microbial chemotherapy are given for urinary tract infections, and bacterial resistance to broad spectrum antimicrobial agents is common in those wards.[14] Clarification of the role of bacteriuria in the atypical presentation of disease in the elderly might thus allow fewer patients to be treated with antibiotics and so reduce bacterial resistance in wards for the elderly.

The effect of treating all asymptomatic elderly individuals with bacteriuria has not been examined; a very large multicentre study would be required to eliminate confounding variables. The elderly with bacteriuria are a heterogeneous population, and better understanding of underlying causes of urinary infection could result in the identification of subgroups of infected individuals who would benefit from prophylactic treatment.

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Campylobacter pyloridis: what role in gastritis and peptic ulcer?

Much excitement has recently been generated by the possibility that *Campylobacter pyloridis* might be the cause of gastritis and peptic ulcer.[1 2] This spiral organism colonises the gastric antrum in 90-100% of patients with duodenal ulcer, over 70% of patients with gastric ulcer, and half of patients with non-ulcer dyspepsia.[3 4] When present, it is invariably associated with histological evidence of gastritis.[5]

Spiral organisms were seen in the stomach of animals before the turn of the century,[6] were reported in man in 1906,[7] and raised further interest in 1940,[8] but their possible clinical importance was not recognised until recently.[9-11] *C pyloridis*,[12] a microaerophilic spiral bacterium, is like many other campylobacters and shows some antigenic cross reactivity,[2] but it differs from others metabolically, morphologically, and in its chemical structure.[1]

The organisms are found on the surface of gastric epithelial cells even when acidity is normal—they are protected from acid by the overlying mucus layer and the alkaline secretion of the epithelial cells.[13] They are mobile in highly viscid material[14] and appear to be specially adapted to the mucus layer above these particular cells as they are not found in areas of intestinal metaplasia within the stomach, and when identified in the duodenum are found only in areas of gastric metaplasia.[10] Ultrastructural studies show adherence pedicles at points of membranous adhesion[1 15]; microvilli are absent or depleted, and intracellular oedema is prominent. These appearances are reminiscent of intestinal epithelial cells infected by enteropathogenic *Escherichia coli*.

Is *C pyloridis* pathogenic? Data from many different centres have confirmed the association with active gastritis,[1 2] but the organisms are less often found in gastritis secondary to duodenogastric reflux[16] and pernicious anaemia.[17] These data, together with the ultrastructural appearances, strongly support a primary aetiological role. Further support comes from an experiment carried out by a normal volunteer who developed an acute self-limiting dyspeptic syndrome with acute gastritis after swallowing the bacteria.[18] Other evidence links *C pyloridis* infection with an epidemic of hypochlorhydric gastritis in 17 of 37 volunteers who underwent acid secretion studies with a pH electrode that had not been sterilised between experiments.[1 19] Eradication of *C pyloridis* with antibiotics or bismuth leads to histological improvement[4] but relapse is common. Serum IgA and IgG titres to *C pyloridis* are appreciably raised in patients with campylobacter,[20 21] and local gastric juice antibodies are also present in some of these.[22]

The clinical relevance of the strong association between gastritis and *C pyloridis* is, however, controversial as gastritis occurs in many of the normal population[23] and campylobacter associated gastritis has been reported in a quarter of normal volunteers. More interesting is its relation with peptic ulcer.[4 10] Numerous studies have confirmed that campylobacter associated gastritis is present in virtually all non-iatrogenic cases of duodenal ulcer. *C pyloridis* may infect the islands of metaplastic gastric epithelium found in the duodenum, thereby weakening the mechanisms which normally protect these cells from acid attack, which leads to a breakdown in mucosal integrity and ulceration.[24] A similar sequence in the stomach leads to gastric ulceration. The evidence for this hypothesis remains circumstantial, but metronidazole, to which *C pyloridis* is sensitive, has had a beneficial effect in both gastric and duodenal ulceration.[25] Further, the lower recurrence rate when duodenal ulcers are healed with colloidal bismuth subcitrate rather than acid reducing drugs may be related to the effect of bismuth on *C pyloridis*.[26]

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Isolating the gene for Duchenne muscular dystrophy

Despite much work on muscle and other tissues we still have no clear indication of what the primary defect is in Duchenne muscular dystrophy, and this makes rational approaches to treatment and prevention difficult. The new recombinant DNA techniques allow identification of a gene without requiring information on what that gene does, and these have allowed research to break out of what might have been stagnation and given five years of remarkable progress.

