Dr C / Public Hospital

A Report by the

Health and Disability Commissioner

(Case 99HDC08824)

Health and Disability Commissioner
Te Toihau Hauora, Hauātanga

Parties involved

Mrs A	Complainant / Consumer's mother
Mr B (deceased)	Consumer
Dr C	Provider / Consultant physician, at the public hospital
Dr D	Registrar, at the public hospital
Dr E	Director of ICU, at the public hospital
Ms F	Customer Services Officer, at the public hospital

Independent expert advice was obtained from Dr Sharon Kletchko, an emergency medicine specialist.

Complaint

The Commissioner received a complaint from Mrs A about the treatment her late son, Mr B, received from Dr C and the public hospital. The complaint was that:

- *Following Mr B's overdose of Tegretol (carbamazepine) charcoal was not administered when all sources of information state it should be.*
- *No x-ray or ultrasound was performed to ascertain whether a pharmacobezoar had formed.*
- *Mr B's ingestion of slow release Tegretol should have made a high bowel washout or gastrotomy a consideration. Despite this neither procedure was carried out.*
- *On 1 November 1998 no action was taken despite Mr B's Tegretol levels having risen above immeasurable levels.*
- *Mr B's Tegretol level was recorded on 2 November 1998. No further levels were recorded until 5 November 1998.*
- *Mr B was not intubated to protect him against aspiration, which occurred on 2 November 1998.*
- *The medications listed on page 7 of Mr B's 'Acute Assessment Discharge form' were incorrect.*
- *In the ICU plan Dr C stated treatment was to be "supportive". Mrs A queries the decision to pursue supportive care when active intervention may have saved Mr B's life.*

The complaint was received on 12 August 1999. An investigation was commenced on 27 October 1999.

Information reviewed

- Clinical records for Mr B from the public hospital
- Clinical records for Mr B from another public hospital
- Information sheet on carbamazepine (Tegretol) from the National Poisons Centre

Information gathered during investigation

Background
Mr B was born in May 1980. When Mr B was 14 years old, an educational psychologist suggested to his mother, Mrs A, that he might have Asperger's Syndrome. (Asperger's Syndrome is an autistic spectrum disorder characterised by impaired social interactions and restricted interests and behaviours.) In 1998, Mr B was referred to IHC. He was subsequently diagnosed as mildly intellectually disabled and was therefore able to access IHC's accommodation and support services. On 20 May 1998, IHC arranged for Mr B to live with one of its contract board provider couples. He stayed with that couple until Friday 30 October 1998 when the couple requested "time out". Mr B was placed with an alternative IHC board provider (two caregivers) for the weekend beginning 30 October 1998.

On the evening of Saturday 31 October 1998, Mr B went to bed at approximately 11pm. At some stage that night, or early the following morning, he swallowed a large number of Tegretol tablets kept in an unlocked kitchen cupboard. (Tegretol is the trade name for carbamazepine and is used therapeutically as a psychotropic and anticonvulsant medicine.) Mr B was found by a passer-by collapsed in the street at approximately 8.30am on Sunday 1 November 1998. An ambulance was called and Mr B was taken to a public hospital where he arrived at 9.11am. The Police were also called and were present when the ambulance arrived.

The ambulance officer's report recorded that Mr B was unconscious, that he was rousable to pain and had a GCS score of 6. (The Glasgow coma scale is a 15-point system used to estimate a patient's level of consciousness. The higher the score, the greater the level of consciousness. Patients are scored according to motor response (from "obeys command", which has a score of 6, to "no response", which has a score of 1), verbal response (from "oriented", which has a score of 5, to "none", which has a score of 1) and eye opening (from "spontaneous", which has a score of 4, to "none", which has a score of 1).) Mr B scored 3 for motor response, 1 for verbal response and 2 for eye opening.

Admission to hospital
An emergency department officer, examined Mr B on his arrival at hospital. He was unconscious but breathing spontaneously. His pupils were dilated, but sluggish when reacting to a light source. His GCS was recorded at 4 (a drop from when seen by the ambulance officer). Mr B's vital signs were taken and recorded. His blood pressure was

137/65, his pulse rate was 105 and oxygen saturation level was 96%. Mr B had brisk reflexes although he had clonus (alternate muscle contraction and relaxation) in both feet. At 10am he was recorded as agitated and combative. He had episodes of sweating, tachycardia (rapid heartbeat) and ataxia (irregular muscle contraction), followed by episodes of inertia.

It was initially thought, following discussion with one of his caregivers, that Mr B had taken 45 x 400mg tablets of Tegretol. A blood sample was taken to test for Tegretol toxicity. It showed that he had an elevated Tegretol level of 129µmol/L (toxic level: >45µmol/L). The emergency department officer contacted Dr D, the medical registrar on call, to admit Mr B for further monitoring.

Dr D reviewed Mr B, who had started having attacks of opisthotonos (form of spasm/fit consisting of extreme hyperextension of the body). Dr D contacted the National Poisons Centre (NPC) by facsimile to obtain information about the treatment of Tegretol overdose. The request form noted that Mr B had ingested "45 500mg" carbamazepine tablets. A copy of the information faxed to Dr D by the NPC is attached as Appendix I. Dr D talked to Mr B's caregiver, who clarified that a bottle of Tegretol had been found with 55 x 400mg tablets missing.

The information from the NPC stated that "single dose activated charcoal is the recommended gastrointestinal decontamination procedure". Dr D contacted Dr C, the consultant physician on call that day. The doctors agreed that Mr B should be transferred to the Intensive Care Unit (ICU) and closely monitored. Intravenous diazepam was to be administered if he developed prolonged fits that would not resolve spontaneously.

Mr B was transferred to ICU at 10.45am. His GCS had dropped to 3. Dr C saw Mr B soon after his transfer to ICU and discussed his treatment with Dr D. Dr D informed me that Dr C advised against performing a lavage (washing out of the stomach) or administering activated charcoal as this could cause more harm, particularly as Mr B was unconscious. During that morning Mr B had frequent fits.

Dr C confirmed to me that he did not order the administration of activated charcoal. He stated that it was not clear whether there was another drug contributing to Mr B's condition. He further advised that as Mr B's serum Tegretol level was already significantly raised on arrival to hospital it was likely that he had ingested the drug by 7am. Dr C advised that the estimated time of ingestion was therefore between 8pm and 7am. It was his view that it was not possible to say when peak serum levels would be expected, but that repeat blood tests would clarify this. (Repeat blood Tegretol levels were ordered for 4pm that day.)

The time of ingestion is important when treating an overdose as the effect of the drug depends on the amount of absorption. In the case of Tegretol poisoning, the information from the NPC stated:

> "Carbamazepine is absorbed slowly from tablets. In therapeutic doses, peak plasma levels are attained in two hours from the syrup formation, within 12 hours from

conventional tablets and within 24 hours from the controlled release formulation … In overdose absorption may be delayed up to 72 hours post ingestion."

Dr C informed me that a diagnosis of severe Tegretol poisoning was made and a management plan formulated that consisted of four aspects: diagnosis, decontamination, supportive care and elimination. Having made the diagnosis, Dr C then considered treatment by means of decontamination. He advised me as follows:

"(a) Lavage: The treatment guidelines states 'The lavage is not generally recommended unless the patient presents obtunded [reduced level of consciousness] within one hour of ingestion'. Because of this, and other reasons mentioned later, I did not advise lavage.

(b) Activated Charcoal: I was not ignorant of the fact that activated charcoal is recommended for the management of Tegretol overdose. However, in my opinion, the process of administering the activated charcoal would cause more harm than benefit to [Mr B] for the following reasons:

(i) The efficacy of activated charcoal decreases as the duration from the time of ingestion of Tegretol increases. Being unsure of the time of overdose, I was not certain of the degree of benefit. (If this was the only consideration, charcoal would still have been given.)

(ii) During, and for several hours after administration of charcoal, it would be mandatory to protect the airway with an endotracheal tube. Given the ease with which the 'seizure' activity could be precipitated, I felt very strongly that an E.T. tube would greatly increase seizure activity thus necessitating heavy sedation, respiratory depression and ventilation. In other words, administering activated charcoal meant artificial ventilation. (The treatment guidelines recommend treating seizures with Diazepam 'taking care that undue depression does not occur'.)

(iii) There was no other indication for artificial ventilation at the time. This procedure has its own inherent problems.

(iv) Another patient was already on the ventilator at the time and it seemed unlikely that she was going to come off for several more days. If the second patient went onto a ventilator then consideration would possibly have to be given to transferring one out to another centre. (If there is a clear indication for ventilation, this is never an issue.)

(v) There was no reason to be certain that [Mr B] would eventually develop an indication for artificial ventilation.

Therefore, after careful consideration of all the above, I felt that it was better to omit the activated charcoal than to commit [Mr B] to ventilator therapy. I would like to reassure [Mrs A] that at that point that was considered the better option for [Mr B] and would also like to add that, from my personal point of view, it would have been easier to order activated charcoal since [Mr B] would then go onto a ventilator and the responsibility for his own ongoing care would shift primarily to another specialist."

Although Dr C decided not to administer charcoal to Mr B, he nonetheless actively treated him. A management plan was prepared and included careful monitoring of Mr B while in ICU. Although a decision was made in the morning not to administer charcoal, Dr C was aware that the Tegretol level could increase and ordered repeat Tegretol levels to be performed that afternoon.

With respect to supportive care, the third aspect of the management plan for Mr B, Dr C informed me that in his view, this was by far the most important element and there was to be no compromise in respect of this component of Mr B's care. Close observation was ordered, but undue stimulation was to be avoided in view of the easily inducible seizures. The important aspects were:

"Respiratory rate and depth
Blood pressure, heart rate and rhythm
Oxygen saturation
Vomiting, retching
Seizures
Temperature."

Dr C also advised me that if Mr B's spontaneous seizures became frequent or prolonged, diazepam was to be used. If there was a drop in respiratory rate or oxygen saturation or evidence of vomiting/retching, then Mr B was to be intubated and ventilated. Dr C ordered chest and abdominal x-rays to be performed later that day.

Clinical notes record that Dr C recommended intravenous diazepam 5-10mg if fits were prolonged and that Mr B should be monitored closely for respiratory depression.

With regard to elimination, Dr C advised that Tegretol is mainly excreted in the urine and that Mr B's renal function was normal. I note that the guidelines from the NPC state that "following an oral dose of carbamazepine, about 72% is excreted in urine". Dr C also referred to the "treatment guidelines" (from the NPC) which stated, under 'Enhanced Elimination' that "charcoal haemoperfusion has been used … The amounts removed are generally relatively small when compared to the dose taken." Dr C informed me that haemoperfusion is not available at the hospital.

Mr B remained unconscious although his fits lessened in both frequency and duration. His GCS remained at 3. A repeat serum Tegretol was taken at 5.45pm which showed >250µmol/L. Nursing staff contacted Dr D but he did not give any new orders with respect to Mr B's care. There is no record that Dr C was informed about the increased Tegretol level. Dr D saw Mr B at 8.15pm and noted that he had not passed urine since admission. Dr D commenced an intravenous saline drip, and catheterised Mr B.

Mrs A advised me that it was she who informed Dr D that Mr B had not passed urine since his admission.

2 November
Nursing notes record that Mr B's neurological condition was stable until 4am on 2 November 1998 when he began grunting and making moaning noises. He did not appear to be fitting. There was a query whether his left pupil was reacting to light. The notes record that at 5am his pupils were fixed and dilated, his oxygen saturation had dropped to 74 and his breathing was laboured. Nursing staff contacted the on-call house surgeon, who assessed Mr B. The house surgeon recorded that he contacted the medical registrar (Dr D), but he did not give any new orders.

Dr D saw Mr B at 6.30am. His breathing had started to deteriorate and Dr D contacted an anaesthetist, who saw Mr B at 6.45am. The anaesthetist intubated Mr B and commenced him on a ventilator. The clinical records note that on intubation, there were "pink secretions +++".

Dr C advised me that after Mr B was ventilated, he was primarily under the care of Dr E, Director of ICU. Dr E saw Mr B at 9am. Dr E recorded his plan of ventilatory support, inotropic (muscle contraction) support, IV antibiotics, volume support (Pentaspan) and IV diazepam if Mr B was seizing. Dr E's impression of Mr B's condition was of "? pulmonary oedema, ? aspiration pneumonitis, ? early adult respiratory distress syndrome (ARDS)". Dr E also recorded that the last Tegretol level was 223µmol/L. This result was obtained from a blood sample taken at 8.25am. A dopamine infusion was commenced (to correct haemodynamic imbalances associated with shock). Dr E inserted a central venous pressure line at 11.30am to more accurately monitor Mr B's fluid levels.

Dr C examined Mr B at 10am. In light of the drop in Mr B's blood pressure, the copious amounts of pink frothy fluid in Mr B's airways, the widespread diffuse changes on x-ray and the normal white cell count, Dr C suspected Mr B had developed myocardial suppression and pulmonary oedema, rather than aspiration pneumonia. Dr C informed me that he advised urgent echocardiography, which revealed that Mr B's left ventricular function was at the lower limits of normal. This was unusual for a young man with no previous cardiac problems. Dr C prescribed antibiotics.

Nursing notes record that during the afternoon of 2 November, Mr B began to wake up, and that he settled with reassurance. The evening nursing notes record that Mr B was quite settled although he remained unconscious.

3 November
Dr E saw Mr B on the morning of 3 November. He noted that Mr B remained very unresponsive, but that his pupils were smaller and reacting to light. Mr B's lungs were congested with "severe crackles" heard in both lungs. The Tegretol level taken at 8 am that day was recorded at 202µmol/L, which Dr E noted as "still very high but coming down". Dr E's plan for Mr B was to continue ventilation, continue dopamine, commence frusemide (a diuretic) to treat the pulmonary oedema, continue with the prescribed antibiotics and commence nasogastric feeds. Mr B was seen by a dietician and a physiotherapist.

Dr C also saw Mr B. He did not order any further treatment.

4-6 November
Mr B continued to receive care in the ICU and was monitored by Dr E, who recorded on 4 November that everything was improving except Mr B's lungs. He recorded "→ severe ARDS".

Dr C recorded that the plan was to continue with Dr E's management. There is no indication in the notes provided to me, that a serum Tegretol level was taken for Mr B on 4 November.

Dr E recorded on 5 November that Mr B was improving and that the plan was to wean him off the ventilator. His GSC was 4-5. The nasogastric feeds, antibiotics and frusemide were to continue. Mr B's serum Tegretol level taken at 8am on 5 November was recorded as 192µmol/L.

During the afternoon of 5 November, Mr B was recorded as having periods of restlessness. His temperature was elevated. He developed a tachycardia, but by 2am the next morning was recorded as being "much more settled".

On 6 November Dr E decided to transfer Mr B to an ICU at another public hospital. Prior to his transfer an intercostal drain was inserted into Mr B's right lung to drain fluid. Dr C informed me that it was necessary to transfer one of the two ventilated patients from ICU. The Discharge Summary from the hospital stated that Mr B was to be transferred "to [another public hospital] for further management = ventilation". Mr B's serum Tegretol level on 6 November, taken at 8am, was 138µmol/L.

On arrival at ICU at the hospital, Mr B had a chest x-ray which showed diffuse patches throughout his lungs. He was treated for 31 days in the ICU. During that time, there was no real improvement in his lung function. Mr B died at the hospital on 7 December 1998, aged 18 years.

Coroner's inquest
An inquest was held into the death of Mr B. Dr C submitted a statement to the Coroner. He stated:

> "[Mr B] was given supportive care and daily discussions were held regarding his condition. … The treatment he received at [the public hospital] was purely supportive."

The Coroner found that the cause of Mr B's death was pulmonary fibrosis and bronchopneumonia and made no recommendations about the circumstances surrounding his death.

Medications listed by Dr D
Mrs A complained that medications listed on page 7 of Mr B's 'Acute Assessment Discharge form' were incorrect. She alleged that Mr B had been taking risperidone and Aropax only and that he had not taken carbamazepine, haloperidol, Cogentin and lorazepam.

The medical records provided to me are not numbered. However, I note that the 'Medical/Surgical Interdisciplinary Acute Assessment/Discharge Form' lists carbamazepine, haloperidol, Cogentin and lorazepam. The notes were written on 1 November 1998.

