

INQUEST INTO THE DEATH OF

L I S A S H O R E

THE EVIDENCE OF DR. STUART MacLEOD

TAKEN JANUARY 20, 2000

BEFORE DR. JAMES CAIRNS, DEPUTY CHIEF CORONER

CORONER'S COURT, TORONTO

A P P E A R A N C E S:

Counsel for the Coroner	MARGARET BROWNE, MS.
Counsel for the Shore Family	FRANK K. GOMBERG, ESQ.
Counsel for the Hospital for Sick Children, et al	PATRICK HAWKINS, ESQ. RENEE A. KOPP, MS.
Counsel for Dr. M. Schily and Dr. M. Catre	ANNE POSNO, ESQ.

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1 DR. STUART MacLEOD, SWORN

2 EXAMINATION IN-CHIEF BY MS. BROWNE:

3 Q. Dr. MacLeod, I have a copy of your CV
4 here which I'm going to have marked in a moment, but
5 suffice it to say that it runs to 31 pages. I'm almost
6 tempted to suggest you must be awfully old. We've
7 heard somewhat from Dr. Mayers today that you're more
8 than a physician, that you're also a pharmacologist and
9 a number of other things; you have a Bachelor of
10 Science in Medicine from the University of Toronto, you
11 have an MD from the University of Toronto, you have a
12 PhD from McGill in Pharmacology and you have done a
13 thesis on something that I couldn't even imagine,
14 hepatic microsomal drug oxidation and electron
15 transport in immature rats, rabbits and humans.

16 A. All of that is correct.

17 Q. You must have a very full lab; rats,
18 rabbits and humans?

19 A. Not at the same time.

20 Q. You are now in the Faculty of Health
21 Sciences at McMaster University and you are a professor
22 in the Department of Clinical Epidemiology,
23 Biostatistics and Pediatrics?

24 A. That's correct.

1 Q. What's the St. Joseph's Hospital, Father
2 Sean O'Sullivan Research Centre? That appears in your
3 correspondence. What is that?

4 A. Oh, that is the research centre at St.
5 Joseph's Hospital in Hamilton. St. Joseph's is a
6 teaching hospital within the academic health science
7 centre in Hamilton, and I'm the director of that
8 research centre.

9 Q. The research centre, does it focus on
10 any one thing, or is it just medical research in
11 general?

12 A. Well, it has a variety of interests, but
13 one particular component of it is a unit called the
14 Centre for Evaluation of Medicines and when I moved to
15 St. Joseph's six years ago, I was the director of that
16 centre, as well, but subsequently, I have abdicated in
17 favour of one of my colleagues.

18 Q. You have also written innumerable
19 treatises on very interesting and impressive topics,
20 which I am not going to summarize now, but let me just
21 -- this is your CV and we'll mark it for the jury. Can
22 you just look at it and tell me if that's it? You can
23 probably update a bit now, but ...

24 A. Oh, yes, there's probably more recent
25 versions, but it's correct as of April of 1999.

1 Q. Can that be marked as an exhibit?

2 THE CORONER: Thank you.

3 CONSTABLE CULLETON: Exhibit 30.

4

5 EXHIBIT NO. 30: CV of Dr. Stuart MacLeod

6

7 BY MS. BROWNE:

8 Q. It might be of some use if I can pass
9 that to they jury while Dr. MacLeod is talking, they
10 could probably have a quick glance at it and give it
11 back. All right, Dr. MacLeod, I understand that you
12 were asked by Dr. Cairns to look at this case and this
13 inquest into Lisa Shore to look over certain aspects of
14 her treatment, of the drugs she was on and the
15 interaction of the drugs, in fact, to just review what
16 happened to Lisa that night in the hospital; am I
17 correct?

18 A. Yes, that's correct, primarily from a
19 pharmacology/toxicology perspective, of course, because
20 that's my expertise.

21 Q. And from a pharmacology point of view,
22 Dr. MacLeod, what were you provided with on which to
23 base your review of this case, what items of
24 information were you given?

25 A. Well, I think I had, to the best of my

1 knowledge, I had complete information about all of the
2 drug therapy that took place on the night -- the
3 evening before and the early morning of the day that
4 Lisa Shore died.

5 Q. And you had access to her chart?

6 A. I didn't -- I at no time had the full
7 hospital record. I have seen the relevant parts of it,
8 I believe, but I've never held the entire record in my
9 hand.

10 Q. Okay. And I gather that one of the
11 questions that you were asked to consider is given the
12 report by Dr. Taylor as read in by Dr. Smith, there
13 seems to be no anatomical cause of death expressed in
14 the post mortem and can you say -- did you come to any
15 conclusion as to the cause of her death?

