

Thrombolysis and the general practitioner

2 Useful after careful evaluation of patients

Robert G Wilcox

Roughly 160 000 people die in the United Kingdom each year of the various manifestations of ischaemic heart disease. Most of these deaths occur outside hospital, many before medical help is sought or there is time to respond.¹ Between half and three quarters of these deaths occur suddenly, usually in patients already known to have ischaemic heart disease, and are caused either by ventricular fibrillation or asystole.² Most of the remainder occur in patients who are in the throes of an evolving myocardial infarction and succumb to primary ventricular fibrillation, other non-viable cardiac rhythms, or pulmonary oedema. The underlying pathological cause is similar in both instances—namely, an atheromatous plaque undergoing fissure with subtotal coronary occlusion and distal platelet emboli in ventricular fibrillation, and total occlusion in the latter.³

Both circumstances require emergency action. Fibrillation requires an almost immediate appreciation by a witness(es) willing to initiate cardiopulmonary resuscitation and to alert the emergency services. Myocardial infarction requires urgent relief of pain and treatment for pulmonary oedema if present. Whereas ventricular fibrillation is a dramatic event likely to precipitate an urgent response, the importance of chest discomfort may not be appreciated or admitted for some time, even when special provisions for help are made available.⁴ In addition, patients with unaccustomed or unusually severe chest pain should seek help sooner rather than later so that treatment which has been proved to increase the chances of survival and reduce the amount of myocardial damage can be started: with intravenous thrombolytic treatment we are confident about increasing survival and hopeful about reducing damage.⁵⁻⁹ The current debate is whether such treatment loses any, or all, of its potential benefit if delayed beyond a few hours; if so, how can it be given as soon and as safely as possible?

Improving survival from myocardial infarction outside hospital

During the evolution of a myocardial infarct irreversible damage spreads outwards from an epicentre over several hours, perhaps even in a staccato fashion.¹⁰ The area of potential damage is governed principally by the site of the occluded coronary artery, its region of perfusion, and the quality of collateral circulation. More acutely thrombosed coronary arteries are probably reperfused by early rather than late thrombolysis.^{11 12} Subgroup analysis of some trials of thrombolytic agents suggests a diminishing return with time and that early treatment achieves the best results—for example, the 47% reduction in mortality in hospital was seen in the 10% of patients randomised to treatment within one hour in the GISSI trial.⁵ If early thrombolytic treatment is best, could its use outside hospital be implemented?

Firstly, the public needs to be educated to summon help immediately in the case of a witnessed collapse or in the event of unexpected or unusually severe chest pain. Secondly, agreement is needed on who should be called for help—the emergency ambulance service, the general practitioner, or both? Thirdly, whoever is

Contraindications to thrombolytic treatment in hospital based trials

Most may seem reasonable but few have been proved to be dangerous

- Any previous stroke
- Transient ischaemic attack in the previous six months
- Increased likelihood of pre-existing left heart thrombus
- Shock with systolic blood pressure <80 mm Hg
- Active internal bleeding (history of overt gastrointestinal or genitourinary bleeding within previous six months)
- Major surgery or trauma within the previous month
- Severe head or spinal surgery or trauma within the previous six months
- Oral anticoagulant treatment
- Known bleeding diathesis, bleeding disorder, or chronic liver disease
- Acute pericarditis, septic thrombophlebitis, or subacute bacterial endocarditis
- Intracranial neoplasm, arteriovenous malformation, or aneurysm
- Severe uncontrolled hypertension (systolic blood pressure ≥ 200 mm Hg or diastolic ≥ 110 mm Hg) (not controlled within 24 hours)
- Proliferative diabetic retinopathy
- Vigorous cardiopulmonary resuscitation within the previous seven days
- Non-compressible arterial punctures within the previous 14 days or required imminently
- Possibility of pregnancy or nursing mother (include women of childbearing age only after a negative result on pregnancy testing)
- Serious organic or psychiatric disease.

summoned should be able to assess the severity of the problem, be competent in basic cardiopulmonary support, and have access to a few cardiovascular drugs, an electrocardiograph, and a defibrillator. At present these requirements would probably be best met by summoning both a well equipped ambulance staffed by a crew trained in advanced life support and the general practitioner or a mobile coronary care unit staffed by a medically qualified team.

Patients with suspected infarcts who have not had vigorous cardiopulmonary resuscitation, should immediately be considered for intravenous thrombolytic treatment, and a mental or actual checklist should be conducted. If the ambulance is already present and the estimated journey time short (say, ≤ 30 minutes) give treatment for pain and pulmonary oedema if necessary, give an aspirin, and speed the patient on the way to hospital, where thrombolytic treatment can be given. If transfer to hospital might be delayed or the journey is long, give thrombolytic treatment unless major diagnostic uncertainty exists.

