worth while was initially considered to be six hours. Data from the Gruppo Italiano per lo Studio della Streptochinasi nell'Infarto Miocardico failed to show significant benefit beyond this time and suggested an adverse trend at nine to 12 hours. These observations were not supported in the second international study of infarct survival in which the reduction in risk achieved by streptokinase and aspirin therapy was 32% at five to 12 hours and 39% at 13 to 24 hours. These apparently conflicting observations were based on relatively small numbers of randomised patients, and the confidence intervals were wide. Two further randomised trials of delayed thrombolysis have been published recently. The effect of alteplase 100 mg was compared with that of placebo in 5700 patients presenting six to 24 hours after the onset of symptoms in the late assessment of thrombolytic efficacy study,[10] while in the trial by the Estudio Multicentrico Estreptoquinasa Republicas de America del Sur Collaborative Group streptokinase 1·5 mU was compared with placebo in 4500 patients, of whom 85% were randomised between seven and 24 hours after the onset of symptoms.[11] Neither trial showed a significant fall in overall mortality at 35 days. Prespecified survival analysis of treatment six to 12 hours after the onset of symptoms showed a significant fall in mortality from 12% to 8·9% in the late assessment of thrombolytic efficacy study[10] and a non-significant fall from 14·7% to 12·7% in the South American study.[11] Neither trial found that treatment between 13 and 24 hours after the onset of symptoms produced a significant fall in mortality. Taken together, these and other studies suggest that thrombolytic treatment between seven and 12 hours achieves a significant reduction in mortality, with 16 fewer patients dying per 1000 treated, while treatment between 13 and 24 hours reduces the number of deaths by five per 1000 patients treated.[12]

The data from all available trials consistently suggest that maximum benefit is achieved by early thrombolysis. Every effort should be made to streamline prehospital and in hospital procedures and to audit performance. On the available evidence, all patients without contraindications to thrombolysis who present with ST segment elevation or bundle branch block up to 12 hours after the onset of symptoms should be treated. The identification of subgroups who may benefit from treatment after 12 hours requires further study.

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What to do about halitosis

Regular use of toothbrush and dental floss

A degree of halitosis (oral malodour or foetor oris) is common in healthy people, particularly after sleep. It seems to originate from the mouth, resulting from the metabolic activity of bacteria present in oral plaque. Halitosis at other times is a distressing complaint from which few people probably escape completely and which is still incompletely understood. The true prevalence is not known, but one recent study suggested that nearly half of a group of young women (dental hygienists) believed that they sometimes had halitosis.[1]

Halitosis generally has as its basis bacterial putrefaction of food debris, cells, saliva, and blood.[2] In particular, proteolysis of proteins to peptides, amino acids, and thence substrates with free thiol groups, such as cysteine and reduced glutathione, gives rise to volatile fluids and sulphides.[3] Acetone, acetaldehyde, ethanol, propanol, and diacyl are also important causes of halitosis but, perhaps surprisingly, amines, indole, and skatole do not seem to be aetiologically important.[4]

People who refrain from cleaning their mouth soon develop halitosis,[5] but any form of oral sepsis can produce appreciable malodour, the most common condition being inflammatory, plaque related gingival disease (gingivitis) or periodontal disease (periodontitis). The amounts of volatile sulphur compounds and the ratio of methylmercaptan to hydrogen sulphide are higher in the mouth air from patients with periodontal disease than in that from people with healthy mouths.[6,7] The source of these compounds seems to be the gingival crevice, periodontal pockets, and the tongue coating.[6,7] Sulphides identified from gingival crevicular sites include hydrogen sulphide, methylmercaptan, dimethyl sulphide, and dimethyl disulphide.[8] Concentrations of these sulphides in mouth air seem to be particularly associated with oral spirochaetes and motile rods.[9] Other oral sources of infection can cause malodour, as can sinusitis, foreign bodies in the nose, and respiratory infections.