16 A. Yes, maybe -- would it be appropriate
17 for me to speak for a moment to my letter?

18 THE CORONER: Yes, please do.

19
20 BY MS. BROWNE:

21 Q. Certainly.

22 A. I'm not sure if everybody -- do you all
23 have a copy of my letter dated November the 5th?

24 Q. Counsel have, the jury does not.

25 THE CORONER: Yes.

1 THE DEPONENT: The jury does not.
2

3 BY MS. BROWNE:

4 Q. So you'll have to explain to them.

5 A. Okay. Well, just for the benefit of
6 Counsel, I want to point out that there are two areas
7 where there are typographical errors in the report
8 dated November 5th, and they have to do with something
9 that plagues all of us who deal in pharmacology and
10 toxicology and that is the units of measurement that
11 are used when we talk about drug concentrations. So
12 under item six in my report, I cite a couple of
13 concentrations of morphine in the syringe -- or the PCA
14 apparatus, and the unit that was in the letter was
15 nanograms or ng per ml.; that should be milligrams,
16 "mg," per ml in both cases in that paragraph.

17 And then in paragraph 11, in talking
18 about the concentration of gabapentin, the unit that
19 was written was ng per ml again or nanograms per ml,
20 but it should be micrograms per ml, so it's a Greek
21 letter "mL" for ml, in paragraph 11, the second
22 paragraph under 11. So it's the range, the therapeutic
23 range reported in adults is between 2 and 8 micrograms
24 per ml.; the concentration reported in the deceased of
25 11 micrograms per ml., it was actually, I think,

1 reported by the forensic lab as 1.1 milligrams per 100
2 ml. And then the last six -- concentrations as high as
3 60 micrograms per ml. It doesn't change any of the
4 conclusions, it's just that the units were incorrect.

5 Q. Okay.

6 A. So you ask if I have, first of all, any
7 comment about the anatomic -- an anatomic cause of
8 death and that is certainly outside my field of
9 expertise, but if you've read my letter of November
10 5th, you will know that in reviewing the pathology
11 record, the post-mortem record, I noted that there were
12 some signs that were at least suggestive of there being
13 a viral myocarditis, some aggregates of cells that are
14 sometimes associated with a viral infection of the
15 myocardium, so I raised that as a possible interacting
16 factor in this death.

17 Subsequently I have seen the results of
18 additional pathological testing that was performed and
19 on the basis of that, I would say that that is not a
20 factor, so I'm not aware of there being any organic
21 disease of the heart or any other organ that would
22 account for this death.

23 Q. Perhaps you could just indicate to us
24 what you have in your letter as a pharmacological look
25 at what Lisa absorbed.

1 A. Well, you know ---

2 THE CORONER: Just so that it's clear that I
3 had written a letter to Dr. MacLeod which
4 summarized basically, the amount of
5 medication she was given. He had the autopsy
6 report, but in addition, he had been given
7 all the toxicology reports from Dr. Mayers
8 who testified earlier this morning and he was
9 able to have some conversations with Dr.
10 Mayers, as well, before he wrote his report
11 and he also had access to the Pediatric Death
12 Review Committee's report, as well, to assist
13 him. Is that a fair ---

14 THE WITNESS: Yes, that's correct. And
15 there was some discussion after May of last
16 year with the forensic lab about additional
17 testing that should be done and so I had some
18 opportunity to request additional data.

19
20 BY MS. BROWNE:

21 Q. And after you did, could you just lead
22 us to conclusions or observations?

23 A. Yes. Shall I just work through my
24 letter? Maybe that would be the easiest way of doing
25 it. I believe in the absence of any obvious anatomical

1 reason for this death or any pathological explanation,
2 it seemed reasonable to me that our attention should be
3 focused on the drug therapy in the case, with -- it
4 seemed a reasonable presumption, at least, that the
5 drug therapy may have played a role in this death, and
6 as I'm sure you've heard in the course of the inquest,
7 Lisa was taking four different -- or was taking three
8 different medications for control of her pain and then
9 was given morphine on the night of her death.

10 So I looked at the possible effects of
11 all of those drugs in this patient and, of course, the
12 first focus of attention was morphine and you know that
13 she received several doses of morphine both given
14 directly and self-administered by the PCA apparatus, so
15 that she received a total of 14.5 milligrams, beginning
16 at 23:50 or 11:50 in the evening on October 21st. And
17 as nearly as I can recall, she received all of that
18 morphine before she went up to the ward from the
19 emergency room. If we can jump ahead from -- and she
20 received no subsequent morphine, to the best of my
21 knowledge.