Department of Medicine,
University Hospital,
Nottingham NG7 2UH
Robert G Wilcox, FRCP,
reader in medicine

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If an electrocardiogram is not available, is normal, or is considered to show old or non-specific changes then the decision to give a thrombolytic drug has to be made on purely clinical grounds. Clearly some circumstances could be catastrophic—namely, aortic dissection and intestinal ulceration or bleeding—but usually no harm should be expected other than the disadvantage of an unnecessary exposure to a thrombolytic drug which might (on theoretical grounds) preclude re-exposure within, say, six months. There are no proved electrocardiographic prerequisites for thrombolytic treatment. Indeed, in one hospital based trial patients with normal results on electrocardiography (of whom about 10% were ultimately diagnosed as having had an infarction) had a better outcome at one month with thrombolytic treatment than with placebo.⁸ However, when relatively simple electrocardiographic criteria are applied the diagnostic accuracy can reach 80-90%.

Another factor likely to influence a general practitioner's decision to give an intravenous thrombolytic drug outside hospital is the ease of preparing the agent and the simplicity of its administration, but the same may not apply to teams in mobile coronary care units or trained ambulance crews with more experience. Currently all the available drugs—streptokinase, anistreplase, and alteplase—need to be reconstituted, and only anistreplase has been given as a bolus dose in both a large (hospital based) trial¹⁶ and in a prehospital trial based in a mobile coronary care unit.¹³ Streptokinase has also been given outside hospital by mobile coronary care unit teams,¹⁴ and a trial using bolus low dose streptokinase (600 000 U) is underway in general practice after a pilot trial based in an accident and emergency department.¹⁵ So far two prehospital pilot trials of alteplase in mobile coronary care units have reported encouraging results.^{16 17}

Conclusions

Clearly more needs to be learnt about simpler administration schedules if these drugs are to achieve widespread use outside hospital under the direction of general practitioners or ambulance crews, or both.

There are also other concerns about thrombolytic treatment. Streptokinase and anistreplase are more likely to cause acute allergic reactions and hypotension, which are not usually seen with alteplase, although these adverse effects are rarely of clinical importance. There need not be undue concern about reperfusion arrhythmias. In none of the large trials has there been

an increase in either early or total serious arrhythmias; in fact some trials report less. Certainly they may occur, but they are no more likely than if thrombolysis is withheld.

In summary, contrary to the recently published recommendations of the British Cardiac Society,¹⁶ I believe that thrombolytic treatment could and should be given out of hospital after a careful evaluation of the patient, particularly if undue delay in transport to hospital is expected. The availability of resuscitation equipment would be advantageous but not mandatory. General practitioners should expect guidance and support from their local cardiovascular physicians and proffer their collaboration in trials of thrombolytic treatment outside hospital.

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THE MEMOIR CLUB

On the subject of buildings for microbiology his [Allan Downie's] advice was eminently practical and sound. His new department had been furnished with abundant completely sealed windows and a plenum system of ventilation without any provision for cooling or opening the windows. On a summer afternoon the heat so built up that the building was unfit for human use by about 4 pm or even earlier. So the advice was to insist on adequate air cooling. If, because of the costs of installation and running, a completely air conditioned system could not be provided, the architect must have detailed advice from a ventilation engineer about how best to arrange for safe and adequate ventilation by opening windows. It is surprising how often these elementary facts are still overlooked in buildings for all sorts of purposes.

When it became obvious, in the early 1960s, that rapid laboratory diagnosis of smallpox must be provided by the Public Health Laboratory Service on a regional scale I went to him for detailed advice. As always, it was eminently sound and sensible. Ideally, the laboratory for smallpox must be next to the roof; and nobody—repeat nobody—must be allowed into it who did not need to be there; and everyone who went in for any purpose must be adequately vaccinated against smallpox. He added, for

good measure, that in another 20 years or less smallpox could be eradicated. The World Health Organisation was persuaded to take this project as a serious possibility. Many regarded it as impossible; but not Allan Downie. His own work and his active collaboration with fellow virologists at home, in the United States, and in India at last made it possible for WHO to declare the world free from smallpox in 1978. It is a happy thing that he lived to see his vision accomplished.

For him, retirement had no meaning in the ordinary sense. He continued, almost to the end, to be available for locum work, which he greatly enjoyed. "What do you most want from life?" I heard him asked one day. I remember the sense of his answer even if not the actual words. His desires were few and simple: "A good and happy family life, which I have; loyal colleagues who keep me on my toes, which I have; and a boat to sail on the open sea, which I can have every time I go back to Rosehearty."

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