Dr D informed me that when Mr B was admitted, the only person he met was Mr B's caregiver, who had started looking after him two days prior to his admission. There was no accompanying documentation indicating what medications Mr B was taking. Dr D read Mr B's old medical notes to confirm his medical status, and to look at the most recent medication list. He informed me that the medications listed in the notes for 1 November 1998 were copied from the medical notes and were not able to be verified or checked during his duty.

Independent advice to Commissioner

The following expert advice was obtained from Dr Sharon Kletchko, an independent emergency medicine specialist:

"ADVICE REQUIRED

To advise the Commissioner whether, in my professional opinion, [Dr C] and [the public hospital] provided [Mr B] with medical services that complied with professional, ethical and other relevant standards.

In particular to answer the following questions:

- What are the specific standards that apply and were they followed?
- Was [Dr C]'s decision not to administer charcoal reasonable in the circumstances?
- Was [Dr C]'s decision not to intubate and ventilate [Mr B] reasonable in the circumstances?
- Was [Dr C]'s decision not to perform a whole bowel irrigation or gastrotomy reasonable in the circumstances?
- Was [Dr C]'s decision not to perform ultra-sound or abdominal x-rays reasonable in the circumstances?
- Was [Dr C]'s treatment of [Mr B] reasonable in the circumstances?
- Are there any other matters you consider relevant in relation to the standard of care provided by [Dr C] or [the hospital]?

EXPERT ADVISOR'S GENERAL COMMENTS

Summary of Events

[Mr B] presented initially to the [public hospital] ED with no available history as to the cause of his 'alteration in mental status'. Ambulance personnel, at 0910 hours, had already confirmed that hypoglycaemia was not involved and that there was a high probability of an overdose or toxic ingestion.

Initial review in the ED at 0920 hours confirmed that [Mr B] had a GCS of 4/15, was breathing spontaneously with a protruding dry tongue, sluggish dilated pupils and brisk reflexes with upgoing plantars. He had an abrasion visible on his left cheek but no other signs of acute trauma. The impression was that the problem was most likely due to an overdose, however there was some concern re: ? intracerebral pathology.

At 1000 hours he was noted to have episodes of agitation and combativeness interspersed with periods of inertia. As well, he was found to be sweating, to be tachycardic and to be ataxic.

However by 1010 hours, a notation in the records indicated that 45+ x 400 mg Tegretol tablets were found to be missing from [Mr B]'s room. The Poisons Centre at […] was contacted and they faxed the 'CARBAMAZEPINE DOCUMENT F105' to [the hospital] ED. A serum carbamazepine level was requested.

By the time [Mr B] was transferred to the ICU, it was determined that he had taken an overdose of 55 x 400 mg carbamazepine totalling 22,000 mg. In the medical registrar's admission note reference to the Poisons Centre advice indicated that there was no known antidote and that activated charcoal was to be administered if the patient was unconscious. It was further noted that side-effects of the overdose included respiratory depression, cardiac suppression, agranulocytosis and seizures. A tegretol level, taken at 0930 hours of 129 µmol/L (normal up to 42), was recorded.

The specified plan, organised by [Dr C], was for 'supportive care' consisting primarily of monitoring [Mr B]'s vital signs. Instructions were provided that if respiratory rate decreased and/or oxygen saturation fell, endotracheal intubation would be considered. In addition if 'prolonged' seizures occurred, staff could consider using iv diazepam 5 mg.

Further instructions requested repeat blood tests for 1600 hours and in the morning, an abdominal flat plate and chest x-ray and the need to withhold all of [Mr B]'s medications. No parameters were defined as to the minimum and maximum acceptable levels for GCS, respiratory rate, blood pressure, oxygen saturation or pulse rate. No standards or policy guidelines were referenced to guide the requested monitoring.

The evening shift nursing note reported that [Mr B] had a GCS of 3/15 throughout the shift noting that the pupillary signs had deteriorated with very little, if any, reaction of the left pupil to light. The nursing note records these findings, along with the fact that

the tegretol level from 1600 was > 250 µmol/L (note this is in excess of the severe toxicity level reported by Montgomery et al of >20 mcg/mL). Discussion was held by the nursing staff with the medical registrar regarding these facts. The nurse recorded that there were 'no further orders (NFO)'. [Dr C] was not notified of the tegretol level.

At 2014 hours the medical registrar who had admitted [Mr B] to hospital, [Dr D], was called by nursing staff as [Mr B] had not passed any urine since admission. As well as corroborating that [Mr B] had indeed not passed any urine, [Dr D] also noted that [Mr B] continued to have repetitive seizures and that the repeat Tegretol level at 1600 hours was high. [Dr D]'s therapeutic intervention at the time was to provide intravenous fluids and undertake fluid balance charting and monitoring. Nursing staff were provided with no other orders. [Dr C] was not notified.

The nursing note subsequent to this indicates that [Mr B] had a urinary catheter inserted and intravenous saline initiated. The recordings noted by nursing staff around this time revealed major fluctuations in blood pressure, heart rate, respiratory rate and oxygen saturation. No mention was made of notifying either [Dr D] or [Dr C] of these fluctuations.

At 0400 hours on 2 November, ICU nursing staff noted that [Mr B]'s condition had markedly declined. He was noted to be GCS 3/15, with an increased respiratory rate to 50 breaths per minute with audible grunting. His left pupil was again noted to be only very slowly reacting to light, if at all.

At 0500 hrs the night duty house officer was called to reassess the patient. The house officer noted that [Mr B]'s repeat oxygen saturation was only 64, that [Mr B]'s temperature was now 38 degrees centigrade and that his pupils were fixed and dilated. The medical registrar was contacted and the nursing staff recorded that no new orders (NNOs) were provided. [Dr C] was not notified.

At 0600 hours, nursing staff recontacted the medical registrar as [Mr B] had visibly deteriorated – no limb movement, pupils fixed and dilated, no response to painful stimuli, tachycardic, hypotensive, hyperthermic, hypoxic and with 'haemo-mucous exudate' suctioned from his mouth.

At 0630 hrs the medical registrar reviewed [Mr B], confirming the nursing observations as to [Mr B]'s physical state, along with recording the presence of bilateral coarse crackles present in both lungs.

The registrar contacted the anaesthetist on-call and [Mr B] proceeded to be intubated. Frothy pink pulmonary oedema-type fluid was found welling up into the endotracheal tube. A provisional diagnosis of acute pulmonary oedema was made and positive pressure ventilation utilising positive end expiratory pressure (PEEP) was initiated. The anaesthetist noted that a CT may be required. [Dr C] was not notified at the time.

[Dr C] reviewed [Mr B] in the morning on a ward round. He indicated that he believed [Mr B] to have '*probable myocardial depression leading to hypotension with*

pulmonary oedema'. [Dr C] felt an echocardiogram was indicated but not a CT. He also recommended coverage with intravenous antibiotics for ?aspiration pneumonitis. The echocardiogram was performed with the Cardiologist noting normal left ventricular function. No CT was performed subsequently. [Dr C] recorded no further note indicating any reassessment was carried out following the negative echocardiogram. While on ventilator support, [Mr B] was under the care of the Intensivist, [Dr E] who initiated an intravenous dopamine infusion for cardiac and renal support.

Subsequent to this, [Mr B]'s condition closely resembled the syndrome of Adult Respiratory Distress (ARDS) a component of the Systemic Inflammatory Response Syndrome (SIRS). [Mr B] also had evidence of acute renal dysfunction and acute hepatic dysfunction.

On November 6, due to fluctuations in his condition with a trend to worsening, [Mr B] was transferred to [another public hospital] where he subsequently deceased.

SUMMARY OF [DR C]'s MANAGEMENT OF [MR B] WITH ANALYSIS BY EXPERT – SUPPORTING INFORMATION 'B'

[Dr C]'s summary, dated November 1999, outlines [Mr B]'s acute presentation to [the public hospital] following an overdose of 22,000 mg sustained release formulation of carbamazepine (CBZ).

[Dr C] outlines his response to what he termed 'a severe tegretol poisoning', that is, diagnosis, decontamination, supportive care, elimination. [Dr C] made no specific reference to 'stabilisation'. As previously included in this report, stabilisation encompasses the ABCs of acute resuscitation, including securing a protected airway, ensuring respiratory stability and monitoring and ensuring circulation stability (see flow diagram [page 41]).

Stabilisation of [Mr B]'s condition was essential as early as his ED attendance given the fact that he had a GCS of 5/15, that he was tachycardic and that he demonstrated peripheral brisk reflexes, upgoing plantars and frequent myoclonic seizures. Clinically he fitted the symptom complex of a severe CBZ intoxication.

[Dr C] proceeds, in his summary dated 19 November 1999 to discuss [Mr B]'s condition, under the following headings:

A. Diagnosis:

He notes that [Mr B] has a 'certain' diagnosis of moderate to severe tegretol toxicity. He further notes that another drug could not be excluded. Even though [Mr B] was found collapsed on the road outside his home and to have a facial graze, no consideration was given to the possibility of a head injury either causing his presentation or contributing to it. [Dr C] negated the recommendation that [Mr B] may require a head CT.

With regard to the Tegretol [Mr B] ingested, [Dr C] does not refer to the type of preparation and does not review the physiological consequences of such a toxic ingestion. No advice from [Dr C] to the medical registrar, [Dr D] was recorded related to the monitoring limits for [Mr B]'s physiological parameters. That is, there was no specified instruction on the minimum or maximum limits that would be tolerated before aggressive management would be instituted for particular vital signs.

[Dr C] provided no guidance on the range of 'stabilisation' goals other than for identification of the toxin as noted above. The 'Goals of Stabilisation', as discussed, must include a consideration of a non-toxicological condition causing or contributing to the patient's presentation.

[Dr C], in his report, makes no mention of the first steps required for 'management of a poisoned patient' namely Airway, Breathing, Circulation, Drugs. This is important from the perspective that at no time in the early course of [Mr B]'s presentation was there any reference as to his ability to protect his airway. There is a note that he was 'spontaneously ventilating' and of within normal oxygen saturation limits. However, there was no discussion of the depth, type or degree of the 'spontaneous ventilation'.

From the Circulation perspective, there is no recorded assessment of peripheral perfusion, pulse pressure or any description of neck vein fullness/waves. All of these are components of 'perfusion' and circulation.

From the drugs perspective – [Dr D], in his admission note, related that there was no antidote available for a carbamazepine poisoning. He noted that [Dr C] had provided some guidance regarding the judicious use of iv diazepam for control of seizure activity. However, as has been discussed, if diazepam is not effective, the next option should be phenobarbitone. [Dr C] did not provide medical or nursing staff with guidance as to what to do if Diazepam failed to control seizures, during [Mr B]'s admission. At a minimum, it is expected that he would request to be called in this event.

B. Decontamination:

[Dr C], in this section of his report, discusses types of decontamination procedures including lavage and activated charcoal instillation indicated for major intoxications. He notes that he did not advise lavage due to the lack of knowledge regarding the timing of the overdose. However, as has been discussed, in cases of suspected severe ingestion of CBZ, lavage is indicated in order to attempt to reduce the total alimentary dose no matter when the overdose was taken. As noted, CBZ has anticholinergic properties that markedly slow bowel movement and transit, an effect which would keep the medication in the stomach and upper duodenum/jejunum for a prolonged period of time.

[Dr C] discusses activated charcoal as recommended by the Poisons Centre's Guidelines. He notes that it was his opinion on the day, that the administration of activated charcoal would cause more harm than benefit to [Mr B]. He then goes on to outline the reasons for his opinion; that is, the efficacy of the procedure – citing a decreased benefit as the duration of time from ingestion of the Tegretol increases. This is not compatible, however, with the known consequences of Tegretol toxic ingestion as previously discussed. Additionally, multiple dose activated charcoal has been shown to be very effective in assisting with the reduction in absorption of Tegretol following toxic ingestion. [Dr C] makes no mention of this strategy. [Dr C] appears to have assumed the less aggressive course of action as being the most appropriate despite the fact that he acknowledges the severity of the toxicity, the fact that he is unaware of the type of tablet (i.e. sustained release formulation), that he did not know when the ingestion occurred and that he was uncertain regarding the involvement of other drugs or conditions.

[Dr C], in paragraph (ii) of his report suggests that if he had administered charcoal, it would have required him to '*protect the airway with an endotracheal tube*'. This statement may be interpreted to imply that [Mr B] did not have a secure airway. [Dr C] attempts to justify not securing the airway by noting that 'seizure' activity could be precipitated by having an ET tube in situ and that this would have required him to provide heavy sedation to [Mr B]. Even in retrospect, this statement is difficult to support as we know [Mr B] continued to have seizure activity despite the liberal use of iv diazepam and that he presented at 0400 hours on 2 November with acute respiratory failure accompanied by a lack of ability to protect his airway.

In point (iii) of his report, [Dr C] indicates that he considered there was no other indication for artificial ventilation. As has been discussed this is not so. As noted in the preceding report, the presence of a low Glasgow Coma Score (<7/15) is enough of a reason for securing the airway, let alone the need to proceed with decontamination procedures.

Under point (iv) of his report, [Dr C] indicates that the 'availability' of a ventilator for [Mr B] if intubated, was unlikely due to the fact that there was already a patient on a ventilator. As has been discussed, if treatments or therapeutic support options including expertise are not available at one site the managing doctor is required to consider the transfer of the patient to an alternative site where the treatments are available. It is not acceptable to withhold a treatment based on the unavailability of the therapy at a particular site.

In point (v) of this report, [Dr C] indicates that the 'likelihood' of [Mr B] developing any further indication for artificial ventilation was, in his opinion, 'uncertain'. Again, the fact that [Mr B] had taken a severe overdose of CBZ, that he had a GCS of between 5-3/15, that he required at a minimum both gastric lavage and activated charcoal and more probably, multiple dose activated charcoal and instillation of cathartics, constituted more than adequate reasons for securing [Mr B]'s airway by endotracheal intubation. Having an endotracheal tube in place, also

does not automatically imply pressure support ventilation is required. However, in [Mr B]'s case the ability to manage his seizure disturbance through the use of iv barbiturate infusion would have required artificial ventilation to be instituted.

C. Supportive Care:

[Dr C] outlines the need for vital signs and symptom management for [Mr B] in this paragraph of his report. However, as mentioned previously, no record has been made of any guidance provided to medical and nursing personnel from this perspective. That is there are no specified limits within which [Mr B]'s vital signs could be said to be stable and outside of which [Dr C] would have expected to have been notified.

For example, it was noted by [Dr D] that [Mr B] should be reviewed for respiratory depression and cardiovascular depression. However, at 0400 hours when [Mr B]'s situation was deteriorating, nurses made note of wide fluctuations in all of his monitored vital signs. Given that there was no explicit request for medical staff to be notified if saturations, for example, dropped below 90% or his respiratory rate dropped below 10 breaths per minute etc., requests by nursing staff to medical staff met with comments of NFO (no further orders). This type of 'implicit' monitoring of signs with no guidance as to requirements if the signs are not met, does not meet the recommended standard of care for a severely poisoned patient.

It is not good enough to state if there is a 'drop' in respiratory rate or oxygen saturation, then the patient is to be intubated. What constitutes a 'drop'? Also, according to the medical notes the term was for '?consider intubation' – there was no definitive recommendation provided by [Dr C].

D. Elimination:

[Dr C] begins this section of his report with the statement that 'Tegretol is largely excreted in the urine'. This is incorrect. As previously mentioned Tegretol is a highly protein-bound compound and therefore, physiologically urinary excretion is minimal. Renal excretion accounts for only 1% to 3% of its total elimination and only 3% of the elimination of its active epoxide metabolite (CBZO).

Tegretol is metabolised primarily by the liver and hepatic metabolism is the major route of elimination of its active epoxide metabolite (CBZO). Hepatic metabolism is also the major route of elimination resulting in the production of the active metabolite CBZO. How well this is done by the liver, is dependent on the chronicity of the tegretol prescription and the development of enzyme pathways within the liver to more rapidly metabolise the drug. Because chronic therapy of CBZ results in the 'autoinduction' of hepatic metabolic enzymes, there is a high intrinsic clearance for CBZ. We know, from [Mr B]'s history, that the CBZ had only recently been started, therefore the likelihood of more rapid metabolism of CBZ was much less than if he had been on the drug for many months.

[Dr C] next discusses the Poisons Centre's Guideline regarding Haemoperfusion. Again, the important issue is that the lack of availability of this technique at any particular institution is not sufficient reason to discount the prescription of the treatment.

