Technology Appraisals Process Series 4

(The National Institute for Clinical Excellence)

Pre-Hospital Thrombolysis

Combined Submission from:
The Joint Royal Colleges Ambulance Liaison
Committee and
The Ambulance Services Association

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Section Headings

Executive Summary

Many lives are being lost in the United Kingdom because of unnecessary delays in the administration of thrombolytic therapy. Determined policies are needed to combat this needless attrition. They include increased efforts to educate the public in the recognition and implications of symptoms of heart attacks, encouraging primary care physicians to provide rapid emergency cover for drug administration where local conditions make this desirable, and eliminating the inexcusably long door to needle times that are common in many hospitals.

The ambulance service must also play an important role in reducing delays by adopting one or more strategies that have been recommended by JRCLAC and ASA. The simplest is to provide the admitting hospital with an expected time of arrival for potential candidates, a practice that can be achieved at little cost but depends for success on cooperation within the hospital. A more complex option favoured by some Ambulance and Hospital Trusts includes transmitting the index electrocardiogram to the admitting hospital to reinforce the warning call. We believe that one or other of these offers the *minimum acceptable practice at the present time*.

The goal, however, must be pre-hospital administration of thrombolytics as a common strategy, especially but not exclusively where transport times are long. Whilst most important for patients in rural areas, this practice would have potential advantages in eliminating unnecessary multiple triage and reducing delays even in some urban areas where call to needle times remain above those recommended in the NSF. Cooperation with primary care physicians should be encouraged, but most pre-hospital administration will inevitably be by paramedics acting either under telephone guidance or autonomously (with or without software aids). Therefore both JRCALC and ASA fully endorse the NHS Plan's aim of training and equipping paramedics within three years to provide thrombolysis safely when circumstances and clinical indications are appropriate.

JRCALC recommends a stepwise progression towards this ideal for the majority of Ambulance Trusts that have not yet adopted pre-hospital thrombolysis, within a time-frame that depends on the completion of training and the acquisition of suitable equipment. This could, for example, start with pre-hospital recognition and hospital alert (where circumstances permit, paramedics might then initiate thrombolysis in hospital under supervision); progress to pre-hospital administration with ECG transmission under physician control; and ultimately to autonomous use where circumstances warrant this strategy.

Possible strategies for speeding thrombolysis, and in particular for pre-hospital administration, are set out in detail in the full document.

1. Introduction

1.1 Large scale trials, mostly but not exclusively with streptokinase and alteplase, have proved conclusively the striking therapeutic benefit of thrombolysis for selected patients with acute myocardial infarction. A combined analysis of studies that had enrolled more than 1000 patients provided an overview based on a total of 58 600 patients in nine trials [1] that offers definitive evidence of the impressive clinical results that can be obtained. *Unsurprisingly, the benefit of thrombolysis in myocardial infarction is time dependent: it diminishes rapidly as time passes and is no longer evident after about 12 hours.* The average mortality reduction in the major trials was approximately 25% over the period of data collection, but the combined analysis suggested that patients who presented in the first six hours with ST elevation or bundle branch block had a mortality benefit of 30 lives per thousand treated, falling to 20 per thousand for those treated at seven to 12 hours. A subsequent re-analysis of available data showed even more convincingly the importance of prompt treatment [2]. *When the drugs are given within one hour of the onset of major symptoms mortality can be reduced by as much as 48% - amounting to 65 (SD 14) lives saved per 1000 treated.* Mortality reduction is believed to depend principally on myocardial salvage as a result of reperfusion when thrombolytics are administered within an hour or so of coronary occlusion [3]. But thereafter the extent of myocardial necrosis has largely been determined irrevocably. Reperfusion may bring hazards of its own that increase mortality during the subsequent 24 hours [1], but appreciable longer-term benefit may still accrue – principally from improved healing of the affected area - so that a net benefit is apparent in those treated within about 12 hours when mortality is judged over 30 days. From after about 12 hours of occlusion, however, the hazard generally outweighs any residual benefit. At this stage treatment ceases to have a clinical advantage and even long-term mortality may be increased.

1.2 Much emphasis has been placed on the benefits of prompt treatment. It's importance was highlighted in recommendations of a Working Party of the British Heart Foundation which called for efforts to be made for treatment to be given within 90 minutes from the patient's call for help [4], later by a Task Force set up jointly by the European Society of Cardiology and the European Resuscitation Council [5] that stressed the value of pre-hospital administration, and most recently in the Government's National Service Framework for Coronary Heart Disease (England) [6] which states that prompt delivery of thrombolytic therapy for patients with myocardial infarction is a principal target with a national standard of a "call to needle time" of 60 minutes. An identical target has been set for Wales [7]. It is appropriate to regard the standard as relevant for the whole of the United Kingdom.