22 And I should say that one of the things
23 I asked the forensic lab to do was to check to make
24 certain that the morphine concentration in the pump was
25 correct, that there hadn't been some error in preparing

1 the morphine for infusion and, in fact, the morphine
2 concentration in the syringe was more or less as it
3 would be expected if somebody had put 50 milligrams of
4 morphine into a 50 millilitre syringe; that is
5 obviously the concentration in those circumstances
6 should be 1 milligram per millilitre. It was actually
7 measured by the forensic lab as 0.8, but that's within
8 the range of acceptable error, and certainly doesn't
9 imply that there was some mistake made in the
10 preparation of the morphine.

11 But then jumping ahead to the post-
12 mortem concentration, that was measured by the forensic
13 lab at 105 nanograms per millilitre. Now, that is
14 about the concentration of morphine that we see in
15 blood when it's given therapeutically for pain relief
16 in relatively high doses as Lisa received, so that
17 concentration would be completely unsurprising had it
18 been taken at 2:00 in the morning at the time when she
19 went to the ward. It's a little bit surprising
20 measured five hours later than that or at some time
21 after her death, but I think it's probably
22 understandable.

23 For one thing, the measurements of
24 morphine in blood after death are not entirely
25 accurate. There is evidence from animal studies at

1 least that morphine concentrations do change after
2 death and the morphine concentration that is measured
3 in blood after death has a tendency to be higher than
4 it would have been in life, so there may be some error
5 on that basis. It's not really an error as such, but
6 just a spuriously high concentration measured at the
7 time of death or after.

8 But in any case, we can take that as a
9 starting point and we then work backwards from there to
10 judge what the concentrations might have been at the
11 time when the last dose of morphine was administered
12 and that was at 1:07 in the morning. So the
13 concentration at 1:07 could have been on this basis as
14 high as 300 nanograms per ml. That would be really
15 considered extraordinarily high, not necessarily -- I'm
16 not suggesting that that's a lethal concentration, but
17 it's a high concentration. But for various reasons, I
18 expect that the concentration at it's maximum was not
19 as high as that. It probably was more in the order of
20 150, maybe 200 nanograms per ml., but it probably
21 wasn't any higher than that.

22 But working backwards, it is likely that
23 her concentration was at its highest at the time when
24 she had a decreased respiratory rate, the time when her
25 respiratory rate was registered at 8 to 10, so that

1 would make, from a pharmacology point of view, that
2 would make sense, that at the time when her morphine
3 concentration was highest, she did show an effect which
4 we associate with morphine, a slowing of respiratory
5 rate. And it's also a time when apparently her pain
6 came under control, as well, so again that would be
7 some indication of morphine effect. We know that she
8 fell asleep at that point, so presumably her pain was
9 controlled.

10 So I think that's -- those are the major
11 observations about morphine, so she would have had a
12 high concentration, but not -- probably not a
13 concentration that would necessarily be associated with
14 a fatal outcome and in any case, we have some physical
15 measurements that go with it, the respiratory rates and
16 the blood pressure that show that while she had an
17 effect of morphine, that she recovered from that or at
18 least compensated to some degree.

19 Q. Where did you get the information about
20 what her blood pressure was that night?

21 A. Well, I took it from the -- I'm sorry,
22 I'm not implying that there are multiple blood pressure
23 measurements, because there are not, but there are one
24 or two, as I recall.

25 Q. I don't know, the information that we

1 have and perhaps you can add to it, if you can, is that
2 there was one blood pressure taken at 1:45 a.m. and it
3 was 90 over 60.

4 A. Right, that's correct.

5 Q. So that you are able to make that
6 conclusion from that one reading?

7 A. Yeah, I'm also interpreting a little
8 bit. So 90 over 60 is a low blood pressure. The other
9 thing we know with some certainty is that her heart
10 rate increased quite dramatically to 125 or there-
11 abouts. Usually when -- the normal effect of morphine
12 on the heart is to slow heart rate, so you would
13 normally anticipate somebody who had enough morphine to
14 lower their respiratory rate, you would expect them to
15 also have a slowed heart rate.

16 Obviously that was not the case in Lisa,
17 so when heart rate accelerates like that, there are
18 some possible explanations. I mean, one possible
19 explanation is that there are some people who simply
20 show an increase in heart rate with morphine, it
21 doesn't always slow a heart rate, it usually does, but
22 not always.

23 Q. You mean that some people have the
24 response to morphine that instead of going down, their
25 heart rate goes up?