The Poisons Centre guideline as well as others reported in this paper support the institution of charcoal haemoperfusion for a CBZ poisoning of this magnitude. This is particularly so, as [Mr B]'s Tegretol level had continued to increase within 20 hours post ingestion and he continued to seize, remained comatose and, in fact, was deteriorating. Even if haemoperfusion had not been considered prior to 0600 hours on 2 November as an option, [Mr B]'s acute deterioration that morning should have led to his referral to a specialist centre, airway, breathing and circulation stabilisation and rapid transfer to a facility that could provide for haemoperfusion treatment.

E. Progress:

[Dr C] begins this paragraph of his report with the statement '*I did not hear about, or see, the patient until the next morning*'. This is true. However, there is no explicit record that he provided the medical or nursing staff with the information upon which they could make rationale judgements as to when it was appropriate or necessary to call him.

All of this 'instruction' is at the best 'implied' and at the least, not specified. Standards of care required for patients who are at considerable risk require the doctor in charge of the patient to demonstrate an 'active duty of care' towards the wellbeing of their patient. An essential component of this duty of care is the necessity to ensure that the patient's condition is well monitored and controlled within stated specific parameters and that clinical colleagues and nursing staff are aware of these parameters. It also requires the doctor in charge or his designate, to be rapidly available for consultation if and when required.

At no time, in any of the documentation, are any existing standards of care policies sited. If these policies are in place, then there is still a requirement for the managing doctor to specify the policy to be adopted and any parameters of care required for specific patients.

SPECIFIC ADVICE REQUIRED BY THE COMMISSIONER'S OFFICE

To advise the Commissioner whether, in my professional opinion, [Dr C] and [the public hospital] provided [Mr B] with medical services that complied with professional, ethical and other relevant standards.

In particular to answer the following questions:

1. What are the specific standards that apply and were they followed?

This paper outlines the specific standards (guidelines, poisoning algorithms and standards, specific requirements for carbamazepine toxic overdose management) that apply to the acute admission of [Mr B] on 1 November 1998. Additionally, throughout the report, discussion has been developed regarding the standards required to ensure that ongoing monitoring of any patient must be performed through the institution of standing orders in existing policies and standards, as well as the 'explicit' parameters within which the individual patient can be considered to remain 'stable'. The specific standards that have been recorded in this report were followed to a point but, in my opinion, did not reach the standard of care required. [Dr C] frequently, in his summary, indicates that it was his individual opinion as to the interpretation of the problem and the care that was provided. However, at no time, other than the initial contact with the Poisons Centre, did he or any of his medical delegates either ask for or seek further expert opinion despite the fact that [Mr B] continued to deteriorate. It is my opinion, that he should have sought such help at least on the morning of November 2 1998 following [Mr B]'s acute deterioration.

2. Was [Dr C]'s decision not to administer charcoal reasonable in the circumstances?

   This question has been responded to under the section dealing with [Dr C]'s summary of [Mr B]'s management. It is my opinion that he was obligated to administer activated charcoal in this instance. It is further my opinion, that he was obligated to secure [Mr B]'s airway through endotracheal intubation in order to undertake nasogastric activated charcoal instillation. It is also my opinion, that a quick literature search along with more expert consultation would have provided [Dr C] with the knowledge that multiple-dose activated charcoal along with intermittent instillation of cathartics was indicated.

3. Was [Dr C]'s decision not to intubate and ventilate [Mr B] reasonable in the circumstances?

   This question has been substantially responded to in the section reviewing [Dr C]'s summary. It is my opinion, that [Mr B] should have had his airway secured through endotracheal intubation in the Emergency Department. At that time, he had been noted to have a GCS between 3-5/15 and was known to have taken a severe overdose of CBZ. [Dr C]'s reluctance to request this treatment, even when asked by [Dr D] cannot be considered an appropriate response. Also, it is extremely inappropriate and below the standard of expected care to make such a decision based on the knowledge that [the hospital] could not support two ventilated patients at this time. According to the algorithm included in this report, [Dr C] should have requested transfer of [Mr B] to a facility capable of delivering the appropriate therapy.

4. Was [Dr C]'s decision not to perform a whole bowel irrigation or gastrotomy reasonable in the circumstances?

Whole bowel irrigation is a very difficult procedure with no evidence of efficacy over the standard therapies of multiple-activated charcoal instillation and intermittent cathartic instillation. It has been proven to be effective in patients who have taken organophosphate insecticide overdoses in order to rapidly eliminate the compound which is very toxic to bowel mucosa. CBZ is not toxic to bowel mucosa and is capable of being bound to activated charcoal and eliminated in this less aggressive way. With regard to gastrotomy, the flat-plate of the abdomen failed to reveal any evidence of a tablet bezoar. Again, these are extraordinary options not indicated over the standard therapies discussed in this report. There is no indication that [Dr C] at any time considered using these therapies – in my opinion, his lack of consideration of these therapies was reasonable.

5. Was [Dr C]'s decision not to perform ultra-sound or abdominal x-rays reasonable in the circumstances?

   [Dr C] requested an abdominal x-ray as well as chest x-ray on admission to the ICU. Abdominal ultrasound would not have contributed significantly more information.

6. Was [Dr C]'s treatment of [Mr B] reasonable in the cir cumstances?

   In my opinion, [Dr C]'s treatment of [Mr B] failed to meet the standards of care required by a Specialist Physician. The reasons for this statement have been developed throughout this report.

7. Are there any other matters you consider relevant in relation to the standard of care provided by [Dr C] or [the hospital]?

   It should be understood by everyone involved with acute illness and/or injury presentations, that the management of any patient presenting with:

   - an altered mental status or coma,
   - potential / probable severe substance or drug intoxication and
   - major physiological symptoms (seizures, tachycardia, respiratory depression)

   requires teamwork, expertise, consultation and the most appropriate provider capable of delivering the expected range of care required.

   Policies, standards, guidelines, algorithms and access to the most appropriate expert advice must be rapidly and easily available to assist health care personnel in performing their obligations and their required duty of care to individual patients in the best and most appropriate way. Doctors not experienced or particularly knowledgeable in managing the extremes of severity of major overdoses and intoxications, should be required to ask for advice or assistance so that patients can receive the most appropriate care in the safest and most effective way.

> From reading through this file, it is obvious that decisions regarding [Mr B]'s care were made with inadequate expertise, lack of available information on probabilities and using assumptions that were not grounded in fact. It is difficult to state whether, if everything that could have been done for [Mr B] had been done, if it would have prevented his death. In this regard, it is my opinion, that by diligently and forthrightly managing [Mr B] according to the evidence and the guidelines developed by overseas and local experts, it is more likely that his survival could have been optimised."

Dr Kletchko subsequently provided the following clarificatory advice:

> "Thank you for requesting some further clarification regarding my report to you dated January 2000.
>
> Specifically you have asked about the basis upon which I concluded that an abdominal x-ray was carried out that failed to reveal evidence of a tablet bezoar.
>
> In my report, … under question 4, I noted the following: '… With regard to gastrotomy, the flat-plate of the abdomen failed to reveal any evidence of a tablet bezoar.' I have re-read the documentation as originally provided and agree that the abdominal flat plate that was requested was never in fact performed. In re-reading the context of question 4, it is my impression/conclusion that I meant to comment that evidence (as provided in the extensive review in the report) suggests that a tablet bezoar would not show up on a flat plate of the abdomen, as Tegretol tablets are not radio-opaque. My wording in this regard was clumsy and led to an inaccurate assumption that an x-ray not showing a bezoar had been performed. My apologies.
>
> Your further request 'what further action, if any, should have been taken when [Mr B]'s Tegretol levels exceeded 250 on 1 November 1998?' As recommended in my report [Mr B] should have had his airway secured and be placed on artificial ventilatory support. He should have had instillation of activated charcoal through a nasogastric tube and have this repeated at a minimum of 4 hourly. Finally, he should have been transferred to a tertiary facility that could have provided the extracorporeal treatment of charcoal haemoperfusion. This treatment would have removed the Tegretol from his system and allowed him to systemically stabilise. I am still very much of the opinion that a high bowel washout and/or gastrotomy was not indicated. Charcoal haemoperfusion would have been the best and least complicated therapeutic option.
>
> Lastly you request some opinion regarding the frequency of serum Tegretol measurements. It is my firm opinion that [Mr B] should have been transferred for urgent haemoperfusion on November 1, 1998 and that this treatment would have removed any need for monitoring of levels of drug over the following days other than to ensure the clinical staff caring for [Mr B] that the active drug had been removed in significant amounts."

Dr Kletchko was asked to comment on the hospital's protocol 'Care of the Unconscious Patient' and advised:

"[You] request:

1. Whether the 'Care of the Unconscious Patient' protocol provided by [Ms F] is reasonable given the circumstances of [Mr B]?

2. Whether the 'Guideline for Assessment and Management of the Poisoned Patient' [in] my original advice dated January 2000 [page 42] and the algorithm on page [50] are in place in [the hospital] and whether they represent reasonable or 'gold' standards of care?

In response to Question 1, the submitted protocol from [Ms F] is a sound nursing management protocol for the unconscious patient. It is not a guideline for medical decision-making for management of the unconscious patient however. It does not provide any direction on when and by what means and for how long care may be required for an unconscious patient. As such it is insufficient guidance for clinical staff who lack the background competencies to manage patients who are unconscious for whatever reason.

In response to Question 2, management of the poisoned patient and the unconscious patient are part of the current available guidelines in [the hospital]. The issue here is guidance on management of patients to ensure appropriate supportive care for their problem until it either improves naturally or is resolved therapeutically. This has always been implicit in care at [the hospital] and explicit since a formal guideline on the ABCs of Trauma was approved by the clinical Board back in the mid-1990s. [The hospital] ED has a guideline manual that contains both the flow outlines found in my original advice. I consider both of these to represent sound, usual and reasonable standards of care. In fact, these standards of care have been the norm in many hospitals around New Zealand since the mid-1980s. [Another public hospital] ICU operated under precisely these guidelines during my employment there as a[n] Intensive Care Specialist."

The remainder of Dr Kletchko's comments are attached as Appendix II.

Response to Provisional Opinion

Dr C responded to my provisional opinion as follows:

"I agree with you, particularly with hindsight, that I put the patient at a disadvantage by not administering activated charcoal immediately on his admission to ICU. Consequently it is very appropriate for me to tender an apology to [Mrs A]. I also do not have any concerns about the Medical Council reviewing my competence.

However I do not at all agree with several conclusions made by your independent advisor Dr Sharon Kletchko. Given that these erroneous conclusions are a result of poor documentation in the patient's clinical notes I appreciate this opportunity of putting

the record straight by providing details which should have but were not recorded by the junior staff and further by detailing my reasoning and plan of action which seems not to have been completely comprehended.

I agree with Dr Kletchko I did not make any reference to 'stabilisation', 'the ABC of acute resuscitation'. The ABC of acute resuscitation is performed immediately on the patient's presentation and NOT one hour later. The patient had already been through the A&E Department where he had been stabilised. He had a pulse rate of 104/min, BP 137/65, normal breathing, oxygen saturation of 96% and although his GCS was recorded as 4/15 he was agitated and combative, attempting to get out of bed. It is totally incorrect to say that I was 'asked by [Dr D] for endotracheal intubation to protect the patient's airway on the basis of severe Tegretol poisoning. The '? Intubate' in A&E refers to sedating and intubating this combative patient so that a CT head scan could be performed to rule out head injury. The patient was certainly past the stage of stabilisation and was ready to move onto the next stage of management. I saw him soon after his admission to ICU.

She will have noted that there is no mention in the notes of the physical signs elicited by me. (It is usually the junior staff, who take down the notes as the consultant conducts the examination etc). I therefore cannot entirely blame her for making the assumption that I did not conduct an adequate examination. As always I performed a thorough enough evaluation to answer all those questions that needed to be answered. The patient was cardiovascularly stable, yes his respirations were normal in rate, depth and rhythm, he had a cough reflex, his JVP was normal, he disliked interference readily withdrawing his limbs when examined, he opened his eyes on minimal stimulation, almost spontaneously, his pupils were dilated but reacted to light, his planters were up-going without clonus and there was no evidence of significant injury. I was fairly confident that the neurological picture was not that of structural brain injury (hence CT not considered essential), but of diffuse brain pathology consistent with tegretol poisoning. Even in retrospect, the only error in my assessment was accepting the Registrar's information that the patient had been on long-term tegretol therapy prior to the overdose 4-15 hours ago. (I felt it was more likely to be 15 hours because apparently the caregivers were out that evening which would have given [Mr B] the best opportunity and he could still have been looking well between 9-10pm before going to bed. Whether it was a slow-release formulation or not was not known at that point).

It is not true that 'no consideration was given to the possibility of a head injury'.

My initial management decisions were made on the above background only and not on subsequent developments. It is also to be remembered that I took into serious consideration the fact that he was not having true seizures but opisthotonic reactions, which were easily induced by interference, particularly when he resisted, and abated significantly when the patient was not disturbed. The NPC document states that 'dystonias can be treated supportively'.

The two possible courses the patient was expected to take were:

a) steadily improve – which was not an unreasonable expectation given that his GCS was better than it was reported to have been earlier and I felt he had probably taken the overdose the previous evening; **or**

b) steadily deteriorate.

If he were to take the first course then the process of administering charcoal (not the charcoal itself) would have been to his disadvantage for the various reasons given in my previous report. (He did get a pneumothorax with ventilation!). When I explained that an ET tube would precipitate more opisthotonic episodes and necessitate heavy sedation leading to a need for continued airway protection, Dr Kletchko somehow interpreted this 'to imply that [Mr B] did not have a secure airway' which is not a valid conclusion. (As one could deduce from the clinical picture, the GCS was at least 7 if not higher). And I did not say that 'the availability of a ventilator for [Mr B] was unlikely'. It was just that the ICU was not staffed to manage two ventilated patients at once except for short periods. (This is the reason why [Mr B] had to be transferred to [another public hospital] eventually.)

In summary the decision to not ventilate (and hence omit charcoal) was not based on any one single but a composite of reasons AND on the significant possibility on very valid grounds that the patient would follow course a.

If the patient followed the second course then at some point he would certainly need airway protection and ventilation hence the reason for the instruction to the staff for close monitoring. The idea was not to wait until 'eg saturation dropped below 90% or respiratory rate dropped below 10 breaths' as suggested by Dr Kletchko but as soon as the downward trend was recognised. For the duration that I was with the patient (along with the Registrar and Nurse) the oxygen saturation was 96-99% and respiratory rate 15-20/min). Any level persistently below these was adequate indication that there was a change in the status. Other variables to be monitored were listed as mentioned in my previous report.

I have to totally disagree with Dr Kletchko that my instructions to the staff were 'at the best implied'. I have always been in the habit of giving very clear instructions and confirming that those concerned are clear about the plans. The staff nurse caring for the patient and the Registrar on call were present and there was not going to be a change in the Registrar on call that day. True I did not provide the staff with further options if Diazepam failed to satisfactorily control the 'seizures'. I considered that it would be more appropriate for me to re-assess the patient myself at this point than for the junior staff to intensify therapy according to a management plan formulated on the initial evaluation. I expected to be consulted if there were any concerns at all and the staff were aware of that.

In summary, intubation and ventilation (and hence charcoal administration) was never totally excluded when the management plan was first formulated. The process put in place was intended to identify at the earliest any indication for intubation or other intervention.

Dr Kletchko disagrees that 'Tegretol is largely excreted in the urine' even though this is what the NPC document states.

Also, I did not discount haemoperfusion because of its lack of availability at [the hospital]. The Guidelines certainly do not suggest that this procedure be performed in the initial stages of admission. It states 'it may be indicated in cases of failure or slow response to supportive care'.

I also do not agree that there was a need for 'a quick literature search along with more expert consultation' **at that stage**. I already had the management guideline, which was perfectly adequate and very helpful in all aspects except for putting me in a slight dilemma of treating the dystonias supportively vs increasing them by attempting to administer charcoal and then having to use more medications to control the same. One could speculate that consultation may have prompted me to choose the other option.

