The Prevention of Intrathecal Medication Errors

A report to the Chief Medical Officer

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Summary

1. Administration of Vinca alkaloids such as vincristine by the spinal route, rather than intravenously, invariably causes death or severe neurological damage. This catastrophic clinical error has arisen because of confusion of the drug with a cytotoxic agent intended to be given intrathecally (usually methotrexate). Five such incidents have occurred in NHS hospitals in the past decade, representing an estimated rate of about 3 per 100,000 intrathecal chemotherapy treatments.

2. This report adopts a systems approach to identify factors which have contributed to these errors and explores possible safety measures to reduce risk.

3. Recommendations are made for an immediate action plan, implemented by national guidance and reinforced by clinical governance. Key elements are:

    - formal designation within each Trust of medical staff competent to give intrathecal chemotherapy;

    - steps to ensure that intrathecal and intravenous cytotoxic drug treatments are given at different times, by different people and in different clinical locations.

4. It is recommended that there should be urgent assessment of the feasibility and safety of dispensing Vinca drugs either in an infusion bag or in a non-Luer syringe allowing intravenous administration only. This would add a level of design safety to the measures set out above.

5. Drug prescribing and administration errors occur with unacceptable frequency, particularly among recently qualified doctors. It is recommended that steps are taken with Medical Schools to ensure that therapeutics and risk management are thoroughly covered in core curricula.

6. Intrathecal injection errors belong to a wider class of misconnection hazard arising from the ubiquitous use of Luer connectors for a wide range of medical devices. Expert opinion is divided on the value of a major design initiative to achieve physical incompatibility of devices used for different routes of access, e.g. spinal/epidural and intravascular. More data are required upon which to base risk-benefit and cost-benefit analyses. It is recommended that the key issues are explored further with users, designers, manufacturers and international standards organisations. Better information on the true frequency of misconnection/disconnection errors within the NHS is urgently required.

Introduction

The brief

1. This report was prepared at the request of the Chief Medical Officer in order to take forward one of the recommendations made in *An Organisation With a Memory*[1]. Among four specific tasks set out in Recommendation 10 of that report was the following:

   "By 2001, reduce to zero the number of patients dying or being paralysed by maladministered spinal injections"

   The report had identified 13 such cases in the past 15 years. Tragically, another case occurred in January 2001, emphasising the urgency of finding fully effective preventive measures against this hazard.

2. The scope of the work presented here was as follows:

   - to identify the factors contributing to the hazard;
   - to consult widely across disciplines to identify interventions which might reduce intrathecal medication errors;
   - to consider the potential effectiveness and practicability of each intervention;
   - to set out the steps required to achieving the goal of zero incidents of intrathecal medication errors;
   - to consider, where relevant, strategies to reduce the overall burden of adverse events in the NHS.

Plan of work

3. In the interests of speed, it was agreed that the task should be undertaken by individual consultation rather than by convening a working group. Those consulted (Annex A) have contributed greatly to the shaping of the report but bear no responsibility for its final form. Many individuals have given much thought and effort to finding a solution to the problem, but the lack of a forum has hitherto been an obstacle. This report provides an opportunity to bring together their ideas and propose a co-ordinated strategy.

4. There is a general point concerning the development of a safety culture in the NHS. Relevant knowledge and ideas are scattered across many professional groups and functions within the NHS. The size of the organisation creates communication barriers both in gathering the available expertise and in implementing preventive measures universally. However, the NHS possesses in its workforce a rich resource to identify and find solutions to clinical hazards. Corporate action could be a powerful force in achieving system solutions.

The hazard

5. Vinca alkaloids (vincristine, vinblastine, vindesine, vinorelbine) are cytotoxic drugs used to treat leukaemias, lymphomas and certain other malignancies. They share a common property of neurotoxicity. Effective drug regimens for leukaemias and lymphomas commonly include a Vinca alkaloid to be given intravenously and methotrexate (or sometimes cytarabine) administered intrathecally to eradicate malignant cells sequestered within the blood-brain barrier. Erroneous injection of the Vinca alkaloid (usually vincristine) intrathecally causes devastating damage to the central nervous system which in most cases has lead to death within days. The few patients who have survived have had severe and permanent neurological damage.