1.3 Despite all that is known of the deleterious effect on prognosis, many patients are still subjected to many hours of delay in the administration of thrombolysis, much of it unnecessary. This delay has three principal components. The first is from the onset of major symptoms to the patient seeking help: this can vary from minutes to many hours and can be corrected only by improved public education, an important issue but outside the principal scope of this report. The second delay is from the call

for help to arrival in hospital. The third delay is that which occurs after admission which has come under considerable scrutiny. Birkhead [8] published the results of an audit of the provision of thrombolytic therapy in 15 UK hospitals up to 1997. The data from the 3714 patients are likely to represent the better end of the spectrum of practice, given that the hospitals had volunteered for the audit because of their interest in promoting improvement. Even in this group, less than 50% of patients were treated within two hours of calling for help, and only 14.5% of those eligible started their thrombolytic therapy within one hour. Although these data represent both 'call to door' and 'door to needle' times, an important part of the delay still occurs after hospital admission - and these are the easiest to correct. Whilst considerable discrepancies exist between hospitals in the average delay to treatment from onset of symptoms (from 29% to 65% within three hours of those audited), these reflect not only hospital practice but the whole system of provision of care - including patient delays and transport times that reflect variations in geography.

1.4   Clearly, much remains to be done to minimise unnecessary delays that so seriously increase mortality and morbidity. In response to this challenge a strategy of pre-hospital administration has been adopted in many countries (especially those that have doctors in ambulances), thus eliminating the third component of delay and replacing the second only by the time taken for assessment at the point of first medical contact. Within the United Kingdom, the more demanding ambulance target response times that have already been implemented are useful, but cannot be nearly as effective.

2.   Benefits of Pre-hospital Administration

2.1   Relevant evidence comes from what has been achieved by the use of pre-hospital thrombolysis either by physicians or by Paramedics acting under immediate but remote physician control. A meta-analysis of six randomised trials comparing pre-hospital with hospital treatment, involving 6434 patients, indicated a significant reduction in mortality with an odds ratio of 0.83 (95% confidence interval 0.70-0.98). An average of 58 minutes was saved in time to treatment [9]. A long-term follow up from one of the three principal studies (The GREAT Trial) showed that the benefits in terms of mortality reduction persisted for at least five years [10]. *Even more striking was the calculation in the same paper showing that, in the first three hours after the onset of symptoms, every 30 minutes of time saved resulted on average in one additional year of life for the patients – in other words every single minute of delay costs 11 days of life.*

2.2   We also have European data on the routine use of thrombolysis when the treatment has been given on the initiative of Paramedics without direct supervision. This has been practised in Rotterdam since 1988 and was reported as the REPAIR study in 1995 [11]. As a result of continuing good results, this strategy is now being used in other parts of Holland. The inclusion criteria have been more restrictive than is common in hospitals and are based on clinical criteria and a qualifying ECG pattern which must be recognised as such both by a diagnostic computer program printed

out by the electrocardiograph and by the attending Paramedic (*both* positive computer and human diagnosis required: neither alone will suffice). Over a six year period (1988 to 1993), 529 patients received thrombolysis initiated during the pre-hospital phase. The time gained was calculated as 50 minutes, based on the delay observed in those who did not meet the precise inclusion criteria for the study but were thrombolysed subsequently in hospital. The rate of complications during transportation and during the first day in hospital was low. Remarkably (for clear-cut cases of infarction characterised by ST elevation), the hospital mortality was only 2% and the 1-year mortality 3%. We know of no better hospital survival from myocardial infarction. Cumulative survival at 5 years was 92%, compared with the 84% 5-year survival observed in a matched (not randomised) group of 230 patients treated with alteplase in hospital. A later editorial [12] provided important additional data from the Rotterdam experience. Of the nearly 2000 patients who had by then been treated with pre-hospital thrombolysis, a false positive diagnostic rate of only 1% occurred; and even in these the likelihood of harm would be very small. The latest figures - maintaining the same pattern - were presented to the annual scientific meeting of the ASA in 2001 and can be made available on request [13]. The Dutch Paramedics are all trained nurses with CCU or ITU experience before joining the ambulance service, but we believe that appropriately trained British Paramedics should be able to achieve similar results. *Clearly results that even approached those achieved in Holland could reduce appreciably the mortality of myocardial infarction for those patients who survive long enough to come under care and fulfil the criteria for pre-hospital treatment.*

3.   Strategies for pre-hospital care in the United Kingdom

3.1   The Joint Royal Colleges Ambulance Liaison Committee (JRCALC) strongly supports the drive for earlier treatment promoted by the Department of Health through the NSF and the NHS Plan. All ambulance Trusts have been encouraged to adopt one or more of five strategies designed to achieve this goal. These are as follows:-

3.1.1 Simple recognition of eligibility for thrombolysis by ambulance paramedics (based on clinical features and 12-lead electrocardiogram) with telephone or radio transmission of this information to the Accident & Emergency department or the CCU in order to reduce delay to hospital administration of the drug. This is simple, safe, and involves no additional pre-hospital delay. A forewarned department should readily achieve shorter 'door to needle' times

3.1.2 Transmission of clinical information together with the electrocardiogram to an A/E department or a CCU in order to reduce delay to hospital administration. This takes more time than the first option but does not require interpretive skills from the paramedics.

3.1.3 The involvement in rural areas of primary care physicians, so that thrombolytic agents can be given either at the place of first contact (for example: the patient's home) or at a Community Hospital that can act as a convenient rendezvous for the ambulance and the practitioner. The same ambulance might then take the patient to the District

General Hospital for continuing skilled supervision. The thrombolytic agents could be held either by primary care physicians, or by the ambulance service, or if appropriate in the Community Hospital.