Up to this point I had deviated from the management Guidelines only in that I had opted not to administer charcoal, a decision I made in good faith and one I felt was justified at that stage of [Mr B]'s illness. However Dr Kletchko's report gives a totally different picture, one that suggests that my performance was very sub-standard with almost every aspect of [Mr B]'s management. I totally disagree with that assessment. The report seems to lack objectivity. It is a result of lack of evidence, which is not her fault, and the fact that whatever evidence is available has not always been used to the best advantage. For example:

a) [Mr B] was managed primarily by the ICU Consultant from early morning of 2nd November but Dr Kletchko continues to hold me responsible;
b) He was agitated and combative and got out of bed when his GCS was recorded as 4/15 suggesting that there may have been some discrepancy in actual vs assessed GCS;
c) An abdominal xray was not performed despite clear documentation, indicating that it was not necessarily unclear instructions from the consultant;
d) Repeat blood tests were performed much later than was planned and documented;
e) There was a significant delay from the time of significant drop in saturation to the time he was intubated, which could not have been because of unclear guidance from the consultant.

Although, once intubated and ventilated [Mr B] was under the care of the Director of ICU who thereafter was the primary Specialist managing his care, I visited him on a daily basis. I had already made one error of judgement and I preferred the Director of ICU had full control over the patient's management. However I was there to give a helping hand. I also evaluated my assessment and management retrospectively. The following are some points:

a) [Mr B] had had Acute Pulmonary Oedema. It was either Cardiogenic or Non-Cardiogenic both of which are described in severe tegretol poisoning. My contribution was to arrange echocardiography. This showed the function to be at the lower limits of normal while he was receiving inotropes (I would have

expected a young healthy male to have a much better left ventricular function even without inotropes) thus not quite able to differentiate between the two possibilities. The clinical picture was certainly not that of typical aspiration pneumonia. Whether or not this event could have been prevented by airway protection earlier was difficult to speculate.

b) By now we knew that it was the slow release formulation of tegretol that [Mr B] had taken. This coupled with the fact that serum level peaked in the evening did lend support to my suspicion that he had ingested the tablets the previous evening.

c) Such severe tegretol poisoning is rare even in medical literature. It would be difficult to say whether medicating such a toxic patient would have conferred any advantage. In other words would a single dose of charcoal at 11 am have made adequate impact on his peak levels to offset the ill-effects of such medications?

d) Maybe I should have asked the Registrar to give me an update at regular intervals or perhaps phoned in myself. (That is the practice I have adopted since.)

My management plan did not produce a favourable outcome and I realise that I have to be held accountable even though some of the factors leading to its failure were not totally under my control. The nature of a Consultant's job is such that one has to occasionally be able to 'switch from automatic to manual' and deviate from a protocol for good reasons, but with the knowledge that if there is adverse outcome then there may be no defence.

I intended getting [Mr B]'s case discussed at one of the Department of Medicine Clinical Meetings but it became the subject of the Coroner's and then HDC's inquiry and I was unable to do so. However as a direct result of my experience with this case I have become very particular with the standard of documentation by junior staff on the ward rounds and more so about feedback to and consultation with the Consultants. I also presented proposals to the Department of Medicine to conduct regular Mortality Audit Meetings and after three unsuccessful attempts I imposed such a regular audit meeting only after I became the HOD last year. (I have also made it compulsory for each of the seven Medical Registrars to conduct any audit of their choice.)

I owe an apology to [Mrs A] and I await your final report before that. As regards the Medical Council reviewing my competence I am confident no deficiencies will be identified."

Code of Health and Disability Services Consumers' Rights

The following Rights in the Code of Health and Disability Services Consumers' Rights are applicable to this complaint:

RIGHT 4
Right to Services of an Appropriate Standard

1) Every consumer has the right to have services provided with reasonable care and skill.

Opinion: Breach – Dr C

Right 4(1)

Right 4(1) of the Code of Health and Disability Services Consumers' Rights (the Code) states that every consumer has the right to services provided with reasonable care and skill. For Mr B, this means that the treatment he received for his Tegretol overdose should have been appropriate. No action or inaction on the part of any provider involved in Mr B's care should have put him at further risk. In my opinion, the treatment provided to Mr B was inadequate and exposed him to further risk from the Tegretol poisoning.

Charcoal was not administered
Mrs A alleged that charcoal should have been administered to Mr B following his overdose of Tegretol. She informed me that, in her opinion, "Mr B would still be alive today had charcoal been administered, had he been intubated, and had lavage been administered in a timely manner." Mrs A referred to the recommendation of the NPC which stated, at page 10 of the document faxed to the hospital on 1 November 1998: "Activated Charcoal: Single dose activated charcoal is the recommended gastrointestinal decontamination procedure." Mrs A also referred me, in her letter of complaint, to *Martindale's Pharmacopoeia* and the *New Ethicals Compendium*. Both of these documents refer to the administration of activated charcoal when treating Tegretol overdose.

Dr C advised me that he was not ignorant of the fact that activated charcoal was recommended for the management of Tegretol overdose. However, he considered that in the circumstances, administering activated charcoal would cause Mr B more harm than good. He referred to the efficacy of activated charcoal decreasing as the duration from the time of ingestion of Tegretol increases. Dr C was unsure of the time of the overdose and was therefore uncertain of the benefit of administering charcoal. He also took into account the need to protect Mr B's airway with an endotracheal tube. Because of the ease with which seizure activity could be precipitated, Dr C was strongly of the view that the placement of an endotracheal tube would greatly increase the seizure activity. If Mr B had been intubated he would have required heavy sedation, which would have resulted in respiratory depression. In addition, Mr B would have required ventilating. Dr C stated that administering activated charcoal therefore meant artificial ventilation, and there was no

other indication for artificial ventilation at that time. Dr C considered that there was no reason to be certain that Mr B would eventually develop an indication for artificial ventilation.

It is clear that Mr B had taken an overdose of Tegretol and required treatment for his overdose. His blood test taken at 9.30am on 1 November showed a serum Tegretol level of 129µmol/L. The NPC guidelines clearly state that activated charcoal is the recommended decontamination procedure. The guidelines also state that nasogastric intubation should be used for comatose adults.

My medical advisor is critical of the care provided by Dr C. She advised that Dr C appeared to have assumed that a less aggressive course of action was the most appropriate, despite the fact that he acknowledged the severity of the toxicity, that he was unaware of the type of tablet (ie, whether the tablet was a sustained/slow release formulation), that he did not know when the ingestion occurred and that he was uncertain regarding the involvement of other drugs or conditions. My advisor stated that, in her opinion, Dr C "was obligated to administer activated charcoal in this instance".

My advisor expanded upon her opinion. She stated that Dr C did not review the physiological consequences of the Tegretol ingestion. She commented that Dr C's decision not to administer charcoal, as it would cause more harm than good to Mr B, was incompatible with the known consequences of Tegretol toxic ingestion. She stated that multiple dose activated charcoal has been shown to be very effective in assisting with the reduction in absorption of Tegretol following toxic ingestion. In my advisor's view Dr C did not reach the standard of care required.

Dr C did give consideration to the administration of charcoal. However, the conclusion he reached was wrong. I am satisfied, on the information provided to me by the NPC and by my expert advisor, that administering activated charcoal was appropriate in the circumstances. It is my advisor's view that Dr C was obliged to secure Mr B's airway in order to undertake nasogastric activated charcoal administration. As my advisor commented, Dr C was uncertain of the time of ingestion of the Tegretol. Accordingly, while the initial result of Tegretol was high (129µmol/L), Dr C had no way of knowing whether the Tegretol level would increase even further. His concerns about Mr B's airway, although they may have been well founded, did not mean that charcoal could not be administered. Steps should have been taken to firmly secure Mr B's airway, and then activated charcoal should have been administered.

I note that my advisor has referred to a number of sources in medical literature in her report. I acknowledge that some of those sources may not have been available to Dr C. However, he did have the recommendations of the NPC available to him, and he decided not to follow them. In this respect, Dr C's actions were unreasonable. While following some of the recommendations (not to administer lavage), Dr C did not follow the prescribed recommendation of administering charcoal.

Dr C advised me, in response to my provisional opinion, that he "deviated" from the NPC guidelines "only in that [he] had opted not to administer charcoal" and that it was a decision

he made in "good faith". Dr C also acknowledged to me that his "management plan did not produce a favourable outcome".

I note Dr C's comment that his decision was made in good faith. Nonetheless, his decision was not a reasonable clinical response in the circumstances. Accordingly, in my opinion, Dr C breached Right 4(1) of the Code.

Intubation not performed

Mrs A complained that Mr B was not intubated until 6.45am on 2 November, despite his oxygen saturation dropping to 74% at 5.00am. She referred to the aspiration of gastric contents as a major danger of Tegretol overdose and has questioned why her son was not intubated to protect him against aspiration, particularly as he was unconscious.

I note that Dr C was not informed about the drop in Mr B's oxygen levels, and that the decision to intubate Mr B at 6.45am was made by other doctors involved in Mr B's case. However, it was Dr C's decision not to intubate Mr B when he was admitted to hospital on 1 November.

Dr C stated that Mr B was not vomiting or retching when he was admitted and that his respiratory rate and depth were normal. He did not consider intubation at the time of Mr B's admission to be appropriate as insertion of an endotracheal tube could have precipitated seizure activity. Also, in Dr C's view, there was "no reason to be certain that Mr B would develop an indication for early ventilation".

My advisor commented on the decision by Dr C not to administer charcoal. As explained above, I accept my expert advice that charcoal should have been administered, and that an endotracheal tube should have been inserted at an early stage to protect Mr B's airway. This would have allowed charcoal to be safely administered. Mrs A referred to the need to protect against aspiration. In my expert advisor's opinion, intubation should have been performed in the emergency department because of Mr B's unconscious state and his GCS of 3.

Dr C stated, in response to my provisional opinion, that he "took into serious consideration the fact that [Mr B] was not having the seizures but opisthotonic reactions, which were easily induced by interference, particularly when he resisted, and abated significantly when the patient was not disturbed. The NPC document states that "dystonias can be treated supportively."

I note Dr C's further comments about the effects of intubation. I am not persuaded, however, to alter my opinion. Mr B had taken a significant overdose. Even though there was a risk, in Dr C's mind, of inducing opisthotonic reactions by intubation, Mr B still required treatment for his Tegretol overdose.

I am satisfied that Dr C's decision not to insert an endotracheal tube at an early stage was inappropriate. In my opinion, Dr C did not provide medical services of an appropriate standard and breached Right 4(1) of the Code.

Opinion: No breach – Dr C

Reference to "supportive care" in ICU plan
Mrs A queried the decision to pursue "supportive care" when active intervention may have saved Mr B's life. The clinical notes for 1 November record the plan for "supportive care".

Dr C informed the Coroner that Mr B was "given supportive care" and that "the treatment he received at [the public hospital] was purely supportive".

Dr C's clinical decision not to administer charcoal was one that was made after consideration of all of the factors affecting Mr B's condition at the time. Dr C's conclusion was that charcoal was not appropriate. While that decision was wrong, in my opinion, that does not mean that Dr C did not actively treat Mr B. Dr C's management plan for Mr B included a "supportive" element, which was to support Mr B's unconscious state.

Dr C's orders were that Mr B was to be carefully monitored. His blood pressure, pulse, respiratory rate, oxygen saturation and temperature were to be regularly taken and reviewed. Seizures were to be treated with diazepam if they became frequent or prolonged. In addition, Mr B was to be intubated and ventilated if there was a drop in respiratory rate or oxygen saturation, or evidence of vomiting or retching.

There is a distinction between "supportive care" for a patient in ICU and palliative care to ease the suffering of a dying patient. I am satisfied that Mr B continued to receive appropriate treatment and not simply palliative care when he was in ICU. In my opinion Dr C did not breach the Code in relation to this matter.

High bowel washout or gastrotomy not performed
The notes from the Emergency Department record that Mr B had taken 45 x 400mg Tegretol tablets. However, consultation with Mr B's caregiver established that 55 x 400mg Tegretol tablets had been taken. I note Mr B's clinical records for 2 November state "check whether was on slow release Carbamazepine". It is not clear what action, if any, was taken to establish this, or whether questions were asked of Mr B's caregiver about this.

In his response to my provisional opinion, Dr C advised me that by the time Mr B was in ICU, clinical staff knew that the Tegretol tablets were slow release.

Dr C advised that he did not consider lavage (stomach washout) was appropriate. He referred to the treatment guidelines as stating that lavage is not generally recommended unless a patient presents obtunded within one hour of ingestion.

My advisor commented that whole bowel irrigation is a difficult procedure and that there is no evidence of efficacy, particularly when compared with standard therapy of administering multiple-activated charcoal installation. She also stated that whole bowel irrigation and gastrotomy are "extraordinary options" and are not indicated over standard therapies. Even when Mr B's Tegretol level rose to >250µmol/L, a high bowel washout and/or gastrotomy was not indicated.

I have reviewed the information provided by Mrs A, which refers to a number of different treatments for Tegretol overdose. I am satisfied, however, after considering all of the information submitted to me, and my expert advice, that Dr C's decision not to perform a high bowel washout or gastrotomy was reasonable. Accordingly, Dr C did not breach the Code in relation to this matter.

X-ray or ultrasound not performed
Mrs A stated that tests should have been performed to ascertain whether a pharmacobezoar (a mass of ingested material within the stomach that would not pass into the intestine) had formed.

Dr C did order a chest and abdominal x-ray. The chest x-ray was performed, via portable x-ray, on 1 November. The results were normal. Dr C advised that the abdominal x-ray was not performed for reasons that are unclear. Dr C did state, however, that the chest x-ray included a significant proportion of the abdomen which showed the entire outline of Mr B's stomach. It was gas filled and no pharmacobezoar was present.

My advisor commented that Tegretol tablets are not radio-opaque and that it is unlikely a "tablet bezoar" would show up on x-ray. She also advised that an abdominal ultrasound would not have contributed significantly more information.

Having considered the matter, I am satisfied that Dr C did not breach the Code in relation to this matter. He ordered an abdominal x-ray which, for some unexplained reason, was not performed. However, in light of the comments of my advisor, I am satisfied that the failure to take an abdominal x-ray and an ultrasound did not adversely affect Mr B.

Recording of Tegretol levels
From a review of the documents provided to me, Mr B's Tegretol levels were taken twice on the day of his admission to hospital (1 November), once on the morning of 2 November, once on the morning of 3 November, once on the morning of 5 November and again on the morning of 6 November, prior to his transfer to another public hospital.

Given that Mr B's serious condition was due to a Tegretol overdose, and that his serum Tegretol levels had been extremely high, I would have expected daily serum Tegretol tests to be performed to assist in monitoring his condition. Mrs A complained that no Tegretol results were recorded for 3 and 4 November. There is no substance to this allegation, although it is not clear why no test was taken on 4 November. It is possible that the test was performed and that for some reason, the result was not included in the documents sent to me during my investigation.

List of medications on Mr B's 'Acute Assessment Discharge Form'
The documents provided to me are not numbered. However, I note that the 'Medical/Surgical Interdisciplinary Acute Assessment/Discharge Form' dated 1 November 1998 lists carbamazepine, haloperidol, Cogentin and lorazepam as Mr B's usual medications.

When he was admitted, Mr B was not in a condition to inform the medical staff what medications he was taking. The only person able to do so was Mr B's caregiver, who had been caring for him for only two days. Dr D informed me that, without anyone else to consult, he referred to the list of medications in Mr B's previous medical notes.

I am satisfied that the information recorded at the time was as accurate as it could be in the circumstances. There were no family members to consult at the time Mr B was admitted on the morning of 1 November. It was necessary to review Mr B's previous medical notes and attempt to ascertain what his medications were. I accept that it was reasonable to list what was recorded in the previous notes. Accordingly, there is no breach of the Code in relation to this matter.

Response to rise in Mr B's Tegretol levels on 1 November 1998
Dr C ordered that Mr B's Tegretol level be re-tested at 4pm on 1 November. The blood test was actually taken at 5.45pm and was reported as >250µmol/L.

My medical advisor commented that the notes record that discussion was held by the nursing staff with the medical registrar regarding the high Tegretol level. Nursing notes record that there were no further orders given. There was no record that Dr C was informed about the increase in the Tegretol level. He was the physician consultant on call. Dr C advised me that he was available on his locator and by telephone for consultation.

Dr C saw Mr B the next morning, after the on-call registrar, on-call anaesthetist and Director of ICU had seen him. By this time Mr B had been ventilated and his Tegretol level had decreased to 223µmol/L. Once ventilated, Mr B was primarily under the care of Dr E, the Director of ICU.