6. This medical accident has been reported in many countries but its true frequency is unknown. A substantial proportion of the known cases and almost all the published literature relate to incidents more than a decade ago. There is undoubtedly greater awareness of the hazard now and all hospitals have taken steps to prevent it happening (see below). NHS experience over the past decade (5 cases), combined with an estimated denominator of 15,000 intrathecal cytotoxic treatments per year, would suggest a recent rate of around 3 per 100,000 such treatments. The order of magnitude is important. In considering preventive measures, this hazard has three key characteristics:

   - it is a rare event;
   - the consequences are invariably devastating and usually fatal;
   - recovery measures taken after the event are of little or no benefit.

   The target of zero incidence is therefore extremely demanding but entirely appropriate. To the personal tragedy of the affected patients and their families must be added the unquantifiable human costs to the health professionals involved and the damage to public confidence in the NHS.

Taxonomy of hazards

7. *An Organisation With a Memory* emphasises the need to collect and analyse accurate data on adverse health care events. This will require a carefully designed taxonomy if it is to have maximum value. The way in which phenomena are classified has significance far beyond the practicalities of storage and retrieval of data; it both influences and reflects our understanding of them. In medicine, the usual aim is to base classifications on ***causes***. Such an approach is problematic for adverse health care events since the causes are usually multiple, interacting and often individually trivial. *An Organisation With a Memory* illustrates this clearly with an analysis of the contributory failures in a fatal incident of intrathecal vincristine administration. A classification of adverse health care events based on ***outcome*** is also likely to be unhelpful: the latter may be strongly influenced by the patient's general medical condition and by the effectiveness of actions taken to recover the situation. Furthermore, an outcome-based classification cannot be applied to the analysis of 'near miss' incidents. A useful taxonomy should direct attention to the most promising ***preventative strategy*** by focusing on the key characteristic which might be modified.

8. At its simplest, the problem considered here could be seen as a ***drug administration error*** specific to the administration of Vinca alkaloids. Preventative measures would then be directed towards ensuring that drugs of this class are only injected intravenously, as intended. However, the hazard is also one of a class of ***misconnection errors***. The defining feature is that a drug intended to be given by one route is erroneously given by another. Almost the mirror image of the intrathecal injection error occurred recently in an English hospital where the anaesthetic bupivacaine was administered intravenously rather than by an epidural catheter inserted to provide epidural analgesia post-operatively. The patient died. Other examples of misconnection errors have included the connection of enteral feeding sets (intended

to be attached to nasogastric feeding tubes) to a central venous catheter in one case and to a haemodialysis line in another.

9. Conceptually related to the misconnections are the ***disconnection errors***. Although no collected data are available, there are many anecdotal reports of serious outcomes (sometimes fatal) following accidental disconnection of central venous catheters from giving sets, leading to air embolism, and of arterial lines causing major blood loss. Whereas the common theme in misconnection errors is over-compatibility of connecting devices, the shared characteristic of disconnection errors is the liability of connecting devices to separate. The characteristic defining the class of hazard points in each case to possible design solutions.

10. Recognition of misconnection errors as a class raises fundamental questions about the compatibility of connecting devices used medically for a wide range of purposes. Although this formulation of the problem may at first sight seem to be a slight digression from the task of preventing intrathecal Vinca injection, it has the following potential advantages:

- it presents the option of design solutions which have not hitherto been attempted;
- it may offer a single solution to a wider range of hazards in the health care system that have not previously been conceptually linked.

A design solution which creates physical incompatibility between devices used for drug delivery by different routes would certainly take longer to implement than measures to increase awareness of the hazard of intrathecal Vinca alkaloids or to alter hospital procedures. It might, however, be a worthwhile strategy to adopt (i) if it prevented intrathecal medication errors with greater certainty than any human factor approach; (ii) if it prevented a wider range of adverse events than intrathecal Vinca alkaloid administration alone.