3.1.4   Transmission of clinical information and electrocardiogram to a physician within the A/E department or CCU (or by special arrangement to an agency elsewhere) who might then authorise the pre-hospital administration of a thrombolytic drug by a paramedic on a named patient basis (the physician sharing responsibility for the decision on the basis of the information he has received).

3.1.5 Decisions and administration by specifically trained paramedics without outside intervention, based on the available clinical information and interpretation of a diagnostic 12-lead electrocardiogram (preferably with the aid of an appropriate decision-algorithm built into the electrocardiograph that indicates whether or not the electrocardiogram is a qualifying tracing for thrombolysis. The Simoons algorithm has been used over several years in Rotterdam with impressive results [9, 10]. It can be made available in two models of electrocardiographs, both in common use in the United Kingdom).

3.2   The first two strategies rely on alerting the hospital to the impending arrival of a patient who qualifies for thrombolysis, and the third encourages cooperation with primary care physicians if local arrangements include their participation. They require little additional training, with little cost except for equipment used in transmission if that is deemed necessary. All three are currently used in a few areas but one or other could be introduced by any services at any time, subject only to local agreements. It should be noted that assessment of transmitted electrocardiograms in local hospitals has not always been successful: the prompt presence of a physician with the necessary skills at the receiving device may not always be feasible. The concept of a central agency for this purpose is being explored, but raises additional problems in relation to clinical responsibility and liaison.

3.3   JRCALC and ASA see these three strategies as interim arrangements of which one or more could (and should) be adopted by all services that do not have current policies for prehospital administration by paramedics. We wish to encourage, however, the moves towards a policy of pre-hospital administration of thrombolytics by paramedics either giving the drugs under the direction of a physician on a named patient basis (after transmission of the electrocardiogram and discussion of the clinical scenario) or acting autonomously.

3.4   Remote but immediate medical control for pre-hospital administration using modern telecommunications has been found to be feasible in the United States [14] and may find a place in a few districts in the United Kingdom, but in most areas reliable availability of physicians with the skill and training to operate such a system will not be feasible. One or more central agencies (NHS or Private) could act on behalf of local trusts, but local agreement with both ambulance and hospital trusts would require careful consideration. Appropriate contracts would have to include provision for shared responsibility and for suitable indemnity arrangements. Advantages of shared responsibility include support for

paramedics whilst confidence if being built (although support software can go some way to meeting this objective), and the likelihood of treating more patients because the indications for prehospital administration could be wider than the current recommendations for autonomous use (Sections 5 & 6).

3.5   Treatment initiated by Paramedics using strict protocols is our preferred option at least as a long-term objective, and we believe that progress towards it should be strongly encouraged. It is the most time-efficient way in which the advantages of pre-hospital thrombolysis can be brought to the population. After the necessary training has been provided, there is no additional cost to the NHS - though arrangements for regional purchase of the drugs would be necessary, and would thereby attract the discounts of large orders. Previous experience of one of the authors in a local scheme used to good effect in the late 1980s [15] together with published recent evidence [16] shows that paramedics can readily be trained in 12-lead ECG interpretation and in the reliable recognition of patterns of myocardial infarction that potentially qualify for thrombolysis.

3.6   We recognise that training *per se* may not impart sufficient confidence for this preferred policy to be widely implemented in the immediate future. Paramedics know that complications - including fatal cerebral haemorrhage - will occur albeit rarely (see 3.1). Those who administer the drugs are likely to be aware of those who have been harmed thereby but cannot identify the appreciably larger number of individuals whose lives are saved, or who benefit by decreased morbidity, as a result of their treatment. This has been a major concern to paramedics in the past (it prevented the agreed introduction of pre-hospital thrombolysis in Brighton in the late 1980s), and merits careful consideration and preparation now.

3.7   The five strategies outlined above are not mutually exclusive within any single Ambulance Trust. Circumstances will vary from location to location, especially in regard to distances that have to be travelled to hospital. One Trust may therefore use more than one strategy initially, although we hope that autonomous treatment by paramedics will ultimately become the norm in all settings.

3.8   Moreover, one strategy may be used as a stepping stone to another in order to build experience and confidence. For example, in some areas paramedics might well start by notifying the hospital of suitable candidates who are treated only after arrival to the Accident and Emergency Departments - but later progress to prehospital administration of thrombolytics under physician control, and later to autonomous use. This can give an opportunity for audit of skill in recognition of qualifying clinical features and electrocardiogram. But a phased introduction can do more in building confidence: we suggest that where agreement can be reached and circumstances permit, paramedics who have correctly identified candidates for treatment should be allowed to initiate administration of the treatment under supervision in hospital.