Many foods and drinks can cause transient malodour, especially garlic, onions, and curries. Smoking and drugs, including occasionally alcohol, isosorbide dinitrate, and disulfiram, may also be implicated. Rare causes include diabetic ketoacidosis and severe renal or hepatic dysfunction. A recent possible link has been suggested between *Helicobacter pylori* and halitosis,[10] but this is unsubstantiated. Halitosis may also be imaginary (delusional halitosis)[11] or a hallucinatory feature in schizophrenia or temporal lobe epilepsy.

The management of halitosis requires establishing the presence of true halitosis and assessing its severity. People are usually good judges of the degree of malodour but, as

measurement of sulphide concentrations in mouth air is reproducible and sensitive and relates well to assessments of malodour assessment by observers,[12 13] measurement with a portable sulphide monitor provides an objective assessment. Gas chromatography may provide a more accurate assessment of the wider range of compounds responsible for malodour and has been adapted for use with small samples of mouth air.[4] The history and examination should be directed towards eliminating any dietary and systemic causes. A full assessment of oral and dental health is always indicated, and, although a dental practitioner is the best trained for this, a periodontologist has special skill in disorders affecting the gingiva and periodontium.

The most reliable management is to reduce the oral flora, particularly anaerobes; this is best achieved by improving oral hygiene by brushing the teeth, cleaning between the teeth, and other means. A simple, inexpensive, and effective treatment is to use a mouth rinse of 0·2% aqueous chlorhexidine gluconate, which is remarkably active against a range of organisms in dental plaque and can also reduce halitosis whether judged subjectively or by decreases in volatile sulphides in the mouth air.[13] Hydrogen peroxide mouthwashes reduce concentrations of salivary thiols and may be useful in the management of acute necrotising (ulcerative) gingivitis, but they are not indicated in most other oral infections. Antimicrobial treatment is rarely needed except in severe or recalcitrant cases, though it can be useful to reduce postoperative halitosis.[14]

Various other products designed to reduce halitosis are under development. For example, cetylpyridinium chloride and a two phase oil-water mouthwash containing olive and other essential oils [15] seem to reduce volatile sulphur compounds in the breath.[15 16] A range of mouth fresheners is also available. Currently, however, the cheapest and most effective management for most cases of halitosis is simple, regular oral cleaning with a toothbrush and dental floss.

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Appropriateness: the next frontier

Appropriateness ratings could revolutionise health care

The health care systems of developed countries share common problems. Firstly, the explosion of costly medical technologies increasingly jeopardises our ability to give everybody all the care that would benefit them. And, secondly, the explosion in medical services has made it virtually impossible to remember the indications, complications, and costs of procedures and drugs—that is, to practise good medicine without additional help.

Studies of appropriateness underline the seriousness of these problems. By appropriate care I mean that for which the benefits exceed the risks by a wide enough margin to make it worth providing. If we could increase appropriate and decrease inappropriate care, the benefits to patients and society in terms of health and wealth would be enormous. Indeed, without methods to detect inappropriate care, society's ability to maintain universal insurance coverage may disappear.[1]

But how do you measure the appropriateness of care?[2] Although the clinical literature is the place to start, it mostly concerns the efficacy of a procedure performed under ideal conditions and tells us little about what happens when the procedure is done under less than ideal conditions.[3] Furthermore, research rarely includes outcome measures that are relevant to patients and practitioners—for example, effects on health status or function.[4]

To measure appropriateness, colleagues and I at the RAND Corporation and the University of California, Los Angeles, have developed an explicit method, beginning with a literature analysis that summarises what is known about a procedure's efficacy, effectiveness, indications, cost, and use. The next step is to develop a list of specific clinical indications based on that review. Using the list of indications and the literature review, a panel then rates appropriateness on a scale of 1 to 9. On the basis of these ratings and clinical data collected from medical records we can measure appropriateness in actual practice.

Some of the findings have been worrying. For example, among Americans aged over 65 being treated in the fee for service system, carotid endarterectomy was performed for reasons that were equivocal, at best, in two thirds of cases.