Levels of intervention for the prevention of errors

11. Two broad preventive strategies are distinguished here. The first, which encompasses all the precautions currently implemented within the NHS to prevent intrathecal injection errors, can be termed the human factor approach. It includes the following:

- training and education;
- ward procedures and protocols;
- pharmacy procedures and protocols.

Each will be examined in the next section. The hospital policies which have been examined generally contain elements of all three; the emphasis varies depending on the professional group which has taken the lead responsibility for writing the guidelines. From this diversity will be highlighted examples of good practice which could usefully be incorporated into national guidance. Recommendations for action are in paragraph 45.

12. The second strategy, which has not previously been attempted in this context, is to seek a design solution. It has been successfully applied in many industrial settings ('engineering safety') and, to a very limited extent, within health care. In anaesthesia, for example, misconnection of gases has been prevented by physical incompatibility of the connectors used for different piped gas supplies. It represents a fundamentally different approach to error prevention and would require the concerted efforts of the NHS and industry. The issues are considered in paragraphs 34-43.

The Human Factor Approach to Intrathecal Injection Errors

13. *An Organisation With a Memory* describes how medical errors commonly arise because of failures at multiple points in a health care system rather than solely because of the action of an individual. In this model, safety is enhanced by examining the several layers of protection available in the system and correcting weaknesses in each of them. The concept has been likened to slices of Swiss cheese; a sufficient number of slices, with sufficiently small holes in each, will form an impenetrable barrier. A distinction was drawn between ***active failures*** of individuals and ***latent conditions*** in the system. These are holes in the Swiss cheese that become apparent only when, in combination with other deficiencies elsewhere, an adverse event is permitted to occur.

14. Latent conditions have contributed to past cases of intrathecal injection error. Fatigue, distraction and stress are well recognised contributors to human error in general. They are endemic to NHS practice and will remain so, at least until capacity and manpower problems have been alleviated by the measures now being implemented under the NHS Plan:

"England has too few hospital beds per head of population compared with most other health care systems. The NHS lacks sufficient doctors, nurses and other skilled staff. There are 1.8 practising doctors per 1,000 people compared with a European Union average of 3.1 per 1,000 population"[2].

15. In the short term, reductions in working hours will relieve fatigue but at the expense of:

- increased work intensity for staff when on duty;
- increased cross cover between specialties;
- reduced informal supervision of inexperienced by more experienced staff;
- less opportunity for more formal training (induction courses, specialty tutorials and audit meetings).

16. Familiar service pressures within the NHS appear as contributory 'latent conditions' in the reports of intrathecal injection incidents:

- pressure on beds, so that inpatient stays are reduced to the minimum;
- outlying of patients on wards where staff are unfamiliar with chemotherapy;
- relatively junior staff carrying out specialised tasks with minimal supervision;
- rotation of staff in training grades, so that they are frequently unfamiliar with their working environment, with patients and colleagues and with previously agreed policies within the organisation.

17. The high overall level of adverse events in the NHS (and in other health care systems which have examined the problem) testifies to a lack of system safety. A wide gulf currently exists between the NHS and industries with a deeply rooted safety culture such as civil aviation. An aircraft crash, like an intrathecal vincristine injection, is a rare but catastrophic system failure. The organisational contrasts, however, are stark. Civil aviation has long operated in a stringent regulatory environment combining primary prevention and the careful analysis of actual and near-miss incidents. Fatigue is minimised by tight controls on duty hours and rest periods. It would not be acceptable to improvise rotas with reduced trained crews on flight decks, or to allow cross cover between pilots trained on different aircraft types. The NHS could not meet impending legal standards on working time, and rising service demand, without measures which add latent factors for system failure – for example fewer staff on site at any one time, greater cross cover between specialties and less direct supervision of junior by senior staff.

18. The reality is that for the next decade at least the NHS will be attempting to develop safe systems in an environment which, for historical reasons, is ill-suited to the human factors approach. The unpropitious starting point makes it even more important that system safety is urgently addressed. Risk management strategy must, however:

- be parsimonious in the use of stretched resources, notably staff time;
- be efficient, by implementing first those changes which will yield most;
- seek, where possible, to develop design solutions which will *prevent* human error in preference to human factor solutions which only *reduce the likelihood* of error;
- be system-wide, with careful consideration of all the consequences of change.