1 A. The heart rate goes up. But more
2 commonly when heart rate goes up, we assume that it is
3 because blood pressure has dropped, okay, so 90 over 60
4 isn't low, low, but it's a low blood pressure and it is
5 certainly enough to suggest that her pressure was on
6 the way down and of course we don't know if it went
7 lower. But the fact that her heart rate went up
8 suggested it may well have gone lower and again this is
9 a common observation with morphine. Morphine
10 indirectly causes a reduction in blood pressure and, in
11 fact, is sometimes used for that purpose in the
12 treatment of some other conditions.

13 Okay, so maybe I'll move on from there
14 to the other drugs. We can go back and fill in some
15 details if you wish, but I think we perhaps could go on
16 to the other drugs. Probably the most significant
17 other drug that she was receiving was gabapentin and as
18 I'm sure you've heard, this is a drug which was
19 developed for the treatment of certain kinds of
20 epilepsy but is also known to have effects in complex
21 pain conditions such as the one that Lisa had. So it's
22 now being very actively studied as a possible treatment
23 for those pain conditions.

24 She was receiving a dose of 1,400
25 milligrams a day, which certainly would have been

1 considered a high dose at the time, certainly an
2 experimental dose, but one which I think she was given
3 by people who were probably very experienced in the
4 treatment of pain conditions and they would not, I
5 think, see this dose as extraordinary, and certainly
6 today there are many people receiving doses two or
7 three times this as part of the treatment of their pain
8 condition, so, it's high compared to the doses that are
9 used in epilepsy, but not high compared to those that
10 are used in the treatment of pain.

11 And again her blood concentration that
12 was measured after death and I must say we know almost
13 nothing about post-mortem concentrations of gabapentin
14 because this is a relatively new drug and there -- it
15 is by all reports an extremely safe drug and so there
16 haven't been many cases of deaths with gabapentin and
17 for one reason or another, it hasn't been studied
18 extensively, so there's not a lot of information.

19 But this level, the level that was
20 measured by the Centre for Forensic Sciences seems
21 quite in keeping with the dose that she was receiving
22 and is highly unlikely to have been the cause of her
23 death. There are a few reports in the literature of
24 people taking larger overdoses of gabapentin and first
25 of all, these are usually not fatal in much higher

1 concentrations. There are concentrations of 60
2 micrograms per ml. that are recorded in people who have
3 survived, so it's highly unlikely that gabapentin alone
4 was the cause of death in this case.

5 The other drugs that she was getting,
6 carbamazepine, is actually somewhat similar to
7 gabapentin in that this is a drug that was developed
8 for epilepsy, but has been known for at least 30 years
9 to have substantial effects in the treatment of some
10 unusual pain syndromes and so it's not surprising that
11 this drug was being used and, again, the post-mortem
12 concentrations are unremarkable and it's, I think,
13 highly unlikely that this drug had anything to do with
14 Lisa's death.

15 The fourth drug she was getting is
16 amitriptyline and this is an anti-depressant drug which
17 has also been studied quite extensively for the use --
18 for it's use in the treatment of some unusual pain
19 syndromes. For reasons that are not fully understood,
20 it is effective in certain kinds of pain and I'm sure
21 the intention here was to try to amplify some of the
22 beneficial effect of the other drugs, the carbamazepine
23 and the gabapentin.

24 Amitriptyline is, in contrast to the
25 other two, a relatively dangerous drug; I mean, we see

1 many deaths when this drug is taken in overdose. It
2 certainly is a drug which is capable of causing cardiac
3 rhythm disturbances and -- but I think that's not
4 relevant here, in that the dose was very small compared
5 to the sorts of doses that are taken in depression or
6 taken by people who are taking an overdose, so it may
7 have been a small contributory factor, but it's highly
8 unlikely that this was a major, major factor.

9 I mean, the thrust of one thing that is
10 worth noting about it is that when taken in overdose or
11 even when taken in normal doses, it may cause some
12 cardiac acceleration; it potentiates the sympathetic
13 nervous system, so it makes your heart beat faster.
14 Given the fact that Lisa did show this rapid heart rate
15 through the hours leading up to her death, it is
16 possible that amitriptyline was contributing to that
17 and that, in turn, might have predisposed her to a
18 problem with cardiac rhythm. So that's the situation
19 as far as the drugs are concerned.