3.9   An issue that has not been fully resolved relates to 'informed consent' that is expected as a norm but is difficult or impossible to obtain in some emergency settings. Patients who are having a myocardial infarction are likely to have severe pain, or to be obtunded by

powerful analgesics. A recent study confirmed that following attempts to achieve informed consent for trials in myocardial infarction, patients had only fragmentary knowledge about the trial they were involved in and most considered that signing a consent form was an unwanted or unnecessary procedure [17]. The problems are even more difficult soon after the onset of the attack, and paramedics have had little experience of explaining the intricacies of risk against benefit. JRCLAC has been advised informally by a Professor of Ethics that even in this situation some knowledge of major unwanted effects should be given to candidates for pre-hospital treatment. We are not convinced that patients in this situation - who are highly vulnerable to adrenaline-related malignant arrhythmias - should have anxiety levels increased by mention, for example, of the consequences of cerebral haemorrhage when they are in no position to balance this risk against the proven benefits. Many would opt inappropriately to forego potentially life-saving treatment. We wish to canvas additional informed views on this point in order to offer the most appropriate advice to paramedics who will have the responsibility of giving the drugs.

3.10   One additional strategy that has not been included above is relevant only for Northern Ireland where some ambulances do have physicians on board and in similar circumstances in some rescue helicopters. We support these initiatives but do not believe they need to be considered in detail in this report that has a remit only in relation to the direct involvement of paramedics.

4   Hazards and Risk-Benefit Considerations

4.1   Even with appropriate use, thrombolytic agents can have serious adverse effects, but the risks are more than offset by the considerable overall reduction in morbidity and especially in mortality that can be conferred by treatment. Until more experience has been gained, however, JRCALC recommends a cautious policy reflected in inclusion and exclusion criteria more stringent than those recommended for hospital use. These are discussed in more detail in sections 5 and 6.

4.2   As a result, some otherwise suitable patients may be denied the advantages of pre-hospital treatment, but we believe it is important to avoid criticism in the event of adverse events until the policy of thrombolytic administration by paramedics has been accepted generally.

4.3   The hazards of thrombolytic therapy relate: first to bleeding because of the dissolution of haemostatic plugs and old thrombus outside coronary arteries; secondly to complications that follow from reperfusion of ischaemic tissue; and thirdly (particularly for streptokinase) to allergy and induced hypotension. The greatest risk is from cerebral haemorrhage which cannot be prevented in all cases and is likely to be disabling or fatal. It is minimised, however, by avoiding treatment in the presence of hypertension, known or suspected cerebral tumours, symptomatic cerebrovascular disease, old age, and recent trauma. Other contraindications relating to unwanted internal or external bleeding include mistaken diagnosis (pericarditis or dissecting aneurysm), recent surgery, peptic ulceration, known bleeding tendency (including anticoagulant treatment), and prolonged chest

compression from cardiopulmonary resuscitation. The adverse effects from reperfusion injury affect principally those treated several hours after the onset of symptoms. Most occur relatively late, but an increased incidence of early ventricular fibrillation (but less late fibrillation) has been observed in some studies – correctable in most cases by defibrillation immediately available in ambulances. Allergy is rarely life-threatening and severe hypotension can usually be avoided by withholding treatment if the blood pressure is already low. In hospital practice, many patients with recognised vulnerability to the hazards listed above are – appropriately – treated on the basis of a favourable risk-benefit ratio.

5.   Pre-hospital inclusion criteria for thrombolysis

5.1   Inclusion criteria are widely agreed and are evidence based, drawn from the results of the large randomised trials. They are simple because they depend on only two variables: the clinical history and the appearance of the ECG. For pre-hospital use by Paramedics, we recommend that initially they be more stringent than those used in hospitals (Annex 1). It has been agreed by a thrombolytic advisory committee set up by JRCALC that includes representation from the British Cardiac Society (membership in Annex 2) that any candidate for pre-hospital treatment should have had continuing major characteristic symptoms for longer than 30 minutes (to minimise the risk of treating unstable angina) and less than 3 hours (when benefits of reducing delay are becoming less important). The electrocardiogram should show pathological ST segment elevation of at least 2 mm in two inferior leads or in at least two contiguous precordial leads (not counting V1 because ST segment elevation here is often physiological and elevation in only V1 and V2 would represent an unusually small infarct). Any pattern of bundle branch block is currently an exclusion in the JRCALC recommendations in prehospital settings because this increases diagnostic difficulty (Section 6).

5.2   In keeping with our wish to be conservative in terms of indications – for an initial period not yet defined – JRCALC generally recommends the use of pre-hospital thrombolysis only when the journey time can be expected to exceed 30 minutes or when the combined journey time and hospital delay is likely to exceed 60 minutes. This is in consistent with recommendations from the European Task Force on the Pre-hospital Management of Acute Heart Attacks [5] and will help to achieve the targets of the English NSF [6].

6.   Pre-hospital **exclusion criteria for thrombolysis**

6.1   A conservative approach has been recommended for pre-hospital use by Paramedics: *any* patients with identified contraindications should be assessed in hospital. Moreover, the contraindications are more stringent than those for hospital use. In particular, left bundle branch block is a recommended exclusion whereas conventional criteria include *new* left bundle branch block; at this stage we do not think it appropriate that paramedics should have the additional anxiety of deciding if bundle branch block is new or old. Right bundle branch block is also recommended

to be a contraindication because electrocardiographic criteria become more difficult to confirm in this situation. And high blood pressure (systolic pressure greater than 160 mmHg) is a contraindication at a pressure lower than is conventionally used in order to minimise the risk of inducing cerebral haemorrhage. We believe it likely that the indications and contraindications will become closer to those currently used within hospitals as experience grows in pre-hospital administration and evidence becomes available to support the clinical efficacy of this policy.