19. The components of clinical governance set out in *A First Class Service*[3] include:

"Clear policies aimed at managing risks:

- *controls assurance which promotes self-assessment to identify and manage risks;*
- *clinical risk systematically assessed with programmes in place to reduce risk."*

Intrathecal chemotherapy is a prime example of a procedure which should be identified within a clinical service as having high risk associated with it. ('High risk' means either that there is a high probability of error, or that the consequences would be severe, or both[1]). Effective clinical governance therefore requires that there is an explicit local strategy to contain that risk.

Safeguards currently in place

20. A number of policy documents implemented by individual Trusts have been reviewed. Such independent initiatives have both strengths and weaknesses. The strengths are that they encourage local scrutiny of practices, accurately reflect local factors such as staffing and the physical environment in which care takes place, and foster local 'ownership' of protocols. Two major weaknesses are the lack of shared learning between NHS organisations, and the need for staff moving from one Trust to another to become familiar with new protocols. In view of public concern over this repeated mishap, there should be a single national document setting out safe practices for the administration of intrathecal chemotherapy. Local protocols should add to it any specific information required, such as the names of designated clinicians and the treatment areas to be used in the hospital.

Education and Training

21. Lack of knowledge has contributed to several incidents of intrathecal medication errors. In one case a Senior House Officer was not fully aware of the magnitude of the hazard of intrathecal vincristine injection (but had read that the drug has neurotoxic side effects). In another case, intrathecal vincristine was given in theatre by an anaesthetist providing cross cover for an oncology colleague who had gone off duty. As an anaesthetist, he was unfamiliar with the drug. In a third case, an enquiry expressed concern at a more general lack of knowledge among recent medical graduates of drug prescribing and administration; this point was taken up with the Dean of the local Medical School and the curriculum for teaching Clinical Pharmacology and Therapeutics was revised.

22. Intrathecal medication errors are part of a much larger problem of iatrogenic drug toxicity. Medical Defence Union data show that 25% of all indemnity paid out following litigation claims after adverse events in general practice results from medication errors[4]. Their contribution to adverse events in hospital is not known but is unlikely to be smaller, in view of the scale and complexity of hospital drug prescribing. Litigation claims cost the NHS £400m in 1998/9.

23. Most prescribing in hospital is done by junior doctors. A US study of prescribing errors in a teaching hospital measured the error rate in nearly 300,000 prescriptions[5]. 'Significant' errors were rigorously defined by their potential to cause harm. The rate (per 1,000 prescriptions) of significant prescribing errors by residents declined by 78% between the first and fourth years of residency training ($p<0.001$) yet first year residents wrote more than half of all prescriptions. Interestingly, attending physicians (equivalent to consultants in the NHS) had error rates between first and second year residents but wrote only 4.3% of the prescriptions. It would appear that training and practice, rather than seniority *per se*, reduce errors.

24. Reforms of the undergraduate medical curriculum set out in *Tomorrow's Doctors*[6] have sought to reduce the burden of factual knowledge placed upon students. This change was necessary but must be selectively applied. Patients are not placed at risk if new medical graduates are no longer expected to know all the branches of the carotid artery, each enzyme of the Krebs cycle or the histological classification of lymphomas – such detailed knowledge is best acquired during postgraduate specialist training. However, every doctor from qualification will be prescribing and administering drugs. The undergraduate curriculum must therefore provide a thorough understanding of drugs and their potential hazards. The 'learning curve' seen in the US study is no more acceptable in pharmacotherapy than it would be in surgical practice.

25. *Tomorrow's Doctors* devotes fewer than a dozen words to this topic. It is reasonable (and proper) that details of dose should be looked up rather than committed to memory. However, prior awareness of contraindications, drug interactions and toxicities is essential for safe prescribing. These in turn require a thorough knowledge of the clinical pharmacology of all drugs in common use. Case studies of drug-related adverse events are valuable in teaching practical therapeutics, both as an aid to understanding risk management and to avoid the excessively didactic approach which has in the past burdened the undergraduate curriculum.