20 So coming back to the question of
21 whether or not there's anything in this story which
22 might account for Lisa's death, I think it's clear that
23 she had an amount of morphine that caused some
24 significant effects, it did slow her respiration, it
25 may have contributed to her tachycardia, to her fast

1 heart rate and I think if she had died at 2:00 in the
2 morning, perhaps we would have been very much inclined
3 to say that it was -- that morphine was the cause of
4 death, but the fact that she didn't die at that time
5 and she appears to have recovered in many ways from
6 those effects, which suggests that morphine -- it would
7 suggest to me at least that morphine alone is not
8 likely the cause of death.

9 Q. You went through the various drugs
10 individually.

11 A. Yes.

12 Q. It is possible that combinations of
13 them, the fact that they were all at the same time in
14 Lisa ---

15 A. Yes.

16 Q. --- had some effect?

17 A. Well, that's really exactly what I was
18 coming to. I think that as I've thought about this
19 over the last seven or eight months, the only -- I
20 guess my first conclusion eight months ago was that
21 there was probably an interaction of some kind among
22 these drugs. There is -- I have in searching the
23 literature looking for some explanation of this found
24 that there is at least one paper that describes an
25 interaction between gabapentin and morphine in animal

1 studies, and it does look from those studies in rats as
2 if morphine is more active, morphine's actions are
3 amplified in animals that are treated simultaneously
4 with gabapentin, so the gabapentin makes the animal
5 more sensitive to the pain-killing effects of morphine
6 and the pain-killing effects are at the same receptors,
7 occur at the same receptors that mediate respiration,
8 so there are respiratory depression. So you would
9 anticipate that the combination of morphine and
10 gabapentin might have more respiratory depressant
11 effect than would morphine alone.

12 Q. Are you referring to this article in the
13 International Association for the Study of Pain? It's
14 called what you were describing, I have a copy of it
15 here, I'll show it to you.

16 A. That's the one, yes.

17 Q. Is this a magazine published that just
18 goes into pain by itself without the causes of pain?

19 A. No, this is a journal that publishes
20 studies related to the causes and treatment of pain.

21 Q. I have an extra one of these, Mr.
22 Coroner.

23 THE CORONER: No, I don't want it as an
24 exhibit.

25 MS. BROWNE: I don't know that it would make

1 any sense to ---

2 THE CORONER: It's a very complex,
3 scientific article and I think we'd be much
4 better with Dr. MacLeod's lay language
5 explanation of what it's saying. I don't
6 think it will add anything to have the jury
7 trying to read it. I read it; it didn't make
8 much sense to me. The jury are much brighter
9 than I am, but at the same time, I think we
10 can benefit most from Dr. MacLeod's
11 interpretation of what that may mean. I hope
12 you don't disagree with me, Doctor?

13 THE WITNESS: No, I don't disagree. I think
14 the conclusion of this paper is, as I've
15 said, that gabapentin and morphine potentiate
16 each other or at least gabapentin potentiates
17 morphine, to be more correct. So that at
18 least is the beginnings of an explanation for
19 a possible interaction that may have affected
20 Lisa.

21 Now, I have to say that there are
22 probably thousands if not tens of thousands
23 of people in the world who have received this
24 combination of morphine and gabapentin and
25 we're not seeing a rash of reports of this

1 kind of death, but that's not to say that
2 Lisa may not be representative of a small
3 group of people who are particularly
4 predisposed to this interaction.

5 We see these kinds of things with drug
6 therapy, not everybody responds in the same
7 way, even with a drug like morphine which has
8 been around for thousands of years. We know
9 that people have differing degrees of
10 sensitivity to morphine, so some people are
11 much more likely to have respiratory
12 depression than others. Some people are much
13 more likely to get pain relief than others,
14 so it's -- there is a range of normal, so I
15 -- but my conclusion from this is that there,
16 in the absence of any other explanation, one
17 should, I think, interpret these events as
18 showing an interaction at least between
19 gabapentin and morphine, maybe involving at
20 least to some degree the other two drugs,
21 amitriptyline and carbamazepine and that
22 somehow the interaction of these drugs at the
23 very least amplified the morphine effect,
24 caused respiratory depression, probably
25 caused a lower oxygen tension in the

1 patient's blood, we don't know that because
2 there weren't measurements, that could have
3 done that, it certainly caused an increase in
4 heart rate by one mechanism or another and
5 that somehow in that situation, she had a
6 disturbance of her cardiac rhythm that was
7 fatal.