The first clue came from the observation of a rarity: the occurrence of several cases of Duchenne muscular dystrophy in girls carrying a chromosome rearrangement affecting the X chromosome.[1] Initially these were thought likely to be incidental changes, but as other cases were reported it became clear that the breakpoint on the X chromosome was at the same site in each—the central area of the short arm of the X known as band p21.[2] Over 15 such cases are now known, and this constancy has remained, leaving no doubt that the break is at the site of the Duchenne muscular dystrophy gene.

Soon after the recognition of these cases it became possible to produce markers for the Duchenne muscular dystrophy gene that could be studied in families.[3] These DNA markers —inherited variations in DNA sequence recognised by producing fragments of different size and known as restriction fragment length polymorphisms—could be localised to the X chromosome by physical methods and then tested in families with the disorder to show whether the markers had been inherited in parallel with the disease. The year 1982 saw the first such markers linked to Duchenne muscular dystrophy,[4] and in 1983 a second marker was placed on the opposite side of the gene.[5] Both firmly placed the Duchenne muscular dystrophy gene at p21, the same site as that suspected from the girls with chromosome defect.

Furthermore, the gene for the milder "Becker" form of muscular dystrophy (previously thought to be quite separate) proved to be at the same site.[6]

These markers opened the way to prediction for the Duchenne muscular dystrophy gene, since by typing the markers in a family—particularly when both markers could be used together—the presence of the Duchenne muscular dystrophy gene itself could be inferred.[7] The search was now on for closer and more informative markers, and within a year at least seven had been detected, greatly increasing the proportion of families who could be helped by carrier detection,[8] and allowing also the possibility of early prenatal prediction by chorion biopsy in occasional cases.[9]

At this stage, around mid-1985, the suspicion became strong that the Duchenne muscular dystrophy gene was not a conventional one. Despite some of the DNA markers being physically close, all showed relatively frequent recombination between marker and disease,[10] suggesting that the gene might be in an unstable site with much mutation and rearrangement. Recent developments have shown that this is indeed the case, thanks to two remarkable pieces of research that have brought us to the threshold of the gene itself.

The first of these, by Lou Kunkel and colleagues in Boston, was based on the study of a boy who had both Duchenne muscular dystrophy and a visible chromosome deletion.[11][12] When DNA sequences isolated from the deleted region were tested against others from patients with "ordinary" Duchenne muscular dystrophy it became clear that some of them were missing the Duchenne muscular dystrophy gene, even though they were chromosomally normal. About 7% of cases are now known to be associated with gene deletions—the first step in molecular analysis of the defect. At the same time Worton and colleagues in Toronto were able to isolate and clone the DNA from the breakpoint on the X chromosome of one of the girls with muscular dystrophy and a chromosome translocation.[13] As predicted this DNA sequence proved to be integrally related to the Duchenne muscular dystrophy gene, showing deletions in most of the cases which were missing Kunkel's "pERT" probe.

These two experiments, reaching the same endpoint from different approaches, might have been expected to have solved the problem and allowed the gene itself to be fully analysed and its product identified. This has not happened, however, and we seem to be dealing with a very large region of DNA (perhaps several million base pairs) in which a change at different points may result in Duchenne or Becker muscular dystrophy. So far there is no sign of a single functional gene in this region.

How does this answer the questions for clinicians looking after families with Duchenne and Becker muscular dystrophy? The first group for whom there has been a real advance is those in whom a gene deletion is present. Here one can offer carriers an accurate and specific first trimester prenatal diagnosis, so it is most important that such boys and their relatives are carefully tested. For the majority not showing a deletion there remains a finite error of around 5% even using the new markers integrally related to the gene. Nevertheless, most carriers may now be predicted accurately by combining DNA analysis with the older approach of creatine kinase testing. If prenatal diagnosis is undertaken the family must realise that we still do not have a totally accurate prediction, though a 95% accuracy rate will be acceptable to some. For all families the rapid progress of the past five years is a cause for real optimism, since we are now