It is not clear what action Dr C may have taken if he had been informed the night before about the increase in Mr B's Tegretol level. I do not consider it appropriate to speculate about the matter. However, Dr C cannot be held accountable for not acting in response to the raised Tegretol level when he was unaware of that increase. Accordingly, he did not breach the Code in relation to this matter.

Opinion: Breach – Public hospital

Right 4(1)

Direct liability
In my opinion the public hospital failed to comply with its duty of organisational care and skill, and therefore breached Right 4(1) of the Code.

The right to receive good quality medical care is central to the Health and Disability Commissioner Act 1994 and the Code of Health and Disability Services Consumers' Rights. The statutory purpose, set out in section 6 of the Health and Disability Commissioner Act

1994, is "to promote and protect the rights of health consumers", or patients. At the core of patients' rights is the right to receive services of an appropriate standard (section 20(1)(f)). This key right is affirmed in Right 4 of the Code, entitled the "Right to Services of an Appropriate Standard". The hospital breached Mr B's right to have medical services provided with reasonable care and skill in respect of the ongoing decision by medical staff not to administer charcoal when Mr B's serum Tegretol level was reported as >250µmol/L.

My medical advisor has commented that Dr C's instructions to junior staff were inadequate. However, a decision was made by staff other than Dr C involved in Mr B's care not to act upon the increased Tegretol level. All of those staff had available to them the information guidelines from the NPC. None of the three medical staff who saw Mr B during the evening of 1 November and the early morning of 2 November revisited the decision not to administer charcoal to Mr B, in light of the substantial increase in his serum Tegretol level. Similarly, the Director of ICU, to whom Mr B's care was transferred once he was intubated, did not prescribe charcoal. Even though the serum Tegretol level had dropped to 223µmol/L, as reported from the blood sample taken at 8.25am, the level was still so significantly high that reconsideration of whether charcoal should be administered was justified. My advisor commented:

> "… [A]t no time other than the initial contact with the Poisons Centre, did [Dr C] or any of his medical delegates either ask for or seek further expert opinion despite the fact that [Mr B] continued to deteriorate. It is my opinion, that [Dr C] should have sought help at least on the morning of November 2 1998 following [Mr B]'s acute deterioration."

I note that by the time Dr C saw Mr B on the morning of 2 November, he had been assessed and treated by three other doctors.

In my opinion, the failure of medical staff at the hospital to respond to the increase in Mr B's serum Tegretol and take steps to reduce the level amounted to a breach of Right 4(1) of the Code.

Vicarious liability

Section 72 of the Health and Disability Commissioner Act states that anything done or omitted by a person as the employee of an employing authority shall, for the purposes of the Act, be treated as done or omitted by that employing authority as well as by that first-mentioned person, whether or not it was done or omitted with that employing authority's knowledge or approval. It is a defence, under section 72(5) for an employer to show that it took such steps as were reasonably practicable to prevent an employee from breaching the Code.

Dr C was an employee of the hospital. His clinical decision not to administer charcoal, in light of the recommendations of the NPC, was inappropriate, as was his decision not to insert an endotracheal tube to facilitate the administration of the charcoal.

The hospital, like other public hospitals throughout New Zealand, did not have formal systems in place to detect whether a doctor was practising safely. I accept that the hospital should have been able to rely on Dr C to provide appropriate services to Mr B. However, I

have received no evidence that the hospital took any steps to ensure that Dr C was practising safely as a physician.

In the circumstances, and in the absence of evidence that, as an employer, it took reasonable steps to prevent the shortcomings on the part of its on-call physician, the hospital is, in my opinion, vicariously liable for Dr C's breach of the Code.

Action

I recommend that Dr C and the hospital take the following actions:

- Apologise in writing to Mrs A for their breaches of the Code. The apologies are to be sent to the Commissioner and will be forwarded to Mrs A.

Further actions

- A copy of this opinion will be forwarded to the Medical Council of New Zealand with a recommendation that a review of Dr C's competence be undertaken.

- A non-identifying copy of this opinion will be sent to the Royal Australasian College of Physicians and will be placed on the Commissioner's website, www.hdc.org.nz, for educational purposes.

Appendix I – Information provided by the National Poisons Centre

"CARBAMAZEPINE

DATE
Physostigmine use updated August 1998 by Stephen Farquhar
ATC codes added 21 June 1997.
Whole document reviewed May 1997 by Ian Weatherall

PRODUCT
CARBAMAZEPINE

FORM
Tablet/syrup
PHYSICAL PROPERTIES (2,3)
White or yellowish-white crystalline powder. Exhibits polymorphism.
Relative molecular mass: 236.6
Melting point: 189-198 degrees Celsius
Solubility: practically insoluble in water or ether, soluble 1 in 10 of ethanol, 1 in 10 of chloroform, soluble in acetone.

COMPOSITION
5H-dibenz[bf]azepine-5-carboxamide
C15H12N20

USES
Therapeutic carboxamide derivative antiepileptic.
A synthetic iminostilbene derivative employed therapeutically as a psychotropic and anticonvulsant agent.
MECHANISM (1)
Cellular mechanism is unknown but it produces a differential inhibition of high-frequency discharges in and around epileptic foci with minimal disruption of normal neuronal traffic.
It shares some structural pharmacological features with tricyclic antidepressants and meprobamate, which together explain much of the adverse effects, including severe overdose (15).

CODES
CAS No: 298-46-4
N03A F01

TOXICITY
ACUTE TOXICITY (5)
ADULTS
43 mg/kg (TDLo, adult): sleep, hallucinations, distorted perceptions, nausea or vomiting (7)
~45 mg/kg (2 g in a 13 yr old): blurred vision, tachycardia (see case report for details)

~70-80 mg/kg (4 to 4.8 g in an 18 yr old): survival
~100 mg/kg (5 g in a 14 yr old): survival
~100 mg/kg (5.8 in a 16 yr old): acute encephalopathy
150 mg/kg (adult): survival
200 mg/kg (adult): survival
200-300 mg/kg (18.2 to 24 g in adults): serious toxicity, survival
640 mg/kg (adult): survival
640 mg/kg (84 g in a 13 yr old): serious toxicity, survival
~850 mg/kg (60 g in a 26 yr old): fatal
CHILDREN
~80 mg/kg (400 mg in a 22 mth old): drowsiness (resolved after lavage)
65 mg/kg (TDLo, child): convulsions, coma and other changes
148 mg/kg (2 g in a 23 mth old): coma and seizures
~500 mg/kg (10 g in a 6 yr old): coma and respiratory depression, full recovery in 24 hr
SERUM CONCENTRATION/TOXICITY RELATIONSHIP
An association between blood levels and toxicity has been observed
Therapeutic plasma concentrations are reported to be approximately 4-12 mg/l
Although optimal plasma levels may fall outside this range in some individuals (5,8).
ADULTS
4-12 mg/l: therapeutic level
(Peak levels)
>10 mg/l (42-127 mcmol/l): ataxia, nystagmus
~10-30 mg/l (42-127 mcmol/l): mild toxicity (somnolence, ataxia, nystagmus, movement disorders, hallucinations, and vomiting
>40 mg/l (170 mcmol/l): serious toxicity (coma, seizures, arrhythmias, respiratory depression and hypotension
Acute encephalopathy following ingestion of 5.8 g of carbamazepine in a 16-year-old male was reported. The plasma level was 10.1 mg/l 86 hours postingestion.
A 34-year-old male, with history of seizure disorder, died four days after admission from complications of carbamazepine overdose. The amount ingested and the time of ingestion were unknown. Carbamazepine serum concentration on admission was 54 mg/l.
CHILDREN
Children may develop severe toxicity at lower levels than in adults (5)
CHRONIC TOXICITY (7)
TDLo Oral woman: 112 mg/kg over 2 weeks intermittently
Gastrointestinal – nausea or vomiting
Blood – thrombocytopenia
TDLo Oral woman: 144 mg/kg over 2 weeks intermittently
Blood – thrombocytopenia
Skin Appendages – dermatitis, allergic (after systemic exposure)
TDLo Oral man: 160 mg/kg over 3 weeks intermittently
Skin and Appendages – dermatitis, other (after systemic exposure)
TDLo Oral child – 1050 mg/kg over 6 weeks intermittently
Behavioral – muscle contraction or spasticity
TDLo Oral man: 258 mg/kg over 6 weeks intermittently

Gastrointestinal – nausea or vomiting
Liver – liver function tests impaired
TDLo Oral child: 19 mg/kg over 4 weeks intermittently
Peripheral Nerve and Sensation – fasciculations
TDLo Oral woman: 28 mg/kg over 4 weeks intermittently
Behavioral – somnolence (general depressed activity)
Gastrointestinal – nausea or vomiting
Nutritional and Gross Metabolic – other changes
TDLo Oral woman: 560 mg/kg over 4 weeks intermittently
Blood – changes in bone marrow (not otherwise specified)
LDLo Oral man: 54 mg/kg over 9 days intermittently
Behavioral – ataxia
Kidney, Ureter, Bladder – urine volume increased
Blood – agranulocytosis
LDLo Oral woman: 1920 mg/kg over 17 weeks intermittently
Blood – aplastic anaemia
TDLo Oral man: 94 mg/kg over 11 days intermittently
Blood – thrombocytopenia
NORMAL THERAPEUTIC RANGE (8)
Epilepsy:
Adult
Initially, 100-200 mg once or twice daily; slowly raise the dosage until – generally at 400 mg 2 to 3 times daily – an optimum response is obtained. In some patients 1600 mg or even 2000 mg daily may be appropriate,
Children
In general 10-20 mg/kg bodyweight daily, ie –
Up to 1 year of age 100-200 mg daily
1 to 5 years of age
200-400 mg daily
6 to 10 years of age
400-600 mg daily
11 to 15 years of age
600 to 1000 mg daily
all amounts to be taken in several fractional doses.
It has also been recommended that for children aged 4 years and less a starting dose of 20-60 mg/day, increased by 20-60 mg every second day. For children over the age of 4 years, therapy may begin with 100 mg/day and be increased by 100 mg weekly.
Carbamazepine is used therapeutically for a number of conditions, however the above doses would reflect at most the largest amounts used.
ANIMAL TOXICITY (7)
Rat
LD5O?oral???1955 mg/kg
LD50?ip???158 mg/kg
LD50?sc???>1500 mg/kg
Mouse
LD50?oral???529 mg/kg

LD50?ip???114 mg/kg
LD50?sc???>1 g/kg
Other
LD50?oral, dog??5620 mg/kg
LD50?oral, rabbit?2680 mg/kg
LD50?oral, guinea pig?920 mg/kg
PHARMACO-/TOXICOKINETCS (9)
ABSORPTION
Carbamazepine is absorbed slowly from tablets. In therapeutic doses, peak plasma levels are attained in 2 hours from the syrup formulation, within 12 hours from conventional tablets and within 24 hours from the controlled release formulation. In one report 72% was absorbed and 28% excreted in the faeces. In overdose absorption may be delayed up to 72 hours post ingestion.
DISTRIBUTION
Volume of: distribution: 0.8 to 1.9 L/kg. It should be noted that Vd varies –

Neonates	1.52 L/kg
Children	1.94 L/kg
Adults	0.59 to 1.2 L/kg
Overdose	3 L/kg (5)

Fraction bound to plasma proteins: 70 to 80%
METABOLISM
Extensively metabolised in the liver (98%). The main metabolite is carbamazepine – 10,11-epoxide (40% of dose) which has anticonvulsant activity of its own. More than 7 metabolites have been identified.
The epoxide metabolite is then hydrated and excreted.
Carbamazepine appears to induce its own metabolism during prolonged treatment which is complete from 3 to 5 weeks with a fixed doing regimen.
Children have enhanced elimination of carbamazepine.
Plasma half life: 25-65 hours after a single dose. Reduces to l6-24 hours after repeated administration and depending on duration of therapy. A mean elimination half-life of 8.76 +/- 0.85 hours has been reported in newborns & children following a mean dose of 17.2 mg/kg.
The average half-life of the 10,11-epoxide metabolite is 6.l hours.
ELIMINATION
Following an oral dose of carbamazepine, about .72% is excreted in urine, 1 to 2% is unmetabolized drug
Renal clearance is dependent on urine flow for carbamazepine and its epoxide metabolite. Glomerular filtration and active tubular secretion has been proposed for mechanism of renal excretion.
Note that there is also faecal excretion of drug.
PREGNANCY AND LACTATION (10)
Interpretation on the effect of carbamazepine use during pregnancy has been difficult due to the frequency of combination drug therapy.
Although a study has suggested that there may be a small likelihood of an increase in the incidence of spina bifida in children, the conclusions reached were questionable. Since the use of folate supplements has been shown to decrease the incidence of neural tube

defects, this agent has also been recommended by some for patients using carbamazepine. It should be kept in mind however, that neither the increased risk of neural tube defects nor the effectiveness of folate supplements has been fully established in patients using carbamazepine.

One commentator has pointed out that seizures pose a greater overall risk to women with epilepsy than do properly used antiepileptic drugs; and epilepsy is not an absolute contraindication to childbearing because available reports suggest that more than 90% of such pregnancies will result in a healthy baby. Concerns about possible neural tube defects, can be addressed using ultrasound and biochemical markers in blood or amniotic fluid.

Carbamazepine enters breast milk (at levels 25-70% of that in maternal blood and accumulation in nursing infants has been reported. Only two reports of adverse effects in infants (exposed to carbamazepine prenatally and through breast milk) have been transient cholestatic hepatitis, a hepatotoxic effect of carbamazepine that has previously reported in adults and children, and hyperbilirubinemia and high concentrations of gamma-glutamyltransferase. While it has been considered probably safe, the benefits of breastfeeding should be weighed against the remote possibility of adverse effects occurring in the infant. If breastfeeding occurs infants should be observed for possible adverse reactions, eg excessive somnolence.

INTERACTIONS

(i) Carbamazepine is a known inducer of hepatic microsomal enzymes and may accelerate the metabolism of the following drugs:

medendazole, alprazolam, tricyclic antidepressants (in particular amitriptyline, imipramine), anticoagulants (in particular warfarin, phenprocoumon, dicoumarol), non-depolarising neuromuscular blockers, corticosteroids, oral contraceptives, clobazam, clonazepam, cyclosporin a, doxycycline, ethosuxamide, isotretinate, felodipine, haloperidol, itraconazole, lamotrigine, methadone, nimodipine, risperidone, theophylline, valproic acid.

(ii) The following medicines may cause an increase in carbamazepine levels requiring dosage adjustment and/or plasma level monitoring:

cimetidine, macrolide antibiotics (eg erythromycin, triacetyloleandomycin), danazol, diltiazem, fluoxetine), influenza vaccine, isoniazid, propoxyphene, sertraline, verapamil.

(iii) In combination with clozapine, there may be an additive effect on bone marrow suppression.

(iv) Desipramine may have decreased effectiveness while increasing carbamazepine levels.

(v) The following drugs increase carbamazepine metabolism:

loxapine, barbiturates, phenytoin, primidone,

(vi) Additive hyponataemic effects have been observed during concomitant diuretic (hydrochlorothiazide, frusemide) and carbamazepine therapy.

(vii) Coadministration of carbamazepine and ketorolac have reportedly produced seizures. Concurrent use is contraindicated.

(viii) Increased development of neurotoxicity has been observed with coadministration of lithium and carbamazepine even with normal therapeutic blood levels of both agents.

(ix) Terfenadine may displace carbamazepine from protein binding sites causing carbamazepine toxicity.

SIGNS AND SYMPTOMS

Patients may present with aggression and excitation but more typically are found to be obtunded with various degrees of respiratory depression and dilated pupils which are sluggishly reactive to light.

Death from carbamazepine overdose is infrequent but may result from severe cardiovascular effects, aspiration pneumonitis, severe hepatitis, or aplastic anaemia.

Note that pharmacobezoar (tablet concretion) formation can occur. This and its anticholinergic properties may lead to symptomology of a cyclic nature and even relapse (4).

SIGNS AND SYMPTOMS (5, 6)

CARDIOVASCULAR

Effects are inconsistent and are usually not clinically significant. Effects reported include sinus tachycardia, sinus bradycardia, sinus arrhythmia and prolonged PR, QRS, and QT intervals.

A retrospective study of 12 cases and found no arrhythmias noted with acute toxicity in patients with levels less than 40 mg/l (170 mcmol/l) (6).