6.2   Contraindications cannot be remembered readily in critical situations, but check lists can provide a reliable prompt. A number of models are available and have been used over several years both in-hospital and pre-hospital (though without published validation). The check list recommended for paramedics is shown with the indications in Annex 1. To avoid confusion it has been worded so that any negative answer is taken as an instruction to avoid pre-hospital treatment. *Whilst precise instructions to Paramedics is the responsibility of individual Ambulance Trusts, most will follow guidelines for inclusion and exclusion criteria that have national support.*

6.3   One specific factor deserves special mention. In some areas, Percutaneous Coronary Intervention (PCI) may be the preferred strategy for patients who can reach a suitable catheter laboratory without undue delay, and substantially the same group might be suitable for treatment by paramedics. On balance PCI is believed to be preferable to thrombolysis [18], though few hospitals will be able to offer the facility, at least on a regular basis. Some evidence suggests that most of the evidence for superiority depends on the particular advantages in high risk cases [19] but all subgroups can benefit from prompt intervention [20]. One important proviso relates to the conditions of trials reported to date: all compared primary angioplasty with *hospital administration* of thrombolysis. Pre-hospital administration is - in general - more efficacious. One trial has been completed, and presented recently though not yet published, that compared primary angioplasty with *pre-hospital* administration [21]. Although there was a non-significant trend favouring PCI for the composite end point (that included non fatal infarction and disabling stroke), no difference was observed in mortality - with the trend favouring pre-hospital thrombolysis. This cannot, however, be regarded as definitive evidence. Policy on treatment modalities must be a matter for local decisions, and may vary either predictably by time of day or unpredictably depending on other factors. This, however, has little impact on general strategies that relate to ambulance contribution to speeding thrombolysis.

7.   Choice of Drug and adjuvant
7.1   We do not believe that the choice of thrombolytic and of adjuvant therapy is the principal remit for this submission. Brief mention must be made, however, because it does have implications for the type of equipment that is needed and for the cost of drugs.

7.2 Streptokinase is the only thrombolytic that can be administered by paramedics under the Prescription Only Medicines (Human Use) Order 1997 (POM Order). JRCALC applied for the addition of a thrombolytic agent (together with five other drugs) to the list under the previous order, and specifically requested streptokinase only because we were advised that no other agent could be considered at that time. Little experience had then been obtained with one bolus drug (reteplase) and the other (tenecteplase) had no licence. The situation has since changed in that both drugs are now in common use. JRCALC has not applied for a further extension of the POM order to take account of this because Patient Group Directions have been introduced: these offer a simpler and faster way of obtaining approval for the pre-hospital use of a drug not on the current POMs Order list.

7.3 We believe that a single or double bolus agent is preferable for pre-hospital use compared with streptokinase though additional cost is an important drawback to a bolus drug. Streptokinase has important disadvantages that could be of special importance in the pre-hospital arena: it causes more hypotension, and an appreciably greater risk of severe allergy than do the newer agents. It may also be relatively ineffective after previous use because of the development of antibodies, with knowledge of previous use being particularly difficult to determine before hospital admission. The need for an infusion pump that can give a reasonably constant flow rate is another drawback for streptokinase. In addition to the training implications, equipping every front line ambulance with a pump would be expensive - going some way to balancing the difference in thrombolytic costs.

7.4 The bolus drugs, similar in structure to alteplase and relatively clot specific, require adjuvant intravenous heparin whereas streptokinase does not. Whilst the future is likely to be with the administration of a low molecular weight agent, none yet has a licence for this indication. Any ambulance policy to use reteplase or tenecteplase under a PGD will therefore require an additional PGD for bolus intravenous heparin or (possibly) low molecular weight heparin. At present only very low dose heparin is permitted under the POM order, intended to keep open vein cannulation.

8. Training

8.1 Training in the administration of thrombolytics would be initiated at a local level and supervised by the Local Ambulance Paramedic Steering Committee - but JRCALC has made recommendations to Trusts that are following this course (Annex 3). It includes revision in the recognition of suspected myocardial infarction, training in the recognition of classical infarct patterns in 12-lead ECGs, training in the preparation of an appropriate dose of thrombolytic while preparing for transport to hospital, and also in the administration of the chosen agent in the prescribed manner. Additionally, training in recognition and treatment of possible adverse reactions including unexpected bleeding has been included. Bleeding, however, is an unusual occurrence during the early pre-hospital phase [22]. All paramedics are already well trained and experienced in IV cannulation, defibrillation, and advanced life support.

9. Audit

9.1 Audit is regarded as essential. JRCALC and the Ambulance Services Association (ASA) are cooperating with the Myocardial Infarction National Audit Programme (MINAP) of the Clinical Efficacy and Evaluation Unit (CEEU) at the Royal College of Physicians to audit the contribution of the ambulance services to the delivery of the implementation of the NSF for Coronary Heart Disease. Development of the infrastructure for audit is well advanced. At present (December 2001) all pre-hospital administration of thrombolytics by ambulance paramedics is recorded in detail, and from early in 2002 many services will be able to provide data on all patients who might be considered suitable for thrombolysis on the basis of cardiac pain and electrocardiographic evidence of ST segment elevation - whether or not the treatment is administered.