26. Combination chemotherapy for the leukaemias and lymphomas is nevertheless a specialised field of practice. Doctors must acquire detailed familiarity with it during their postgraduate training in the relevant specialities, supported by personal teaching and example from more senior staff. Because of the known hazard of intrathecal administration error, this form of treatment should only be carried out by *designated* staff who have had *explicit* instruction in it. Such a restriction would have prevented most of the adverse incidents considered here. Instruction would include familiarisation with the national guidelines proposed below. Each unit administering intrathecal chemotherapy should maintain an updated list of medical staff who are authorised to administer it, as part of clinical governance.

A national protocol will make it simpler for the training status of specialist registrars to be ratified as they move from one Trust to another.

Ward procedures relating to intrathecal medication

27. Examples of good practice which have been implemented to prevent intrathecal injection errors seek to separate the injection of intravenous and intrathecal cytotoxic drugs *in time, place and person.* For example:

- the intravenous and intrathecal treatments are given at a different time of day or on a different day;
- intravenous treatments are given on the ward, whereas intrathecal therapy is given in a designated side room or in theatre;
- intravenous chemotherapy is given by a nurse specialist and intrathecal treatment is given by a doctor.

These strategies should ensure that the Vinca alkaloid syringe will never be at hand when intrathecal chemotherapy is being given.

28. Experience has shown that such ward procedures can be subverted by unforeseen and seemingly innocent factors. Separation in time of intravenous and intrathecal treatments may be compromised by a well intentioned effort to minimise the duration of the patient's stay. Agreed procedures may break down because of a failure of communication when staff hand over between shifts, when staff cover for absent colleagues or because new staff are simply unaware of them. The designation of competent staff should avoid these eventualities.

Pharmacy procedures, warnings and prompts

29. The preparation of cytotoxic drugs for injection has gradually become a sub-specialty of pharmacy, though not formally recognised as such. Prescribed doses are made up in a dedicated area of the pharmacy department, labelled, checked and sent to the ward when required. The prescription of parenteral cytotoxic treatment has increased substantially over the past decade; one large cancer centre pharmacy is now producing three times as many doses as in 1990. Hospital pharmacies are now preparing an estimated 700,000 parenteral cytotoxic doses nationally each year. However, the use of intrathecal chemotherapy is thought to be relatively stable since the regimens concerned have altered little in recent years.

30. Procedures have been introduced by pharmacists in each Trust to prevent intrathecal medication errors. Although no national framework has been circulated, a document produced by the NHS Executive London Regional Office[7] has been influential. The following specific precautions have been culled from a review of a number of local guidance documents:

- hazard warnings on outer packs of Vinca alkaloids (only to be removed immediately before administration) reminding the clinician that it is for intravenous use only and/or that it is fatal if given by any other route. (Pharmacists are reluctant to specify that the hazard is the *intrathecal* route, since the appearance of that word on the label might cause confusion by association);

- doses of Vinca alkaloid to be diluted in pharmacy to at least 10ml, the logic being that intrathecal injection of this volume would be unusual and therefore the clinician would be alerted to the possibility of error. There have been instances, however, of intrathecal injection errors occurring despite such dilution;

- doses of Vinca alkaloids for intravenous use to be packed separately from all other drugs, transported separately to the ward and stored separately on the ward prior to use;

- intrathecal injections (e.g. methotrexate) to be sent to the ward at separate times from intravenous drugs forming part of the same treatment regimen. In some hospitals, intrathecal doses will not be sent from pharmacy to ward until it is confirmed that the intravenous drugs have been given.

Possible additional pharmaceutical precautions

31. **Novel prompts/reminders to be attached to syringes:**

    i. a syringe cap coded by colour, shape and printed text as being e.g. for 'INTRAVENOUS' or 'INTRATHECAL' administration. Prototypes were produced by NHS staff about 10 years ago, after an intrathecal injection incident; the patent is held by an NHS Trust. The rationale is that the syringe cap is removed just as the injection is given, when a visual prompt is likely to be most effective. Manufacturers could not be persuaded to take this device into production, however, since they doubted that there was sufficient demand to make it commercially viable.

    ii. use of over-printed or colour-coded syringes to indicate the route of administration.

    iii. use of route-indicating labels cross the cap of the syringe, which have to be torn in order to remove the cap. This device is already in production for other purposes ('Steri-Tamp™').