Decreased myocardial contractility, hypotension and pulmonary oedema have been reported in severe carbamazepine toxicity.

Hypotension or hypertension can occur.

RESPIRATORY

Respiratory depression requiring mechanical ventilation may occur. Apnoea has also been reported in at least one case.

CENTRAL NERVOUS SYSTEM

Common signs and symptoms include lethargy, slurred speech and variable degree of coma. Cyclic coma may occur possibly due to delayed absorption or enterohepatic recycling.

Other clinical effects include ataxia, asterixis (motor disturbance causing intermittent lapse of assumed posture), encephalopathy, irritability, aggression, hallucinations, EEG changes, adiadochokinesis (inability to perform rapid alternating movements), seizures, myoclonus, decreased or increased deep tendon reflexes, and opisthotonus (a form of tetanic spasm). Note that seizures have been reported in patients with no history of epilepsy.

Choredathetoid movements, orofacial dyskinesias and other dystonias have been reported.

Neuroleptic Malignant Syndrome has been seen in mixed drug overdose as well as during chronic therapy.

GASTROINTESTINAL

Spontaneous vomiting is common and there may be decreased gastrointestinal motility.

OCULAR

Mydriasis, nystagmus, divergent strabismus and Ophthalmoplegia (paralysis of eye muscles).

HAEMATOLOGICAL
Neutropaenia, agranulocytosis, pancytopaenia, thrombocytopaenia, and aplastic anaemia have been reported during chronic therapy.
Leukocytosis was noted in 2 patients who overdosed on carbamazepine.
OTHER
Hypothermia or hyperthermia.
Hepatitis has been reported after chronic therapy. Elevated liver enzymes and rarely hyperammonaemia have also been seen.
Carbamazepine has antidiuretic properties causing oliguria and urinary retention. Glycosuria and acetonuria may occur.
Hyponatraemia and hypokalaemia have been reported.
Bullous skin formation.

TREATMENT
(1) EMERGENCY MEASURES
(a) Stabilization
Support respiratory and cardiovascular function.
(b) Decontamination
Emesis: Use of emesis is not recommended due to its limited efficacy, possible complications and interference with more effective decontamination procedures.
Lavage: Lavage is not generally recommended unless the patient presents obtunded within one hour of ingestion.
Activated charcoal: Single dose activated charcoal is the recommended gastrotestinal decontamination procedure.
Single dose activated charcoal regimen:
Adult 50 to 100 g
Child 1 to 2 g/kg
The majority of children will tolerate an oral dose of activated charcoal if given in an encouraging and positive manner, preferably in the presence of a parent/caregiver.
For the few children refusing an oral dose, administration via a nasogastric tube should be undertaken. Refer to the 'nasogastric intubation' datasheet for instructions.
Nasogastric intubation or orogastric intubation, if required for lavage, should be used for comatose adults.
Activated charcoal tablets have no place in the treatment of poisoning.
Repeat charcoal may enhance elimination and is indicated for large ingestions.
In this case an initial dose of charcoal with added cathartic has been recommended.
In large overdose (particularly of the SR form) a pharmacobezoar (tablet concretion) may form. This may cause relapses due to later release of drug.
Ultrasound or x-ray may show such a mass.
Whole bowel irrigation may be indicated if a pharmacobezoar is observed or when the SR formulation has been ingested.
(2) SUPPORTIVE CARE (5)
(a) CARDIOVASCULAR
ECG should be monitored for 24 hours after admission. Circulatory status and blood pressure should also be monitored.
Hypotension may be treated with IV fluids or careful use of vasopressors.

(b) CNS
Monitor level of consciousness.
If seizures occur, treat with diazepam taking care that undue respiratory depression does not occur.
Choroid dystonias can be treated supportively with airways protection and observation.
Precautions should be made to avoid ataxic injuries during recovery.
(c) OTHER
Carbamazepine levels should be established in symptomatic patients. Individuals with carbamazepine levels greater than 20 mg/l should be considered at risk of serious complications. (11)
Monitor renal and hepatic function.
Obtain a complete blood count, monitor fluids and electrolytes.
Maintain body warmth.
(3) ENHANCED ELIMINATION (5)
Charcoal haemoperfusion has been used to remove carbamazepine from the blood. The amounts removed are generally relatively small when compared to the dose taken.
It may be indicated in cases of failure or slow response to supportive care.
(3) ANTIDOTE
PHYSOSTIGMINE SALICYLATE
(a) Indications
The antidotal use of physostigmine is controversial and is considered to be a treatment of last resort. It has been used in patients with extensive agitation or delirium, repetitive or long-lasting seizures, severe sinus or supra-ventricular tachycardia, or extensive hyperthermia resistant to mechanical cooling.
(b) Recommended dosage and administration
The duration of effect is only temporary and repeat doses are often required.
Child: 0.02 mg/kg physostigmine salicylate IV, injected over two minutes at a rate not greater than 0.5 mg/min. Repeat every 5 to 10 minutes until toxic effects are relieved, cholinergic effects develop, or until a total of 2 mg has been administered.
Adult: 2 mg physostigmine salicylate IV injected over two minutes at a maximum rate of 1 mg/min. If there is no response, 1 to 2 mg can be given every twenty minutes until reversal of toxic antimuscarinic effects occur or cholinergic symptoms arise.
(c) Adverse effects
Physostigmine can induce cholinergic toxicity including bradycardia, asystole, increased salivation, seizures, diarrhoea, bronchospasm, or respiratory arrest. These adverse effects result from its pharmacological action of increasing acetylcholine levels.
(d) Contraindications
Physostigmine should not be used to treat cardiac conduction defects or ventricular tachyarrhythmias. Severe bradycardia may result from concurrent use of physostigmine and beta-adrenergic blockers.

FIRST AID
INGESTION: Do not induce vomiting. Do not give fluids to dilute. Seek medical attention immediately.
EYES: Flush with water for at least 15 minutes and seek medical advice.

SKIN: Wash well with plenty of water and soap whilst removing contaminated clothing. If a large area is affected, seek medical advice.

EXPOSURE HAZARDS
Harmful if swallowed or absorbed through skin.
Irritant to skin and respiratory tract. Mild irritant to eyes.

OCCUPATIONAL HAZARDS
Avoid contact with eyes, skin or clothing. Avoid breathing dust or mist. Use with adequate dust control. Wash thoroughly after handling. Wear fresh clothing daily. Wash contaminated clothing before reuse. Do not permit eating, drinking or smoking near material (12).

MANAGEMENT FIRE
This material is assumed to be combustible. As with all dry contact with dry material to dissipate the potential buildup of static electricity. When heated to decomposition material emits toxic fumes of NOx. Emits toxic fumes under fire conditions.
Use water spray, dry chemical, carbon dioxide or foam as appropriate for surrounding fire and materials (12).

MANAGEMENT GENERAL
Store in air tight container. Protect tablets from areas of excessive moisture (6).

MANAGEMENT – SPILLS
Wear approved respirator and chemically compatible gloves. Vacuum or sweep up spillage. Avoid dust. Place spillage in appropriate container for waste disposal. Wash contaminated clothing before reuse (12).

SYNONYMS
Carbamazepinum
Tegretol tablet
Tegretol CR
Tegretol Syrup
Teril tablet
Convuline."

Appendix II – Further comments provided by Independent Expert

"SUMMARY OF MAJOR EVENTS AS RECORDED IN THE HOSPITAL NOTES

Ambulance Officer's Report –

At 0857 hrs on 01.11.98, the ambulance service received a call to dispatch a vehicle to […].

At 0909 they found a young male unconscious ? [query] overdose lying in the middle of the road. They noted that he was rousable to pain, had no identification and that no history was obtainable. The police were present.

A finger tip blood glucose level was 8.0 mmol/l. They did not perform baseline vital signs due to the closeness of the hospital. GCS, however, at the scene was noted to be 6/15 [3 motor flexion; 1 no verbal response, 2 eye opening to pain].

The patient was noted to be breathing spontaneously, oxygen via mask at 8 litres/min was applied, the patient was placed in the left lateral recovery position and the Emergency Department – [the hospital] [ED] was notified of the patient via radio.

The ambulance arrived at ED at 0909 hrs, 01.11.98.

Admission to Emergency Department [the hospital] [ED] –

The ED record notes the arrival time of 0911 hours. Triage category was 'Stat' with the history recorded as: '*Found lying in middle of* […] *– dilated pupils, protruding tongue, dry mouth. Roused eventually but no sensible conversation. Vital signs: BP 137/65; HR 105; Oxygen saturation: 96% on 8 litres via mask; Right and Left Pupils = 6; BM: 8*'.

Clinical notes (medical) record the following: '*Found unconscious in the middle of the road. 20 year old Asperger's Syndrome. On arrival GCS 4/15, oxygen sats 96%, breathing spontaneously, Pupils dilated and sluggish. Heart sounds: s1 and s2 normal, ejection systolic murmur. Bilateral upgoing plantar reflexes, clonus both feet. Brisk reflexes. Abrasion to left cheek. Diagnosis: Overdose,? intracerebral pathology.*'

Clinical note (added by nursing staff): 45 X 400-mg Tegretol tabs missing from house.

Medication: cogentin 2-mg i.m. at 1010 hours.

Clinical Notes Continuation: '*1000: agitated and combative → onto floor. Sweating, tachycardic, ataxic, etc. then episodes of inertia. For monitoring in ICU. Anaesthetist input to sedate him ?intubate for C.T. ?? hx head injury; ?? intracerebral bleed.*'

Carbamazepine Poisons Information –

In the notes is a copy of information from New Zealand Poisons Centre faxed to the ED [note the date shown is 28/3/98 – time 22:46:58 ? correct] entitled: CARBAMAZEPINE (Document F105) – 8 pages.

The following 'content' was noted by [hospital] clinical staff by either being underlined or highlighted →

1. Toxicity – adult: 200 – 300 mg/kg (13.2 to 24 g in adults: serious toxicity, survival; '[Mr B] – *258 mgs per kilo at 85 kg'*.

2. Acute encephalopathy following ingestion of carbamazepine in a 16-year-old male was reported. The plasma level was 10.1 mg/l 36 hours post-ingestion.

3. Gastrointestinal – nausea or vomiting; Behavioural – somnolence (general depressed activity); Behavioural – ataxia; Blood – agranulocytosis; Blood – aplastic anaemia; Blood – thrombocytopaenia.

4. Peak plasma levels are attained in 2 hours from the syrup formulation; within 12 hours from conventional tablets and within 24 hours from controlled release formulation. In overdose absorption may be delayed up to 72 hours post ingestion.

5. Distribution: Overdose 3 L/kg (Posiondex 1996 database)

6. Signs and Symptoms: Patients may present with aggression and excitation but more typically are found to be obtunded with various degrees of respiratory depression and dilated pupils are sluggishly reactive to light. Death from carbamazepine overdose is infrequent but may result from severe cardiovascular effects, aspiration pneumonitis, severe hepatitis or aplastic anaemia.

7. Central Nervous System: Common signs and symptoms include lethargy, slurred speech, and variable degree of coma. Encephalopathy. Note that seizures have been reported in patients with no history of epilepsy.

8. Treatment: Lavage: Lavage is not generally recommended unless the patient presents obtunded within one hour of ingestion. ECG should be monitored for 24 hours after admission. Circulatory status and blood pressure should also be followed. If seizures occur treat with diazepam taking care that undue depression does not result. Precautions should be made to avoid ataxic injuries during recovery. Physostigmine has been used to control dystonic reactions. However due to the potential for severe adverse effects it is not recommended for use in treatment of carbamazepine overdose.

Admission to Intensive Care Unit –

November 1, 1998 –

Intensive Care Plan for [Mr B], 19/05/80, 1/11/98 under [Dr C].

- Diagnosis/Reason for admission: *Overdose of carbamazepine 55 x 400 mg tabs. ??time - ?0700 hrs 1-11-98.*

- '*observe for fitting; nausea /vomiting; respiratory depression; coma. See carbamazepine document in notes. Hyper/hypotension. For repeat tegretol level at 1600 hours.*'

- Problem List: Tegretol Overdose – no action plan outlined.

Admission Note recorded by Medical Registrar – [Dr D], 1.11.98:

'*18-year old male known to ward* […]. *Previous overdose with digesic. Aspergers Syndrome (?autism-like – had CT head 4/98 ⇒ Normal. Awaiting EEG – arranged by psychiatrists. On carbamazepine 200 mg bd; haloperidol 5 mg bd; cogentin 2 mg mane; lorazepam 1 mg nocte. Found in the middle of the road by police. Unconscious. In ED had tonic clonic seizure. Given cogentin im 1 mg with no effect. Caregiver doesn't know any previous history. Started to look after him 2/7 ago. They found an empty container of tegretol 400 mg X 55 tabs missing = 22,000 mgs probably taken this morning. Nobody saw this at home. Last night was okay.*

On examination, unconscious – GCS 4/15; HR 120/min regular; BP 140/70; temp normal; oxygen sat 95% air; pupils dilated, fixed; plantars upgoing. Lungs clear. Heart sounds normal, nil else. Abdomen soft. Having myoclonus, opisthotonus. Call to Poisons Centre → no antidote; charcoal → unconscious. Side effects: respiratory depression, cardiac suppression, seizures, agranulocytosis. Tegretol level 0930 129 µmoll/L (normal up to 42). Discussed with [Dr C]*: ? CT head impossible with his agitation; if oxygen saturation decreased or respiratory rate --? ? intubation. Bloods: urea and electrolytes normal; liver function tests normal; white cell count 12 (neutrophils); alcohol level nil; paracetamol level nil.*

Plan: Supportive care. ICU → respiratory rate, BP, oxygen saturation. If gets bad, fit "prolonged" consider iv diazepam 5 mg and start iv. Repeat Blood 1600 hours and mane. Chest and abdominal x-ray. Withhold all his meds.'

The ICU Nursing Notes indicated that [Mr B] had a GCS of 3 on admission to ICU, that he was spontaneously breathing and that his neuro-obs were stable other than for equally dilated pupils (7 mm) with slow reaction to light. [Mr B] also noted to be having frequent tonic fits lasting about 1 to 3 minutes every 10 to 15 minutes.

The nurses further noted that [Dr C] saw [Mr B] and recommended iv Diazepam 5 to 10 mg if fitting prolonged. Subsequently the nurses noted that he was requiring iv

Diazepam approximately ½ to 1 hourly. They note the requirement to monitor closely for respiratory depression.

[Dr D] undertook a ward round at 2014 hours noting: '*didn't pass urine since admit. Still fitting with some response to valium. Tegretol level >250 µmol/L. Start iv saline 150 ml/hr x 1 litre then dextrose saline 1 litre q 8 hrly. Catheterise, fluid balance'*.

Nursing P.M. shift note: '*Patient remains unconscious. GCS=3 throughout shift. Hourly neuro obs continue. Fits have become less in duration and infrequent through the afternoon. 1 x valium diazemules (5 mgs) required at 1700 hours. Neuro obs: pupils left sluggish → ? reaction at all. Right reacting-both very dilated size 7 mm. Repeat Tegretol level 1600 hours >250 mmol (up from 129 mmol). Discussed with* [Dr D] *– no further orders. BP 150/82 to 178/102; HR 117-110; RR: 7-18; SA02: 98-99% (decreases to 85-89 during fits)'*.

November 2, 1998 –

Nurses noted that [Mr B] was stable until 0400 hrs when he developed grunting, moaning noises with laboured breathing. The overnight house officer was called at 0500 hrs to see [Mr B]. The house officer noted that [Mr B] was '*still unconscious / tachypneic 50 per minute and temperature 38; oxygen saturation 64; fixed dilated pupils; medical registrar contacted → she is happy to come to assess the patient'*.

Nursing note records 0530 hours → '*registrar contacted. No new orders.*'

At 0600 hrs the nursing staff recorded: '*BP 121/54; HR 118; temp 38; pupils fixed dilated; no limb movement; not responding to painful stimuli. Condition appears to be deteriorating. Registrar recontacted – will come in. Cares – turned left to right side – mouth cares given – haemo-mucous exudate from mouth. Attempted to suction down back of throat with little success.*'

At 0630 hrs, note from medical registrar: '*patient became tachypnoeic, oxygen saturation decreased to 75% from 98%; RR 35/min; temp 38; pupils dilated. Fitting on & off. Lungs bilateral coarse crackles. Impression: aspiration pneumonia. Plan increase oxygen to 100%, ABG, discussed with Anaesthetist for assessment. ETT ? pulmonary oedema.*' Mechanical ventilation, positive end-expiratory pressure initiated.