9.2 Pre-hospital data will be linked to that of the hospital data for all cases who are admitted, providing information on delays, all treatments including thrombolysis, any complications as a result of the illness or its treatment, and outcome.

10. Cost implications

10.1 Ambulance Trusts will face widely different additional costs for strategies to speed thrombolysis depending on current practice, the size of the Trust and current practice, which model(s) of care will be adopted (see Section 3), the level of existing skills, the choice of agent, arrangements for bulk purchase, joint funding arrangements with Hospital Trusts etc. Only an approximation can therefore be given.

10.2 Training costs. All paramedics directly involved must have be able to record and recognise a normal ECG and the changes of ischaemia and infarction. Software that can complement teaching by instructors has been endorsed by JRCALC and is available without cost as a CD Rom [23]. With appropriate aids and pre-course learning, we believe that a 2-day course is sufficient for professional development. A course involving 12 students with a single training manager is likely to cost around £1440. Validation and practice of skills may cost an additional sum for each student - of the order £100 to £150. The use of a private agency for ECG interpretation - if this policy were to be adopted by any trusts - would involve additional cost on a per patient basis and probably software costs as well.

10.3 Equipment Costs. Services have already received some additional national funding to purchase 12-lead ECG machines, and most will allow telephone ECG transmission that many wish to use at least in the first instance. This strategy will involve a receiving unit in the hospital at about £1000, and telephone cards cost up to £10 per month per machine. (Essex Ambulance Trust with 250 paramedics has indicated that the annual bill for telemetry will be around £16 000 per annum). Had it not been necessary to equip for thrombolysis, simpler 3-lead monitor/defibrillator units would have been suitable for Trusts, costing up to £3000 less than the units now needed. But in addition, some (not all)12-lead equipment is too heavy for use

as a defibrillator remote from the vehicle, so that most ambulances in many Trusts will require an AED at up to £3000 each. JRCALC commends the use of the Simoons software as an adjunct to autonomous use of thrombolytics by paramedics. We understand that there will be no additional cost for those buying new interpretive equipment from the two manufacturers currently offering this facility.

10.4   Drug costs. Pre-hospital delivery simply shifts the drug cost to the pre-hospital environment if the same agent is used in both settings. Streptokinase is, however, still widely used in hospitals but is not likely to find favour for pre-hospital administration for the reasons mentioned in section 7. The cost of bolus drugs will be of the order £400 to £600 per patient. (Note that reteplase is given as two bolus doses 30 minutes apart. The second dose will therefore often be administered in hospital). We do not anticipate any major costs for storage.
Syringe drivers will not be required unless any Trusts decide to use streptokinase which seems unlikely.

10.5   One 'hidden' cost relates to the additional ambulance time that may be required. Even if the thrombolytic is to be given in hospital, transmission of electrocardiograms, which seems likely to be used by some Trusts, will add some minutes to a journey. Local decisions may also dictate that patients must be taken directly to CCU - a practice thatcan add 20 minutes to hospital turn-around times.

10.6   Appraisal of additional costs for pre-hospital administration will be very different when considered only from an ambulance perspective compared with consideration of total costs to the NHS. Cooperation between Hospital Trusts, Ambulance Trusts, and purchasing authorities can minimize additional expense. JRCALC and ASA hope that appropriate arrangements and liaison will be adopted wherever the policy of pre-hospital thrombolysis is adopted.

11.   Recommendations

11.1   The ambulance service must be supported in the training, implementation, and audit of strategies designed to reduce delays to the administration of thrombolysis.

11.2   All ambulance paramedics should be trained to be competent to record and interpret a 12-lead electrocardiogram at least to the extent of recognizing a normal pattern and the changes that occur characteristically as a result of myocardial infarction.

11.3   All ambulance Trusts should *already* have in place strategies that will help to speed the administration of thrombolysis to eligible patients. In addition to meeting the standards for response to calls for patients with chest pain, the minimum that should be regarded as acceptable is the recognition of the clinical and electrocardiographic criteria for treatment - permitting an alert to the receiving hospital. This may or may not be associated with the transmission of the index electrocardiogram if the Hospital Trust deems this necessary before preparing for drug administration within minutes of hospital admission.

11.4   All ambulance Trusts with commitments to rural areas should be working towards pre-hospital administration of thrombolytics by paramedics if the standards of the NSF in England and in Wales cannot be met in other ways.

11.5   Although autonomous decisions by paramedics on eligibility for treatment and the administration of an appropriate drug is the ultimate goal where pre-hospital treatment is appropriate, we recommend that Trusts consider an interim step to help build confidence and experience. Support software ("Simoons algorithm") - that has been shown to be highly effective over several years of use in Holland - is available from at least two manufacturers of diagnostic electrocardiographs. An alternative option is cooperation with hospital physicians after the clinical details and the electrocardiogram have been transmitted.

