shown about 33% of normal adults are colonised with *H pylori*.⁵ In developing countries 67% of asymptomatic adults and 40% of children under 10 years old are colonised in the absence of peptic ulcer disease.⁵ Thus in most patients *H pylori* must be considered as a fortuitous and non-pathogenic agent.

Koch also stated that after being isolated and grown in pure culture the organism should be able to induce the disease. There are two studies which need to be considered. In the first one by Marshall *et al* inoculation

resulted in dyspepsia on day 7 and biopsy proved gastritis in the presence of *H pylori* at day 10.⁶ Gastric biopsies on day 14 showed a decrease in gastritis, and organisms could no longer be recovered. Morris and Nicholson also found dyspepsia at day 3, biopsy proved gastritis at day 5, and gastritis associated with *H pylori* colonisation at day 11.⁷ However, between days 11 and 19 there was hypochlorhydria (intragastric pH 7.6 to 7.9). Duodenal ulcers are known to develop in patients with high acid production, and achlorhydria is generally regarded as protective. Not surprisingly in these studies there was no endoscopic evidence of peptic ulceration. Other studies have also commented on epidemic hypochlorhydria that has developed after measuring 24 hour intragastric pH. The hypochlorhydria has been attributed to coincidental infection from a contaminated pH electrode, probably with *H pylori*.⁸

Can *H pylori* be eradicated?

Many studies have shown that eradicating *H pylori* is difficult. Traditional remedies for peptic ulcer disease, including H₂ receptor antagonists, proton pump inhibitors, and sucralfate do not affect antihelicobacter activity. But bismuth chelates have minimum concentrations to achieve 90% inhibition of 16-25 mg/l.⁹ A large range of antibiotics have high activity against *H pylori*, with minimum inhibitory concentrations ranging from 0.03 mg/l for ampicillin to 1 mg/l for rifampicin.⁹ However, when used singly antibiotics are largely ineffective for eradicating *H pylori*. Thus amoxycillin 375 mg eight hourly for 28 days resulted in only a 30% elimination rate, while 500 mg 12 hourly of tetracycline failed to eradicate any organisms.¹⁰ In a meta-analysis amoxycillin on its own eradicated 23% of