Ward round by [Dr C] queried myocardial depression as a cause of the pulmonary oedema. Echo study showed left ventricular function within normal limits.

[Dr E], […] noted that [Mr B] continued to have a depressed level of consciousness (GCS 4-5/15). Evidence of raised creatinine (acute renal failure) and raised liver enzymes. Carbamazepine level at 0700 hrs was 223 µmol/L. Plan instituted consisted of: ventilatory support; inotropic support; iv antibiotics; volume support (pentaspan) and iv bolus diazepam if noted to be seizuring. Impression was that of query pulmonary oedema, query aspiration pneumonitis, query early Adult Respiratory Distress Syndrome (ARDS).

Course over November 3 through to 6, was one of fluctuating improvement and decline in condition. By November 6, ARDS had worsened and the decision was made to transfer [Mr B] to [another public hospital]. A muscle enzyme test, the creatine kinase enzyme returned markedly elevated at 4394 (normal 30-190).

RELEVANT BIOCHEMISTRY

The table below outlines key and relevant biochemical serological parameters for [Mr B] during his admission to [hospital] November 1 through to 6, 1998.

Date	Serum Carbamazepine	Serum Creatinine	Serum ALT	Serum AST	Anion Gap
0930 hrs 1.11.98	129 µmol/L	0.091mmol/L	34 U/L	36 U/L	
1745 hrs 1.11.98	>250 µmol/L				
0825 hrs 2.11.98	223 µmol/L	0.207mmol/L	58 U/L	219 U/L	25 mmol/L
0800 hrs 3.11.98	202 µmol/L	0.181mmol/L	54 U/L	185 U/L	17 mmol/L
0800 hrs 5.11.98	192 µmol/L	0.109mmol/L	60 U/L	158 U/L	13 mmol/L
0800 hrs 6.11.98	138 µmol/L	0.126mmol/L	64 U/L	138 U/L	14 mmol/L

It is important to note the Carbamazepine level in particular. The first level obtained was on admission to the Emergency Department and measured 129 µmol/L. The normal maximum therapeutic level is 40 µmol/L. The follow-up levels are important with regard to the fact that [Mr B] ingested a sustained release formulation.

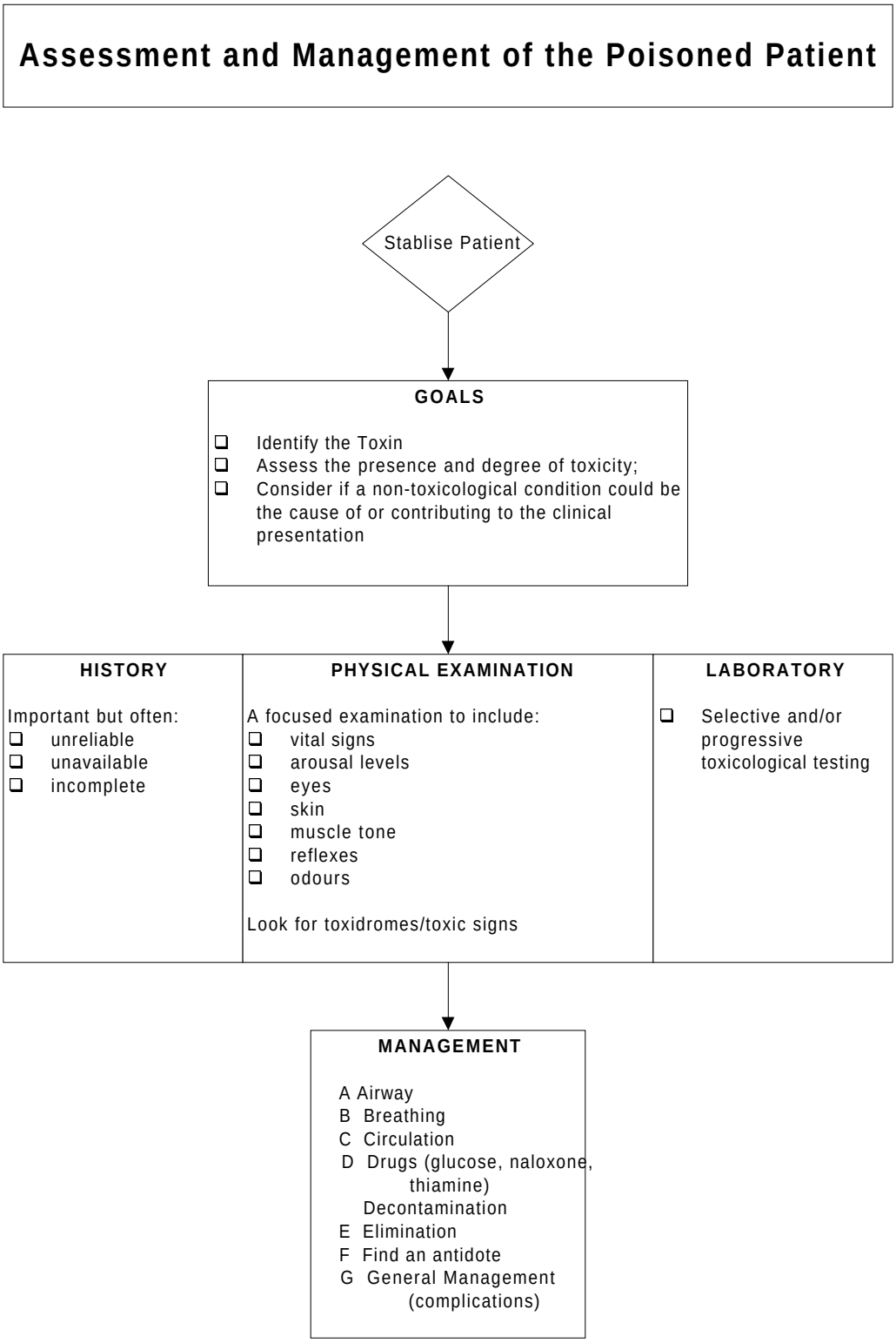
The last level taken on 6.11.98, prior to his transfer to [another public hospital], continued to be greater than four times the maximum therapeutic level.

GENERAL OVERVIEW: MANAGEMENT OF ACUTE POISONING

The general approach, according to current standards of care, to the poisoned patient can be summarised as:

1. stabilisation
2. history
3. examination
4. diagnosis,
5. decontamination
6. enhanced elimination
7. poison-specific treatment, and;
8. disposition.

GUIDELINE FOR ASSESSMENT AND MANAGEMENT OF THE POISONED PATIENT



Medical Practitioners should have a high index of suspicion and be quick to consider an alternate toxin or medical condition or trauma in cases where the history is inconsistent with the patient's clinical presentation.

In difficult cases, the Emergency doctor should consult with the Poisons Centre to obtain up-to-date advice on the best management of their patient's condition.

1. **Stabilisation**

- Stabilisation is the first priority in managing toxic ingestions.
- The patient should be rapidly assessed to determine adequacy of airway and ventilation, mental status, and cardiovascular function. At this point, the doctor should also search for and correct hypoxia and hypoglycaemia.
- Initial management priorities are maintenance and protection of the airway, support of ventilation, and support of circulation.
- Unstable patients should be placed on a cardiac monitor with measurement of vital signs every five to 15 minutes until the patient is stabilised to the point where monitoring is no longer necessary.
- The potential for rapid changes in the patient's condition should be considered in making decisions about airway and ventilator support.

2. **Managing Common Complications**

- Common complications of poisoning include depressed mental status, seizures, agitation, hypotension, bradycardia, and vomiting.
- Most of these can be treated empirically without knowledge of the toxin involved and without specific antidotes.
- Management of these complications occurs concurrently with history, physical examination and specific laboratory tests.

(a) Coma and Altered Mental Status [note: see the appendix – Clinical Policy for management of the patient with altered mental status]

- ❒ Concurrently with the 'ABCs', (airway, breathing, circulation), the Emergency doctor must search for and treat hypoglycaemia, hypoxia, head injury, CNS infection, sepsis.
- ❒ If possible, oxygen saturation should be measured in all comatose patients or patients with altered mental status. All of these patients should be given supplemental oxygen.

- ❒ Bedside glucose testing should be performed in all patients with altered mental status. Administer intravenous dextrose (adults: D50W; children D25W 2-4 cc/kg). Glucose should be given immediately to all persons with **suspected** hypoglycaemia even if the BM reading is normal (since false negatives can occur). It is dangerous to wait for the formal laboratory measurement of glucose before giving D50W.

- ❒ Naloxone may be given to all obtunded patients or reserved for those with hypoventilation, small pupils, or history of opioid use. In apnoeic patients the initial dose of naloxone is 2 mg. If the patient is ventilating, it is reasonable to start with 0.2 mg of naloxone and titrate to effect. This approach is less likely to cause opioid withdrawal in habituated patients. Most patients will respond to small doses of naloxone but up to 10 mg may rarely be required.

- ❒ Flumazenil, a benzodiazepine antagonist should NOT be routinely administered in the patient presenting with coma or altered mental status. Reversal of benzodiazepine effect in a mixed drug ingestion involving cyclic antidepressants and chloral hydrate may result in seizures or dysrythmias with fatal outcomes.

(b) Seizures

- ❒ Toxic seizures are often transient, in which case no specific treatment is required.

- ❒ When treatment is required, benzodiazepines (e.g., diazepam or lorazepam) are usually effective.

- ❒ If benzodiazepines fail, barbiturates (e.g., phenobarbital) almost always suffice.

- ❒ Phenytoin probably has no role in toxin-induced seizures and is theoretically harmful in tricyclic poisoning.

- ❒ Phenytoin also has no role and is harmful in theophylline overdoses.

- ❒ Isoniazid and some toxic mushrooms may cause severe seizures that respond poorly to the usual treatment. Pyridoxine (vitamin B6) is required in these unusual poisonings.

(c) Agitation

- ❒ Severe agitation presents a risk to both the patient and health care providers and should be considered as a medical emergency.

- ❒ Police or paramedics who bring a severely agitated patient to the hospital should be asked to remain until the patient has been safely restrained and adequately sedated.

- ❒ Immediately life-threatening causes such as hypoxia, hypoglycaemia, head injury, and CNS infection should be considered and treated as indicated.

- ❒ Management consists of pharmacological sedation, judicious use of physical restraint and a diligent search for a life threatening cause of agitation.

- ❒ Venous access can usually be achieved with sufficient manpower and it is preferable to use intravenous rather than intramuscular sedation.

- ❒ Benzodiazepines such as diazepam or lorazepam (titrated to effect in aliquots of 5 to 10 mg every 5 minutes) are the drugs of choice for rapid sedation in most cases of toxin-induced agitation but carry the risk of respiratory depression in patients poisoned with alcohol or another sedative.

- ❒ Agitated patients often develop life-threatening hyperthermia, so an accurate measurement of temperature is imperative in all of these patients. Patients who feel hot to touch should be cooled empirically if there is any delay in obtaining an accurate temperature.

(d) Hypotension

- ❒ Drug-induced hypotension is most often caused by vasodilatation or volume loss and usually responds to fluids or catecholamine vasopressors.

- ❒ Bicarbonate may be required for hypotension caused by tricyclic antidepressants or other drugs that inhibit sodium channels.

- ❒ Hypotension caused by cardiotoxic drugs such as ß-blockers, calcium channel blockers, or sodium channel blockers may require glucagon, calcium, or catecholamine vasopressors. The Poisons Centre should be involved early in the management of such cases.

(e) Drug-Induced Bradycardia

- ❒ Agents causing bradycardia include opioids, cholinergic agents (carbamazepine included), organophosphates, antiarrhythmics, digoxin, beta-blockers and calcium channel antagonists.

- ❒ Opiates cause moderate bradycardia that responds to naloxone.

- ❒ Standard doses of atropine (0.5 to 3mg) may be effective in mild cases of drug-induced bradycardia.

- ❒ Large doses of atropine may be required to treat bradycardia and other toxicity caused by cholinergic agents such as organophosphate insecticides.

- ❒ Pacemakers should be considered when bradycardia fails to respond to atropine. Pacemakers should be avoided in digoxin overdose because of the risk of inducing ventricular arrhythmias.

- ❒ Digoxin induced bradycardia may require Digibind®.

- ❒ Bradycardia caused by calcium channel blockers or ß-blockers is often difficult to treat and may require glucagon, catecholamine infusions, or more specialised therapy.

- ❒ The Poisons Centre should be consulted for patients with significant drug-induced bradycardia, especially if it does not respond to atropine.

(f) Intractable Vomiting

- ❒ Toxin-induced intractable vomiting usually responds to metoclopramide. The initial dose is 10 mg intravenously and a total dose of up to 1mg/kg may be required.

- ❒ When metoclopramide fails, a more potent agent such as ondansetron (8 mg IV over 15 minutes) may be required.

- ❒ Vomiting associated with activated charcoal administration may be treated by having the patient take charcoal through a straw or through a nasogastric tube. Administering activated charcoal through the nasogastric tube by slow drip rather than by push may be successful in these circumstances.

- ❒ When vomiting complicates whole bowel irrigation the procedure should be stopped until vomiting is controlled, then restarted at a lower rate.

- ❒ Numerous toxins may cause vomiting in overdose. Common causes of severe vomiting include digoxin, lithium, iron, theophylline, heavy metals, paracetamol acetosalacylic acid.

History

- History and physical examination are performed concurrently with stabilisation.

- The history should include the five 'Ws'

  - ***Who:*** the patient's age, weight, relationship to others present, and gender;

  - ***What***: the name and dosage of medication(s), substance(s) of abuse or other co-ingestants and amount ingested;

- ***When:*** the time and date of ingestion;
- ***Where***: the route of poisoning; and
- ***Why***: whether intentional or accidental, and associated details.

- Other important historical points include a review of systems, specifically the presence of seizures, agitation, coma, vomiting, headache, and shortness of breath.
- Doctors should be aware that in some cases the history is unreliable. Patients may not know what they ingested, communication may be impeded by the patient's altered mental status or psychosis, or the patient may intentionally mislead the doctor.

Physical Examination

- A complete physical examination should be performed to detect complications and to help with the diagnosis.
- Specific attention should be paid to vital signs, mental status (depressed or agitated), respirations (depressed, evidence of pulmonary oedema or aspiration), pupils (size, reactivity, presence of nystagmus), skin (diaphoresis or abnormally dry, blisters), bowel sounds (increased or decreased).
- Based on findings from physical examination, the clinician should specifically consider the presence of a toxidrome.

Diagnosis

- Identification of the toxin involved is based on history, physical examination and clinical course as well as selected diagnostic tests (see below).
- Specific drug levels (as discussed below) may be helpful in confirming the diagnosis and in making management decisions.

Consultation

Consultation is required if:

- the patient is unstable;
- clinical presentation is inconsistent with suspected toxin;
- assistance is needed with any of the following:
  - selection of appropriate investigation and therapy;
  - interpretation of test results;

  - recommendations regarding selective and progressive testing;
  - transfer decisions;
- access to medical toxicologist is desired;
- patient fails to respond to treatment.

Diagnostic Tests

Laboratory evaluation is indicated in the following cases:

- when the ingested substance is unknown;
- when the toxin has the potential to produce moderate to severe toxicity;
- the patient has more than minimal symptoms.

Additional tests for an intentional overdose include the following:

- An electrocardiogram as a screen for poisoning with tricyclic antidepressants or other cardiotoxic agents. (Tricyclics cause widened QRS intervals and tachycardia.);
- Chest radiographs are useful to detect pulmonary damage in patients with suspected aspiration, non-cardiogenic pulmonary oedema, or other lung injury;
- Abdominal radiographs are useful screening tools in patients who may have ingested radio-opaque material such as a lithium, iron, lead, and other heavy metals. Drug packets and enteric-coated compounds may also be detectable on plain films.

Decontamination

- After the patient is stabilised, consideration should be given to removing the toxin. The choice of decontamination should be made based on the clinical status and the suspected toxin.
- Inhalational exposure: patients with an inhalational exposure should be removed from the source, with care taken to avoid exposure of the rescuers.
- Cutaneous exposure: when toxic compounds have been splashed into the eyes or onto the skin, copious irrigation with water is usually enough to remove the poison.