8
9 BY MS. BROWNE:

10 Q. Those are my questions. You will be
11 questioned by others here.

12 THE CORONER: Dr. MacLeod, I know that one
13 of the comments you made to me, you phoned me
14 about was that it would have been of some
15 assistance to you if, in fact, you had
16 further blood pressure readings, particularly
17 when her respiratory rate was 8, which is
18 considered to be low, that you would have
19 liked to have seen an evaluation at that time
20 that included her pulse and her blood
21 pressure and subsequent blood pressure
22 readings would have helped you to be less
23 theoretical about this and would have given
24 you a closer picture of what was going on; is
25 that a fair comment?

1 THE WITNESS: Oh, no question. One can only
2 interpret these events by interpolation.
3 There is not a great deal of data other than
4 the blood concentration measurements that
5 came after death and, of course, the factual
6 knowledge of what drugs were administered.
7 The physical measurements that we would need
8 to interpret this for the most part are not
9 there.

10 THE CORONER: Mr. Krkachovski?

11 MR. KRKACHOVSKI: Thank you, Mr. Coroner.
12

13 CROSS-EXAMINATION BY MR. KRKACHOVSKI:

14 Q. Just to pick up on the last comment,
15 Doctor, I gather what you're saying is there is lack of
16 data in Lisa's chart, which, really, the flow sheet?

17 A. That's correct.

18 Q. I'm not sure what exhibit number the
19 bristol board is of the flow sheet; perhaps we can get
20 it up there? So, for example, in determining or trying
21 to determine a cause of death, it would have been
22 helpful to have blood pressure readings throughout?

23 A. Absolutely, particularly here at 2:50 --
24 particularly at 2:50, yes, as the Coroner has said,
25 when -- when the respiratory rate went down to 8 or

1 even 10, at that point it would have been, I think,
2 important to know what the blood pressure was.

3 Q. Now, you indicated that in your view,
4 the morphine concentration would have been the highest
5 when the respiration was at its lowest, which would be
6 8, which would be at 2:50 a.m.; am I correct?

7 A. Yes, that's correct. It probably was at
8 its highest somewhat before that, given what we know
9 about the absorption of morphine, but it's not unusual
10 that the maximum physical effect of the drug follows by
11 some time the maximum blood concentration.

12 Q. That's exactly what I'm getting at, that
13 whatever respiratory consequence there might be would
14 occur some time after the drug is administered?

15 A. Yes, that's correct.

16 Q. In fact, the records indicate that the
17 last time Lisa actually got morphine was at 1:08, the
18 request was 1:07 and the administration was 1:08 a.m.,
19 which would be roughly an hour and 40 minutes before
20 the concentration is at it's highest?

21 A. Yes. Well, I'm sorry, that was an hour
22 and 40 minutes before we saw the maximal effect.

23 Q. Right.

24 A. I don't know when the concentration
25 would have been at its highest, but probably at about

1 1:30 or something like that.

2 Q. But the maximal effect is about an hour
3 and 40 minutes later?

4 A. That's correct.

5 Q. Okay. Now I note that at 2:50 the
6 depression is 8 -- or, pardon me, the respiration is 8
7 and 10 and then at 4:15, it's back down to 10. Does
8 that suggest to you that the respiratory depression is
9 continuing? If you have a look, you'll notice ---

10 A. Yes. No, I see where you're looking.

11 Q. There's a good deal of fluctuation from
12 2:50 to 4:15 when it goes back to 10 at some point.

13 A. I must say, I mean, that number 10 there
14 looks anomalous to me, you know, given the fact that
15 that's the figure at 4:15 and at 4:20 it's 16 and at
16 4:05 it's 14, I wouldn't want to interpret it very
17 much. I think it's very unlikely that the respiratory
18 rate really went down to 10 and back to 16. It's much
19 more likely that, you know, it was really 12 or -- but
20 I wasn't there, I don't know how the nurse recorded
21 this respiratory rate, how long she took, how long she
22 observed the patient, but I wouldn't want to pin a lot
23 of interpretation on a single reading at that time.

24 Q. Are you familiar with the Corometric
25 monitor at all?

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A. No, I'm not.

Q. All right.

A. Well, was that read from a monitor?

Q. Well, we won't know until the nurses testify but that's what I was alluding to, that presumably if she read it off a monitor as opposed to taking it herself physically, it would more likely be a correct number; would that be fair?

A. Oh, yes, absolutely, yes. I forget what this says over here. Can anybody help me with that notation there?

MR. GOMBERG: Which one?

THE WITNESS: Under "very drowsy," what does it say?

MR. GOMBERG: It says "head of bed," "HOB up."

THE WITNESS: "Head of bed elevated," okay, right, HOB. So, of course, if that was a monitor reading, it's probably correct and I could only say that respiratory rates do fluctuate, usually not quite that dramatically and it may depend on whether she was sleeping or -- we all breathe quite a bit slower when we're sleeping.