32. Any such prompts would have to be used consistently for all cytotoxic injections. They would potentially have greater impact than currently used warning labels on syringes and packs but they would still not constitute an absolute barrier to an injection error. They represent an extension of safety procedures already in use which have occasionally been breached, but could be expected to reduce error rates further. None of the above would be technically difficult to implement, though (i) would require a new manufacturing process to be set up, and (ii) and (iii) would require modification of existing processes.

33. **Vinca alkaloids to be dispensed in another way than in a standard Luer syringe.**

    i. A syringe with a non-removable needle attached. It would then be impossible to connect the syringe to a spinal needle. The fixed needle would be passed through the rubber connector on an intravenous giving set to deliver the Vinca alkaloid safely. However, it is not currently possible to fix an irremovable needle to a syringe in pharmacy. If that were done, there would be technical problems preventing drug leakage through the needle in transit, or loss of sterility. Pre-filled syringes of Vinca alkaloids might be supplied by manufacturers with an integral needle, but this would make dose adjustment difficult. The dose depends on body size over a possible 10-fold range.

ii. Dispensing Vinca drugs in a non-Luer syringe, supplied with a compatible (non-Luer) needle so that the drug can be injected into the rubber connector of the intravenous giving set. No such syringe and needle are currently on the market. This would nevertheless be a relatively simple design solution to introduce, requiring the manufacture of perhaps two sizes of syringe (2ml and 10ml) and a single size of needle.

iii. Using Luer lock and Luer slip syringes (see para 34) to differentiate treatments for intravenous and intrathecal use. This is the practice in some hospitals. However, either can be attached to the hub of a spinal needle; the 'prompt' depends on the operator being aware of the significance of the difference. The Luer fitting is considered in more detail below.

iv. Dispensing Vinca alkaloids into 50ml or 100ml bags for intravenous infusion, rather than in a syringe. These drugs cause serious local tissue damage (including skin necrosis) if they leak out of the vein. It is therefore routine to set up an intravenous saline drip and to inject the Vinca alkaloid into the giving set once secure intravenous access is confirmed. Potential problems with infusion from a bag have been suggested:

- additional time taken to give the drug would increase nursing time and might result in a lower level of nursing supervision for possible extravasation;
- some pharmaceutical development would be needed to confirm drug stability at high dilution (a pH of 3.5-5.0 is required).

If it could be implemented safely, this modification to practice would be equivalent to a design solution for the intrathecal injection hazard. It would be physically impossible to connect the infusion bag to a spinal needle. However, some development work is needed to confirm that an infusion bag system does not increase the incidence or severity of extravasation events or of thrombophlebitis. It should be noted that only a small percentage of Vinca alkaloid treatments form part of a regimen including an intrathecal agent. It is therefore essential that any change in practice to prevent erroneous intrathecal injection in this minority does not increase other hazards (such as extravasation injuries) in a much larger group of patients.

Design Changes to Differentiate Spinal and Intravenous Routes

34. The Luer connector was patented in 1898. It comprises a male and a female component with a 6% taper. It is simple to manufacture from a range of materials and easy to use. It has therefore become almost universal as a connector for medical devices. International standards recognise two variants: the Luer slip, and the Luer lock which has a threaded collar. These are not incompatible but the latter reduces the risk of disconnection.

35. The Luer connector has come to be used for a multitude of medical applications, ranging from fluid delivery by the enteral, intravascular, spinal and epidural routes to the insufflation of gas into intravascular balloon devices, endotracheal cuffs, sphygmomanometers and the like. Its ubiquity creates the risk of misconnection error, intrathecal administration of drugs intended for intravenous use being but one example.