Transfer

Consider the transfer of the patient in the following circumstances:

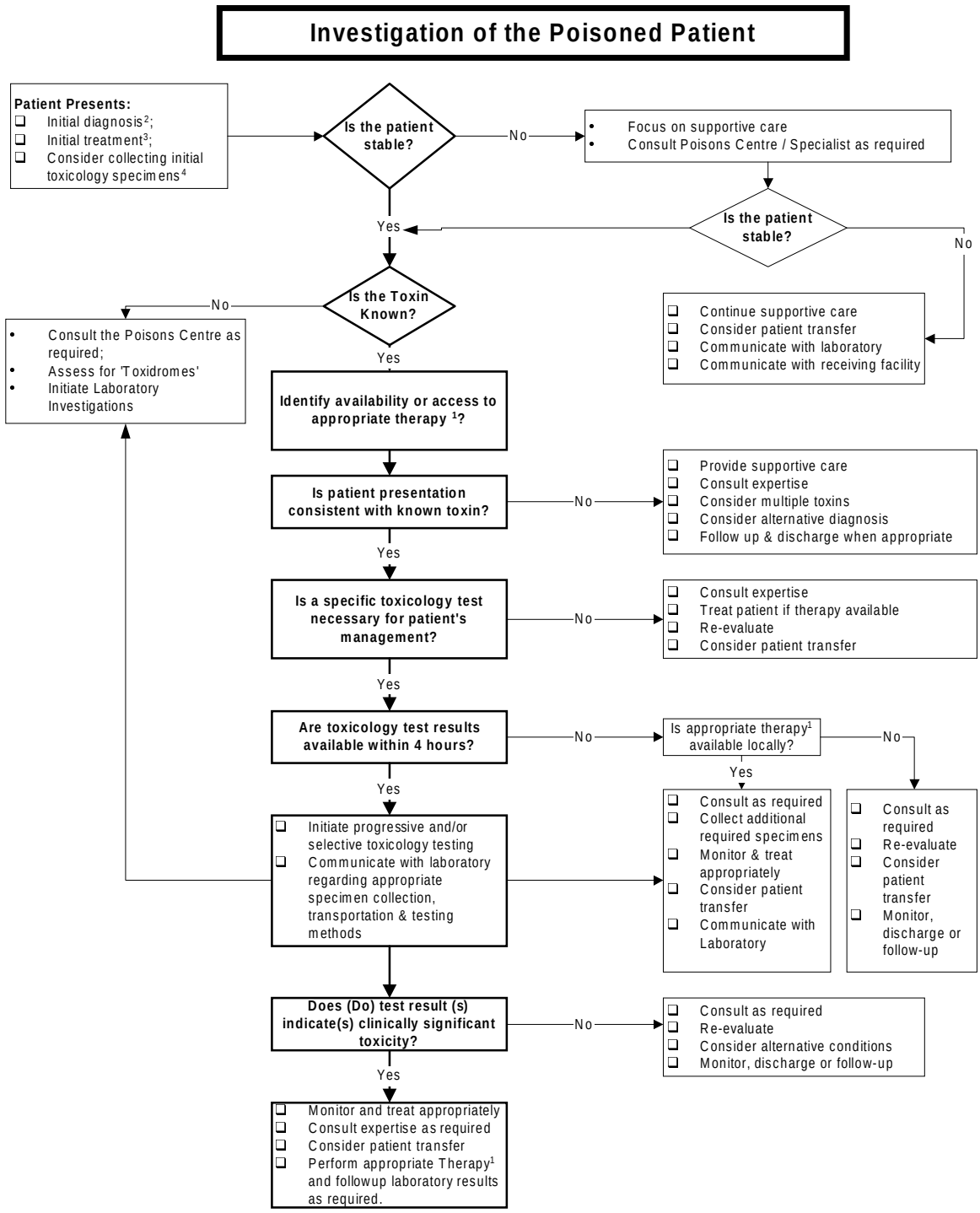
- Inability to stabilise patient;

- Deteriorating patient;
- Resource limitations including staff, timely diagnostic testing and monitoring equipment;
- Clinical judgement suggests a need for transfer;
- Inability to provide patient with ongoing maintenance;
- Lack of availability of toxin-specific therapy.

ALGORITHM FOR MANAGEMENT OF THE POISONED PATIENT

(Note the algorithm on page [42] that outlines the decision-making standards currently required for appropriate management of the poisoned patient). This algorithm was developed and provided by the Alberta Canada Guidelines Group and presented in a comprehensive monograph on Assessment and Management of Poisoned Patients published in 1998.

The primary focus is on assessing the patient's stability, focusing on supportive care that includes maintenance of airway, breathing and circulation; considering transfer of the patient to access appropriate therapy and ensuring that alternative conditions that may be contributing to the patient's condition are considered. The algorithm continues to remind clinicians that at any time in the course of the intoxication, where the patient's condition is seen to deteriorate, then they must consider transfer.



FOOTNOTES

1. Therapy includes but is not limited to pharmacotherapy, appropriate antidote therapy and treatments such as dialysis;
2. Rapid blood glucose, Pulse oximetry, cardiac monitoring, ABGs, ECG, Point-of-care 'elicit drugs kit' etc.
3. 50% dextrose, naloxone, thiamine
4. Urine: 10 ml (minimum volume)
Blood: One FULL collectin tube
adults - 10 ml
child - 3 ml

Names have been removed to protect privacy. Identifying letters are assigned in alphabetical order and bear no relationship to the person's actual nam

CARBAMAZEPINE POISONING

Carbamazepine (tegretol) is an anticonvulsant medication that shares some structural and pharmacological features with tricyclic antidepressants and meprobamate which together explain much of the adverse effects found with severe overdose (carbamazepine levels >85mumol/L [>20 mcg/mL] are associated with more severe toxicity[1].

1. Diagnosis:

a) Symptoms: nausea, vomiting, bradycardia, AV block, hypotension or hypertension, respiratory depression, lethargy, coma, dystonic posturing, anticholinergic symptoms, syndrome of inappropriate antidiuretic hormone (SIADH), abnormal deep tendon reflexes, seizures, ataxia.

b) Serum levels poorly correlate with toxicity, treatment should proceed based on clinical status with respiratory depression, coma and seizures being the most worrisome.

c) ECG may show prolonged PR, QRS, or QT intervals, but malignant dysrhythmias are rare.

2. Treatment:

a) Maintain airway and cardiovascular status

b) Activated charcoal and cathartics for significant ingestions; multiple doses of charcoal should be used particularly for patients who have ingested large doses and/or slow release formulations.

c) With prolonged coma [> 16 hours] charcoal haemoperfusion[2] should be considered.

d) Limited use of physostigmine for dystonic/athetoid posturing.

e) Seizures should be treated with benzodiazepines and phenobarbital.

[1] Montgomery VL, Richman BJ, Goldsmith LJ, Rodgers GC Jr. Severity and carbamazepine level at time of initial poison centre contact correlate with clinical outcome in carbamazepine poisoning. J Toxicol Clin Toxicol – 1995;33(4):311-23.

[2] Low CL, Desai R, Bailie GR. Treatment of acute carbamazepine poisoning by haemoperfusion. American Journal of Emergency Medicine. Vol 14; No. 5, Sept 1996.

MULTIPLE-DOSE ACTIVATED CHARCOAL AND HAEMOPERFUSION IN ACUTE CARBAMAZEPINE POISONING

The risk and severity of toxicity increases as plasma carbamazepine concentrations increase above the therapeutic range. The prognosis after massive overdose is unpredictable with between 5 to 38% of comatose patients dying[3].

Treatment is supportive, however, dialytic therapies have been used as adjunctive therapies for the management of severe poisoning with carbamazepine (CBZ).

CBZ is highly bound to plasma proteins (80%) with a moderately large volume of distribution (Vd 1.0 to 2.0 L/kg). Renal excretion accounts for only 1% to 3% of its total elimination and 3% of the elimination of its active epoxide metabolite.

Hepatic metabolism is the major route of elimination resulting in the production of the active metabolite. For these reasons, haemodialysis and peritoneal dialysis would not contribute significantly to its elimination.

Treatment with haemoperfusion (HP) has met with some success although the efficiency of HP is unclear, since it is apparently dependent on whether the patient has been on chronic CBZ therapy prior to the toxic ingestion. Because chronic therapy of CBZ results in autoinduction of hepatic metabolic enzymes, haemoperfusion may not contribute significantly to the already very high intrinsic clearance of CBZ.

In reports, clearances of CBZ have been between 2 mL/hr/kg and 10 mL/hr/kg. More rapid clearance of CBZ may be inhibited by the fact that absorption of CBZ in overdosed patients can be greatly delayed because of the anicholinergic effect of CBZ. This is known to lead to a slowing in gut motility. It has been reported that the time for peak serum concentration can be delayed to 72 hours after ingestion due to this physiological response to the drug.

In situations where CBZ levels are found to be increasing even 20 hours after ingestion, two methods assist in actively decreasing plasma levels. These two methods include multiple doses of activated charcoal and charcoal haemoperfusion.

Multiple-dose activated charcoal has been demonstrated to increase the elimination of CBZ. Studies have utilised diluted charcoal administered through a nasogastric tube at a dose of 1 g/kg every 4 hours, and a saline cathartic at the same dosage administered every 12 hours. In even the most severe poisoning cases, clinical improvement occurred after 12 to 24 hrs. In one study by Montoya-Cabrera et al[4], activated charcoal was

[3] Litovitz TL, Felberg L, Soloway RA, et al: 1994 Annual Report of the American Association of Poison Control Centres Toxic Exposure Surveillance System. Am J Emerg Med 1995;13:551-597.

[4] Montoya-Cabrera MA, Sauceda-Garcia JM, Escalante-Calindo P et al. Carbamazepine poisoning in adolescent suicide attempters. Effectiveness of multiple-dose activated

administered as above to 8 consecutive adolescent suicide attempters with all but one very severely intoxicated patient demonstrating clinical improvement in less than 24 hours. Their conclusion was that '*Multiple dose activated charcoal is an effective procedure in enhancing CBZ elimination in overdosed patients as well as being relatively free from serious side-effects, widely available, inexpensive and non-invasive*'.

Haemoperfusion has been shown to increase the clearance of CBZ fivefold, shortening the $t_{1/2}$ of CBZ from 30 hours to 6 hours during the treatment process. [5,6,7]

CLINICAL POLICY FOR THE INITIAL APPROACH TO THE PATIENT PRESENTING WITH ALTERED MENTAL STATUS[8]

Altered Mental Status is a collective phrase that denotes an undifferentiated assortment of disorders of mentation. These disorders include impaired cognition, attention, awareness, and level of consciousness. Alterations may be transient, sustained, fluctuating, or progressive.

Patients presenting to EDs with a principal complaint of 'altered mental status' present a formidable challenge to the doctors, as there are a number of conditions that need to be considered.

Most of the actions involved in the initial management and diagnosis of patients with acute alteration in mentation are the basic ones of monitoring, stabilisation and support (that is, airway assessment, cardiac monitoring, consultation and clinical assessment).

Altered mental status is a common presenting complaint in the ED. Although alterations in mental status occur at all ages, the elderly are at especially high risk of morbidity and mortality from the underlying problem(s) causing the 'alteration in mental status' observed on acute admission.

Common causes of altered mental status in the elderly include drugs, infections, metabolic disturbances, trauma, cancers and cardiovascular disease. For younger patients the primary aetiology is most commonly drug overdoses, accidental poisoning,

---

charcoal in enhancing carbamazepine elimination. Arch Med Res – 1996 Winter; 27(4):485-9.

[5] Groot G, Heijst ANP, Maes RAA: Charcoal hemoperfusion in the treatment of two cases of acute carbamazepine poisoning. Clin Toxicology 1984;22:349-362.

[6] Gary NE, Byra WM, Eisinger RP: Carbamazepine poisoning: Treatment by hemoperfusion. Nephron 1981;27:202-203.

[7] Vree TB, Janssen TJ, Hekster, et al: Clinical pharmacokinetics of carbamazepine and its epoxy and hydroxy metabolites in humans after an overdose. Ther Drug Monit 1986;8:297-304.

[8] Annals of Emergency Medicine February 1999 – volume 33 number 2.

infections and trauma. Acute poisoning due to drug overdose is the most likely cause in younger patients presenting with altered mental status.

For patients presenting with the clinical symptoms of 'alterations in mental status', an accurate and thorough history is an essential part of the database that must be collected. Often this is at a time when the patient is least able to provide it himself or herself. It is extremely important, therefore, to interview family members and care providers regarding the patient's baseline condition.

In the absence of knowledge of the patient's condition, it must be assumed to be an acute change from baseline. It is equally important, even when information is available, not to accept a predetermined diagnosis without adequate consideration of the history, physical examination and selected diagnostic studies.

For all patients with 'altered mental status', the first consideration should be airway adequacy and the potential for cervical spine injury. All patients require rapid glucose determination/50% dextrose administration and consideration of oxygen saturation measurement. Provision of naloxone and thiamine provides some advantage for patients given the potential possibility of either a narcotic overdose or acute thiamine deficiency causing the altered mental status.

Frequently, the most challenging aspect of patient care for those presenting with altered mental status, is the recognition and identification of a toxic substance exposure as a potential cause of the patient's symptoms.

Emergency doctors must maintain a high level of clinical suspicion and consider toxicological causes for patients presenting with 'alterations in mental status'.

Because different institutions have different resources and capabilities in the management of these patients, the recommendation to admit a patient (or to obtain a specific toxicological or poisons consultation) may require transfer of the patient to an institution better able to deal with the patient's specific needs.

Initial stabilisation and treatment focus on removal of the toxicological agent to prevent further exposure and toxicity.

Gastrointestinal decontamination represents an area of tremendous controversy. Although some issues involving gastrointestinal decontamination are unresolved, the majority of the current literature supports the following conclusions:

1. Activated charcoal adsorbs almost all commonly ingested drugs and chemicals and usually should be administered to most overdose patients as quickly as possible. Commonly ingested substances not adsorbed include iron, lithium, ethanol, and potassium.

2. Syrup of ipecac generally is believed to be of little value in the ED.

3. Gastric lavage is of unproven benefit for routine use. In general, this procedure is best reserved for patients who may have recently ingested a life-threatening overdose. In these cases, administering a dose of activated charcoal before lavage is of theoretical benefit.

4. The use of cathartics is also of unproven benefit, but a single dose is commonly administered with activated charcoal to speed gastrointestinal transit and prevents charcoal inspissation. Multiple doses of any cathartics should not be used because dehydration and electrolyte imbalances may occur.

5. Whole-bowel irrigation has been shown to be effective under certain conditions, especially when activated charcoal lacks efficacy.

No definitive recommendation can be made on the use of ipecac, gastric lavage, cathartics, and whole-bowel irrigation for all patients. If any of these modalities are used, the choice should be based on consideration of the offending toxic substance, time of exposure, and condition of the patient. The use of forced diuresis, haemodialysis, and charcoal haemoperfusion to eliminate toxic substances must be based on the suspected toxic substance and physiological status of the patient.

Effective treatment may be provided without a toxicological screen after obtaining a history and physical examination focused on identifying the toxic substance, or a clinical toxic syndrome, and establishing the physiological status of the patient.

Specific treatments must be based on the patient's physiological condition and suspected or known toxic substances.

Supportive care is successfully combined with removal or elimination of the toxic substance for most cases.

For some toxic substances such as paracetamol, methanol/ethylene glycol, lithium, carbamazepine, tricyclics, digoxin and salicylates, specific quantitative tests may be useful in determining appropriate treatment and disposition. The physician for individual patients must determine the value of quantitative and qualitative toxicological tests in patients who have ingested unknown substances.

Some patients may be effectively treated with specific or non-specific antidotes. Generally, the use of antidotes should be individualised to the toxic substance and physiological condition of the patient.

The large number of potentially toxic agents and their diverse effects may require Emergency Doctors to access specific expertise, information, or both. Toxicologists, poison information centres, toxicology references, and computerised databases may aid the doctors in the treatment of some patients.

The majority of toxic exposures are readily managed in the ED with the following:

1. General supportive care

2. Treatment of respiratory, cardiovascular, and neurological complications
3. Attempts to identify the toxic substance(s)
4. Appropriate decontamination techniques
5. Specific therapy for treatable toxic exposures
6. Consultation/reporting with medical toxicologists or poison information centres when appropriate
7. Psychiatric evaluation/referral when appropriate."