1 BY MR. KRKACHOVSKI:

2 Q. Now, the nursing evidence is anticipated
3 to be that when the vital signs were checked
4 physically, they were also checked against the monitor
5 to make sure that the two coincided and the two
6 coincided so that again I use the word "anticipate;" I
7 anticipate the nursing evidence will be that, in fact,
8 at 4:15 her respiration was 10 as recorded on the flow
9 sheet. If that is, in fact, the evidence, what would
10 you conclude from that?

11 A. Well, I would probably relate it to this
12 statement up here that she was very drowsy and perhaps
13 she went into a deeper sleep. We know for certain that
14 she had morphine present in her system, she had a good
15 amount of a respiratory depressant, so it's not -- a
16 respiratory rate of 10 is not in any way inexplicable.

17 I, frankly, would have been more focused on the heart
18 rate of 134, which is really, really quite extra-
19 ordinary. Had I been there at the time, I would have
20 said, "I want to know why she had a heart rate of 134."

21 But I think the reaction as reflected here is
22 appropriate. It looks like the nurse came back five
23 minutes later to check. They are sufficiently
24 concerned about a heart rate of -- a respiratory rate
25 of 10 that she came back five minutes later to check

1 and found it was 16 and then stayed up at that rate
2 from that point on, so if it was really 10, there was
3 appropriate attention paid to that from the record.

4 Q. Would you have expected the nurse to do
5 anything other than what is reflected in the record,
6 given the reading of 134 at 4:15?

7 A. Well, this is one of many points at
8 which I think, at least, reacting as a physician, I
9 would have wanted to know what her blood pressure was,
10 and probably her oxygenation and, you know, normally a
11 patient in this situation, you would want to monitor
12 their oxygen tension, if you could.

13 Q. How would they do that?

14 A. Well, usually through an oximeter in a
15 critical care situation or it could be by sending a
16 sample for blood gasses to the laboratory.

17 Q. Is the oximeter the monitor that goes on
18 the finger?

19 A. I don't -- I guess they use it on the
20 finger at Sick Children's, do they? I don't ...

21 Q. All right. Would sedation and pain
22 scores been helpful also?

23 A. You're outside my field of expertise. I
24 think, of course, this is a child who was admitted for
25 the treatment of pain. It's fairly important to know

1 if the pain was relieved. I suppose, though, looking
2 at the record, the fact that she was able to sleep is
3 pretty good presumptive evidence that the pain was
4 relieved.

5 Q. I just want to mention a few things
6 about your report, if you can just turn to that, if you
7 would?

8 A. Mm-hmm.

9 Q. Page two, item nine, and just because
10 the jury doesn't have a copy, I'll read the portion for
11 their benefit. You state:

12 "... In examining the flow sheet
13 completed after transfer to the ward
14 [and the flow sheet is what we have up
15 on the board] it is clear the
16 respiratory rate declined between 1:45
17 and 2:50. At 2:50, respiration was
18 recorded at a rate of 8 to 10. Such
19 slowing of respiration is certainly
20 compatible with morphine effect and in
21 retrospect, treatment with a narcotic
22 antagonist might have justified ..."

23 Now let me just pause there. What does
24 that mean, "narcotic antagonist"?

25 A. Well, one of the reasons that drugs like

1 morphine are so popular for the treatment of pain is
2 that they can be reversed, so when they have side
3 effects, in particular respiratory depression, you can
4 reverse that respiratory depression almost
5 instantaneously by using a drug which displaces the
6 morphine from its receptors.

7 Q. Should the nurse have wanted to
8 administer such a drug, would she have done it of her
9 own accord or would she have needed a doctor's
10 permission?

11 A. That's a question of policy at the
12 Hospital for Sick Children and I'm not sure. Normally
13 it would be done with a doctor's prescription. It is a
14 prescription drug, so I would assume that she would
15 have needed to contact the doctor on call or the pain
16 service to do that.

17 Q. You continue:

18 "... A decision was made at 2:50 to stop
19 PCA administration of morphine and a
20 recheck of respiratory rate at 3:20
21 found a rate of 12. It is also
22 noteworthy that at 2:50, in spite of the
23 slow respiratory rate, air entry was
24 described as good and the chest was
25 described as clear ..."

1 I just want to make clear the importance
2 that you take from the fact that her air entry was good
3 and the chest was clear.