36. The European Committee for Standardisation (Comité Européen de Normalisation, CEN) set up a task group to examine this problem. Its report[8] (which did not specifically consider the intrathecal and epidural routes of delivery) recommended:

"That the use of Luer connectors is restricted to devices intended to be connected:

- *To the **vascular system** for delivery or sampling purposes or to assist in making some sort of measurement;*
- *To a **hypodermic syringe** in order for the syringe or a connected device to achieve its intended purpose."*

European medical device manufacturers raised a number of objections to the report and its recommendations, asserting that the proposals could create more hazards for users and would be costly to implement[9]. In addition to the CEN proposal of differentiated respiratory (gas), enteral and vascular routes, it would be necessary to add a fourth "neuraxial" route for intrathecal and epidural uses if the hazard considered here were to be prevented. Since spinal needles are widely used for spinal and epidural anaesthesia, Luer fittings would have to be removed from all such devices. The list of devices to be re-designed would therefore include:

- the full range of spinal needles, in different gauges and lengths for adult and paediatric use;
- epidural catheters;
- in-line filters used with epidural catheters;
- low friction syringes for epidural placement;
- standard syringes in a range of volumes;
- giving sets for epidural infusions.

37. To prevent intrathecal administration of intravenous drugs (and vice versa), spinal needles with Luer hubs would have to be removed from NHS hospitals. Whatever alternative standard fitting were adopted, the change would affect all user groups, including:

- oncologists and haematologists;
- anaesthetists;
- neuroradiologists, neurologists and neurosurgeons;
- general physicians and paediatricians.

38. Of these, it is the anaesthetists on whom the greatest impact would fall. Epidural anaesthesia is a technical skill acquired by long practice; expert opinion is that any change to the 'feel' of the equipment used would be likely to increase the number of failed procedures (e.g. inadvertent dural puncture) at least in the short term. Design modification would require a larger connector than at present (since a smaller one would lack sufficient mechanical strength) or a 'keyed' fitting. In either case, the change should be the most limited which would achieve incompatibility with Luer devices. A risk assessment and piloting of prototypes would be essential for any proposed design modification.

39. Several non-Luer connectors have been designed, some of them patented and some freely available. One family of connectors (IsoLock) has been patented and developed with the support of Department of Trade and Industry awards. The design has a locking device to prevent disconnections. Prototypes have been produced in several mutually incompatible sizes. The locking mechanism is not required for the intraspinal route and makes the connector too bulky for this application, but has the potential to prevent a range of disconnection errors.

40. Spinal needles and epidural catheters are Class 2A devices[10]. Any new manufacture would have to include the relevant conformity assessment by the Medical Devices Agency, to include an agreed testing or audit of quality assurance. Product development would probably take 1-2 years. If an international initiative were to be pursued through CEN, consultations would take additional time. The UK could act independently, however, provided no barriers to free trade were created.

41. Manufacturers have in the past been reluctant to develop design modifications of high volume, low cost products such as needles and syringes in the absence of a known market for them. A design initiative of the scale required here would have to be customer-led, using the resources of the NHS Purchasing and Supply Agency to put the work out to tender. Since the manufacturing base is global, the size of the market offered by the NHS would be an important factor for companies. Contracts would need to provide the scale and duration required to cover product development costs.

42. The steps required to achieve design incompatibility of spinal and intravenous devices are therefore the following:

> ***Policy.*** Is the aim to achieve spinal/intravenous incompatibility, or to combine this with the more ambitious project (intravascular, respiratory and enteral differentiation) proposed in the CEN document? The latter implies up to four variants of syringes being stocked in NHS hospitals, with a complete range of new non-Luer devices for non-vascular connection. Should the design approach address disconnections as well as misconnections? Should action be initiated by the UK alone or internationally through CEN?

Risk/benefit assessment. Potential hazards and disadvantages of the proposed changes would need to be carefully considered in collaboration with users, offset against the anticipated gains in patient safety.

Design. Options include several existing designs or modifications of them. Consultation would be required with all user groups. Users and product designers would need to work together on both the design and evaluation phases.

Regulatory approval. MDA approval would have to be obtained for manufacture of redesigned devices at Class 1 or 2A level as appropriate.