11.6   JRCALC / ASA support existing schemes available in a few areas that involve pre-hospital administration of thrombolytics by medical practitioners, with the cooperation of the ambulance service. We doubt, however, if this can ever be a major strategy in England and Wales.

11.7   JRCALC / ASA support the use either one of the bolus drugs currently available as being more suitable than streptokinase. These require the use of a Patient Group Directive, whereas streptokinase can be used under the current amendment of the POMs order.

11.8   JRCALC / ASA commend the use of coordinated purchasing policies to rationalize the division of cost between Hospital and Ambulance Trusts and to effect the maximum economies available from large scale purchases of drugs.

11.9   JRCALC / ASA urge that careful agreements are drawn up between Hospital and Ambulance Trusts that will cover any shared responsibilities in diagnosis and treatment. Discussions may need to be at national level if private companies are involved in management strategies using telemedicine.

11,10 JRCALC / ASA are emphatic that careful, coordinated, central audit must be maintained, and that the necessary support to permit this must continue to be available.

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Annex 1

Primary Assessment

1.   Can you confirm that the patient is conscious, coherent, and able to understand that clot dissolving drugs will be used?
2.   Can you confirm that the patient is aged 75 or less?
3.   Can you confirm that the patient has had symptoms characteristic of a coronary heart attack (i.e. pain in a typical distribution of 30 minutes duration or more)?
4.   Can you confirm that the symptoms started less than 3 hours ago?
5.   Can you confirm that the pain built up over seconds and minutes rather than starting totally abruptly?
6.   Can you confirm that breathing does not influence the severity of the pain?
7.   Can you confirm that the heart rate is between 50-140?
8.   Can you confirm that the systolic blood pressure is more than 80 mmHg and less than 160 mmHg?
9.   Can you confirm that the electrocardiogram shows abnormal ST segment elevation of 2 mm or more in at least 2 standard leads or in at least 2 adjacent precordial leads, not including V1 ? (ST elevation can sometimes be normal in V1 and V2).
10.   Can you confirm that the QRS width is 0.14 mm or less, and that bundle branch block absent from the tracing?
11.   Can you confirm that there is NO atrioventricular block greater than 1st degree? (If necessary after treatment with IV atropine).

Secondary Assessment (Contraindications)

12.   Can you confirm that the patient is not likely to be pregnant, nor has delivered within the last two weeks?
13.   Can you confirm that the patient has not had a peptic ulcer within the last 6 months?
14.   Can you confirm that the patient has not had a stroke of any sort within the last 12 months and no permanent disability from a previous stroke?
15.   Can you confirm the patient has no diagnosed bleeding tendency, has had no recent blood loss (except for normal menstruation), and is not taking warfarin (anticoagulant) therapy?
16.   Can you confirm the patient has not had any surgical operation, tooth extractions, significant trauma, or head injury within the last 4 weeks?
17,   Can you confirm that the patient has not been treated recently for any other serious head or brain condition? (This is intended to exclude patients with cerebral tumours).
18.   Can you confirm that streptokinase has not been given previously? (If the patient has had thrombolytic treatment and does not know which agent was used, you should assume that it was streptokinase). *Note: relevant only if streptokinase is the drug to be used. Not required for reteplase or tenecteplase.*
19.   Can you confirm that the patient has not had chest compression for resuscitation for a period of longer than 5 minutes?
20.   Can you confirm that the patient is not being treated for liver failure, renal failure, or any other severe systemic illness?

Annex 2

<u>Members of Thrombolytic Steering Group</u>

Professor D A Chamberlain (Cardiologist, Chairman JRCALC)

Dr Tom Clarke (JRCALC)

Dr Liam Penny (Cardiologist, JRCALC)

Dr Tom Evans (Cardiologist, JRCALC)

Dr Judith Fisher (Primary Care, Ambulance Service, JRCLAC)

Dr Howard Swanton (Cardiologist, BCS)

Professor Stuart Cobbe (Cardiologist, BCS)

Dr Alan Mackintosh (Cardiologist, BCS)

Professor Richard Vincent (Cardiologist, BCS)

Mr Barry Johns (ASA)

Mr Gron Roberts (ASA)

Mr Tom Quinn (ASA)

Mr Andrew Marsden (Scottish Ambulance Service)

Dr Roger Boyle (Department of Health)

<u>**Annex 3**</u>

The model course has drawn on existing courses prepared within four Ambulance Trusts. It has been through a process of wide consultation with individuals from Trusts that have already prepared for pre-hospital thrombolysis, and from an expert advisory committee representing JRCALC, the ASA, the British Cardiac Society, and the Department of Health. It is intended to be used only as a resource which training departments may find helpful in drawing up their own courses for their own particular needs.

Course content is grouped under subject headings. The topics that are presented in bold are believed to be "core" and might properly be the subject of evaluation and tests of competency. The topics that are not in bold are suggested only as background information that may not be taught in depth, and that may not generally be included in competency testing.

