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Appendix 4: Reports of accidental intrathecal injection of vincristine

This document summarises the reported cases of accidental injection of vincristine by the intrathecal route cited in the literature review. A full list of references is provided in that document; refer to Appendix 3.

Abbreviations used: **ALL** acute lymphocytic leukaemia **CSF** cerebrospinal fluid **CYT** cytarabine **FFP** Fresh Frozen Plasma
IT intrathecal **IV** intravenous **LL** lymphocytic leukaemia **MTX** methotrexate **NR** not recorded

| Ref No | Author | Year of Publication | Country | Details | Contributing factors | Dose of vincristine | Management | Outcome | Notes |
|--------|-----------|---------------------|---------|--|---|------------------------|--|--------------------|-------|
| 2 | Schochet | 1968 | USA | 2.5yo female with ALL | IT MTX | 3mg | CSF exchange | Died on day 3. | |
| 3 | Shepherd | 1978 | USA | 5.5 yo child with ALL | IT MTX, CYT,hydrocortisone. 2nd dose vinc instead of IT CYT. | 1.2mg | Recognised immediately. CSF removed, IT hydrocortisone. | Died 12 days later | |
| 4 | Slyter | 1980 | USA | 29 yo woman with stage iv-a lymphoblastic lymphoma | IT MTX, CYT,hydrocortisone. | 2mg | Recognised immediately. CSF removed, IT saline, oral dexamethasone. | Died on Day 14. | |
| 5 | Solimando | 1982 | USA | refers to two unpublished cases | Syringes not labelled - only outer wrap which was removed prior to placement on the tray. | NR | NR | Died. | |
| 6 | Manelis | 1982 | Israel | 5 yo female | Due to procedural errors. | 0.9mg | Recognised after 30minutes. | Died 17days later. | |
| 7 | Gaidys | 1983 | USA | 23month old female with ALL, in remission | IT MTX, CYT,Hydrocortisone. Vincristine instead of IT MTX. | 0.68mg in 6.8ml 2mg/m2 | Recognised immediately but not treated for 4.5hours, aggressive treatment including CSF exchange and folinic acid. | Died on Day 6. | |

High-risk medication alert for vincristine injection – Appendix 4

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| 8 | Williams | 1983 | USA | 16 yo male with ALL | IT MTX. ? Syringes incorrectly labelled, administered by local physician. | 2mg | Referred to hospital 48 hrs post dose. High dose folinic acid, IV dexamethasone. | Brain dead by day 7, life support discontinued day 36. | |
| 51 | The Sydney Morning Herald | 1987 | Australia (Adelaide) | 17yo female | IT MTX. Administered by a doctor (intern) with inadequate experience. Failed to read labels. | NR | NR | Died after 8 days. | |
| 9 | Dyke | 1989 | USA | Adult male with Burkitt's lymphoma | NR | NR | Aggressive early treatment with ventriculolumbar CSF lavage using lactated Ringer's solution and ffp over 24 hours + glutamic acid IV over 24 hours followed by oral glutamic acid. | Survived but died 3months later from lymphoma | |
| 10 | Bain | 1991 | UK | 56 yo male beta cell LL | Oral MTX | 0.3mg (2mg syringe) | Error notice during administration, only part dose given. Sent home as no ill effects anticipated, CSF aspirated. | Respiratory arrest 9 days later, brain dead at Day 30. | |
| 11 | Bleck | 1991 | USA | 23 yo male with ALL | IT MTX, hydrocortisone. | 2mg | Recognised immediately. CSF lavage, IV dexamethasone, folinic acid, vitamin B12, thiamine and IV pyridoxine. | Brain dead at Day 29, died day 348 after active support withdrawn when primary disease returned. | |
| 24 | Brahams | 1991 | UK | 16yo male | IT MTX. Two junior doctors, new at the Hospital. No senior staff available. | NR | NR | Died. | Two junior doctors convicted of manslaughter, later overturned |

High-risk medication alert for vincristine injection – Appendix 4

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| | | | | | | | | | on appeal. |
| 12 | al Fawaz | 1992 | Saudi Arabia | 15month old male with ALL | IT MTX. Fourth dose of vinc, second of combination. All drugs brought to treatment room. | 0.7mg (1.5mg/m2) | Realised 3hrs later. Folinic acid rescue, IT hydrocortisone. | Died 75days later, after respiratory arrest and artificial respiration since Day 7. | |
| 13 | Zaragoza | 1995 | USA | 6 yo male with ALL | IT MTX. | NR | Recognised immediately. CSF drainage/lavage, IV folinic acid, glutamic acid, pyridoxine. | Survived with paraplegia, requirement for nocturnal respiratory assistance at 24months. | |
| 65 | The Age | 1995 | Australia (Geelong, Vic) | 27yo male | NR | NR | NR | Survived with quadriplegia. | |
| 14 | Lau | 1996 | Singapore | 27 yo female with ALL | IT MTX. A junior doctor was assigned to administer the chemotherapy accidentally gave the vincristine via ommaya reservoir. | 2mg | Mistake realised the following day. CSF lavage, folinic acid and oral glutamine. | Died 10 days later. | |
| 15 | Michelagnoli | 1997 | UK | 10 yo female with b-cell lymphoma | IT MTX, CYT and IV vincristine were scheduled to be given under general anaesthesia. | NR | Recognised immediately. CSF drainage/lavage, folinic acid, pyridoxine, glutamic acid, iv caffeine. | Paraplegic at 18months. | |