Purchasing for the NHS. Having specified the range of products required, the NHS Purchasing and Supply Agency would act for the NHS as a whole to procure the redesigned devices. NHS Logistics would be required to provide the necessary distribution facilities for a considerably enlarged range of sterile disposable products.

Communication, training and roll-out. Phased implementation of new devices would be preferable but each phase would need to be properly co-ordinated so that new devices for a particular route were not in service concurrently with superseded (Luer) designs. For example, to achieve the aim of removing all Luer spinal needles from NHS premises would require that all non-Luer devices for neuraxis work be made available simultaneously. This would include all equipment used for spinal and epidural anaesthesia.

43. A number of experts consulted have offered cogent arguments against the re-design of connectors. The management and logistical challenges are large. Even a limited goal of having non-Luer connectors on all devices used for intrathecal and epidural access would, realistically, take at least 2 years to achieve and a more ambitious programme several years longer. The central issues are, in order, the risk-benefit and the cost-benefit analyses. We currently lack essential data on the scale of misconnection and disconnection errors in the NHS to make an informed judgement. Would a requirement to stock multiple ranges of incompatible disposable syringes (up to four) create unforeseen hazards? Overall, would any marginal increment in safety (over and above what could be achieved without re-design) justify the cost? Cost here includes not just financial cost but also managerial and clinical resources needed to implement change. There may be more efficient ways to improve patient safety (see para 18). In view of the urgency of preventing further intrathecal injection errors, such a radical strategy should be pursued separately from the immediate introduction of other safety measures.

Conclusions

44. Intrathecal injection of a Vinca alkaloid is a rare but catastrophic error which has caused a number of deaths and damaged public confidence in the NHS. There is an urgent need to prevent any recurrence of this particular adverse event by establishing a secure system of safeguards throughout the service. This review has also identified wider safety issues in two areas which require action to protect patients: a range of hazards relating to the connectors used in medical devices, and an unacceptable level of drug prescribing and administration errors. Progress in these two areas will require action over the longer term but would yield large gains. The recommendations set out below can be divided into those for immediate action and those which should be initiated now but which will only show results over a longer timescale.

45. **Proposals for immediate action:**

Recommendation 1

The NHS should issue national guidance on safety procedures to be followed in the administration of intrathecal chemotherapy. This guidance should incorporate best medical, ward and pharmacy practice from the many local protocols which have been written.

Recommendation 2

Within each clinical service in which cytotoxic chemotherapy is given, there should be an agreed and regularly updated list of individuals permitted to administer intrathecal chemotherapy. The named individuals must have received training on the protocol to be followed and have been provided with current copies of that protocol. Trust chief executives should be responsible for ensuring that this safeguard is implemented forthwith as part of clinical governance.

Recommendation 3

National NHS guidance should include measures to ensure that administration of intravenous and intrathecal cytotoxic agents is carried out by different trained staff, at different times and in different clinical locations. Drugs should be checked by two staff with chemotherapy training. Trusts should specify local implementation arrangements as attachments to the national guidance.

The above measures would have prevented past incidents of intrathecal Vinca alkaloid injection. Together, they provide multiple robust levels of security and can be implemented with minimum delay.

Recommendation 4

The dispensing of Vinca alkaloids either (i) in a non-Luer syringe or (ii) only in 50ml or 100ml bags for intravenous infusion should be urgently explored.

The first option requires sourcing of syringes and needles not currently available, whereas the second could be implemented without new equipment. However, the latter needs to be piloted to ensure that pharmaceutical and nursing concerns over extravasation risks can be resolved. Either option would add a 'design' element of security to intrathecal Vinca alkaloid administration.

46. **Strategic initiatives to be taken forward concurrently:**

Recommendation 5

Medical schools should ensure that their core curricula provide a thorough knowledge of safe drug prescribing and administration. Proper assessment in these areas is essential to minimise the occurrence of therapeutic errors, particularly during general professional training.

Recommendation 6

Policy decisions are required on a possible programme of redesign of connecting devices. The costs, benefits, risks and feasibility of such a programme will need to be examined in the light of quantitative data on adverse events arising from misconnections and disconnections in the NHS. Research is likely to be required for risk assessment and health economic analysis.

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Annex A

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