1.   <u>***The Genesis and Recording of the Electrocardiogram***</u>

- Revision anatomy of the heart including the coronary arteries.
- The conducting system
- How an ECG is generated
- Concept of spread of excitation and vectors
- **Leads and placement**
- **ECG recording paper, calibration, and intervals**
- **Indications for taking a 12-lead ECG**
- **How to take a 12-lead ECG**
- **How to transmit an ECG (core topic for Trusts using transmission)**

2.   <u>***The Normal ECG***</u>

Possible familiarity of 10 criteria for a normal 12-lead training:-

2.1.   *The PR interval should be 120 to 200 ms* (3 to 5 little squares). A longer PR implies first degree block, a shorter PR may indicate a vulnerability to supraventricular arrhythmias.

2.2.   *The width of the QRS complex should not exceed 110 ms* (less than 3 little squares). A wider QRS is sometimes seen in healthy people, but may represent an abnormality of intraventricular conduction.

2.3.   *The QRS complex should be dominantly upright in leads I and II* (otherwise there is axis deviation).

2.4.   *The QRS and T waves tend to have the same general direction in the standard leads* (I, II, III, AVR, AVL, AVF). For example, if the QRS in AVL is dominantly positive then the T wave in that lead should also be positive, but if the QRS in AVL is dominantly negative then the T wave should be negative as well.

Slight disparities are likely to be normal: for example a QRS in AVL that is barely positive overall may have a normal T wave that is barely negative.

2.5. *All waves are negative in lead AVR*. This has to be so: AVR represents electrical activity as "seen" from the right shoulder. The sinus node is placed top right in the heart nearest to the right shoulder, and the electrical activity is moving downwards and leftwards towards the left ventricle

2.6. *The R wave in the precordial leads must "grow" from V1 at least to V4* where it may or may not decline again. A spurious abnormality frequently occurs in R wave size or "growth" because of faulty placement of precordial leads.

2.7 *The ST segment should start isoelectric except in V1 and V2* where it may be elevated. The normal ST then curves gently in the direction of the T wave and should not remain exactly horizontal (sometimes called plane depression which can indicate ischaemia).

2.8 *The P waves should be upright in I, II, and V2 to V6*. By implication they may be flat or negative in the other leads.

2.9 *There should be no Q wave or only a small q less than 0.04 s (1 little square) in width in I, II, V2 to V6*. A narrow q is expected in V6, and represents the early septal activation.

2.10. *The T wave must be upright in I, II, V2 to V6*. The end of the T wave should not dip below the baseline - this is sometimes seen in unstable ischaemia.

3. ***Arrhythmia Revision***

- **Sinus tachycardia**
- **Sinus bradycardia**
- **Atrial extrasystoles**
- **Ventricular extrasystoles**
- **Supraventricular tachycardia**
- **Ventricular tachycardia**
- **Atrial fibrillation**
- **Atrial flutter**
- **Ventricular tachycardia, unusual forms (Torsades)**
- **Ventricular fibrillation**
- **Bundle branch blocks and all degrees of heart block**
- **Pericarditis**
- **Paced beats**
- **ECGs of pulmonary embolus**

4. ***Coronary Artery Disease***

- Pathology of CAD and myocardial infarction
- Epidemiology of CAD
- **Symptoms and signs of acute coronary syndromes**

- **Differential diagnosis especially Dissection, Pericarditis, Pulmonary Embolus, Chest wall pain, Pleurisy, Hiatus hernia**
- **Complications of myocardial infarction: Heart failure, Shock**
- Complications of myocardial infarction: Other

5. *Electrocardiograms in Coronary Artery Disease*

   - **ECG in ischaemia**
   - **ECG in infarction (including localisation)**

6. *Treatment of Myocardial Infarction: Thrombolysis*

   - Concept and results of thrombolysis
   - **Indications and contraindications thrombolysis**
   - **Thrombolytic agent used within the Ambulance Trust**
   - Other thrombolytic agents in common use
   - Other treatments: primary angioplasty.
   - **Complications of thrombolysis and their management**

7. *Treatment of Myocardial Infarction : Other*

   - **Oxygen**
   - **GTN**
   - **Aspirin**
   - **Nalbuphine**
   - **Morphine**
   - **Anti-emetics (metoclopramide)**
   - **Epinephrine (adrenaline)**
   - **Atropine**
   - **Lidocaine (lignocaine)**
   - **Furosamide (frusemide)**

8. *Testing Competency*

   i) Lead Placement & ECG acquisition in 6 patients (including female patients if practicable)
   ii) Recognition of ECGs (MI) appropriate for thrombolysis. Use of 50 tracings of which half should suggest need for thrombolysis.
   The requirement should be 100% specificity (25/25 correct) and 92% sensitivity (23/25 correct).
   iii) Arrhythmia recognition (10 12-lead ECGs or rhythm strips).
   iv) Written paper, preferably MCQ. Suggested topics:-
      - ECG placement
      - Calibration
      - Intervals
      - Signs and symptoms of acute coronary syndrome

- Differential diagnosis
- ECG in ischaemia
- ECG in infarction
- Indications and contraindications of thrombolysis
- Adverse events
- Drugs/Treatments of MI

v)   Scenarios should also be presented to indicate competency in clinical situations. This should include ECGs in less-than-straightforward situations.

9.   ***Retraining and validation of Course***

These should be achieved by seeking evidence of skill retention (by appropriate re-testing at 6 months and annually thereafter) and by careful audit of procedures in the field.

(Annex 3 generated 23/10/2000)