High-risk medication alert for vincristine injection – Appendix 4

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| 16 | Meggs | 1998 | USA | 59 yo female with ALL | Intraventricular CYT (omaya reservoir). Vincristine instead of IT CYT. | 2mg in 10ml | Recognised immediately. CSF lavage, glutamic acid, ffp. 95% of dose recovered. | Died day 40. | |
| 18 | ISMP Alert | 1998 | USA | 59 yo female | IT CYT. | 2mg vinc | Recognised immediately, optimal care. | Died 9 days later. | |
| 17 | Fernandez | 1998 | Canada | 7 yo female with ALL | IT MTX, CYT, hydrocortisone (Childrens Cancer Group Protocol 1992). Vincristine administered instead of IT hydrocortisone. Experienced and competent physician. The oncology ward was full thus admitted to another ward where the injection took place (treated some oncology patients in the past). The IT chemotherapy was not delivered or stored separately, nor was it brought into the room by the physician. The IT chemotherapy was identified by reading the labels when it came into the room however the presence of the fourth syringe (vincristine) was not recognised. . The chemotherapy was not placed on the lumbar puncture tray by the administering physician and the tray was | 1.5mg | Recognised immediately. CNS lavage, folinic acid, glutamic acid, dexamethasone. | Died 13 days later | |

High-risk medication alert for vincristine injection – Appendix 4

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| | | | | | adjusted in such a way as to be above eye level of the seated physician. Finally the intrathecal (and intravenous) chemotherapy labels were not read again by the administering physician prior to administration. | | | | |
| 19 | Al Ferayan | 1999 | Saudi Arabia | 7 yo female with ALL | | 0.5mg | CSF lavage commenced within 2 hours. Ringers, glutamic acid. | Motor paraparesis at 34months. | |
| 20 | Kwack | 1999 | Korea | 3 yo male with ALL | NR | NR | NR | Died after 6days. | |
| 31 | ISMP Alert | 2000 | USA | Adult male with Burkitt's lymphoma | IT MTX. | NR | NR | Died 10 weeks after injection. | |
| 21 | Dettmeyer | 2001 | Germany | 5yo female with ALL | IT MTX. Doctor prepared syringes and was then absent when a colleague confused the syringes even though they were inscribed. | NR | Recognised immediately. | Died 7 days later. | preliminary investigations led to the reproach of negligent killing in both cases. Civil claims were regulated by legal liability insurance. To avoid a main trial the two charged doctors accepted a pecuniary penalty and a sceond pecuniary penalty only if they become punishable during probation. |

High-risk medication alert for vincristine injection – Appendix 4

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| 21 | Dettmeyer | 2001 | Germany | 57 yo male with LL | IT MTX, CYT. Syringe with IT drug was missing and the resident took the vincristine. | NR | NR | Died four weeks later. | |
| 23 | Dyer | 2001 | UK | Same case as below (25) | | | | | 2 Doctors suspended and charged with manslaughter |
| 25 | Dyer | 2001 | UK | 1999 case - 12yo male | NR | NR | NR | Died | 2 doctors cleared of manslaughter after prosecutors decided death was caused by 'chance events and failings'. |
| 22 | Dyer | 2002 | UK | 18yo male | IT MTX. Both drugs administered IT. Registrar ordered senior house officer to inject even after a query. New staff unfamiliar with procedures. Syringes delivered together. | NR | Recognised within 15minutes. | Died | Doctor charged with manslaughter. Trial halted due to ill health of the defendant (64). |
| 26 | Alcaraz | 2002 | Spain | 12yo female with ALL | IT MTX, CYT, hydrocortisone. | 2mg in 20ml | Recognised after 30minutes. CSF washout/exchange, glutamic acid. | Died day 83. | |
| 27 | 7.30report | 2004 | Australia (Sydney) | 28yo male with Burkitt's lymphoma | IT MTX. Doctor (radiology) wrote 'vincristine and methotrexate given intrathecally as requested'. Warning label on vincristine incomplete. Small type on labels, darkened room. | NR | Recognised 5 days later after paralysis of lower limbs. CSF drainage | Died after 28+ days. | |

High-risk medication alert for vincristine injection – Appendix 4

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| 73 | Mercury News | 2005 | USA | 21yo male with non-Hodgkin's lymphoma | Wrong drug | NR | NR | Died 3 days later. | Hospital to cease preparation of vincristine in syringe and warning labels to be required. |
| 74 | ISMP Alert | 2005 | USA | Same case as 73. | A syringe containing vincristine for another patient had been accidentally delivered to the patient's bedside. A physician administered the drug intrathecally, believing it was a different medication intended for that route of administration. | NR | As above | As above | As above |