4 A. Well, normally when somebody writes
5 that, as they have here, I think that says "chest
6 clear, clr, good air entry" and then it says "took away
7 morphine pump." The significance of the good air
8 entry, I think, for physicians at least that usually
9 means that you can hear breath sounds in all quadrants
10 of the chest. There are no areas that are silent and
11 the fact that the chest is clear suggests that there is
12 no fluid or infection in the air spaces of the lung.

13 Q. Turning the page to item 10, the very
14 last sentence reads:

15 "... The resulting morphine
16 concentrations apparently produced pain
17 relief ..."

18 I think I should read the sentence
19 before so it makes sense to the jury.

20 "... In summary, it seems clear that
21 there was a relatively high morphine
22 concentration blood in the period after
23 1:07 when the last dose of morphine was
24 given. The resulting morphine
25 concentrations apparently produced pain

1 relief and may also have caused
2 respiratory depression, hypotension and
3 tachycardia ..."

4 You've spoken about the depression and
5 the tachycardia; I'm just wondering about the impact of
6 the hypotension, what does that bring to the mix?

7 A. Well, I think, if, in fact, her blood
8 pressure was low and we do know that it was relatively
9 low at 1:45, 90 over 60, I mean that certainly is
10 suggestive of some diminished circulation and suggests
11 a likelihood that there might be hypoxia, although
12 oxygen, a lower oxygen tension associated with it. It
13 would also, as I think I said a few moments ago, it
14 might also account for the more rapid heart rate that
15 she had. As blood pressure goes down, your heart rate
16 goes up to -- in an attempt to compensate for that.

17 Q. And then in the last page, the middle of
18 the last full paragraph, you mentioned -- or you state:

19 "... In summary I believe that the cause
20 of death in this case will not be made
21 definitively on the basis of
22 pharmacology or toxicology analysis. I
23 do, however, think it is likely that
24 death was caused by a cardiac conduction
25 disturbance which may have resulted from

1 a complex interaction among the
2 therapeutic drugs, the patient's
3 physical condition and a concurrent
4 viral infection ..."

5 Now, I think we've ruled out viral
6 infection?

7 A. I think -- in my opinion, that's been
8 ruled out by other tests that have been done since.

9 Q. All right. Is the patient's physical
10 condition still a factor?

11 A. Oh, I think so. The fact that she was
12 hypotensive, tachycardic, possibly hypoxemic, hypoxic.

13 Q. All right. And what do you mean by
14 "cardiac conduction disturbance?"

15 A. Well, this is -- I suppose the commonest
16 cause of sudden death is some change in the way in
17 which an impulse forms in your heart and then spreads
18 through the heart, causing the heart to beat, so that
19 there is a system that has an architecture and
20 something can go wrong at various places in the system.

21 Certainly we don't know enough about Lisa's case to
22 even begin to guess where the problem might have
23 occurred, but it is, I think, the most likely cause of
24 death.

25 Q. Thank you.

1 THE CORONER: Ms. Posno?

2
3 CROSS-EXAMINATION BY MS. POSNO:

4 Q. Doctor, I'm Anne Posno, we represent Dr.
5 Shily who was the pain fellow who prescribed the
6 morphine while Lisa was in emergency on October 21st.
7 I have a couple of areas to cover with you. What I'd
8 first like to do is just make sure I understand your
9 findings in a summary fashion. First of all, as I
10 understand, each of the four drugs that Lisa Shore was
11 on alone, each of them by themselves, you do not think
12 were causative of the death?

13 A. That's correct.

14 Q. So the morphine alone, the gabapentin
15 alone, the carbamazepine alone, and the amitriptyline
16 alone, we can rule those out as possible causes of
17 death?

18 A. I'd just qualify that to say with
19 varying degrees of certainty. The only one in which
20 I'd be less than 100 percent certain about is morphine.
21 I mean, it is clear that she had effects of morphine
22 and, you know, had she died at 2:50 in the morning, I
23 think we would have said this is morphine.

24 Q. You read my mind, I was going to go
25 exactly there. If the death had occurred earlier at a

1 time when the effects of morphine would have been at
2 their highest, then we would be more likely to say that
3 the cause of death was related to the morphine?

4 A. Yes, much more likely.

5 Q. Okay. So the drug alone we're not
6 concerned about, what we are concerned about is the
7 potential interaction amongst the drugs and in
8 particular you have identified the morphine and the
9 gabapentin?

10 A. That's correct.

11 Q. And the gabapentin, the existence of it
12 may enhance or magnify or amplify the effects of the
13 morphine in some situations?

14 A. That's what we know from animals. To be
15 correct, from one animal study.

16 Q. So there has not been a study on people
17 with respect to those effects?

18 A. Not to the best of my knowledge, and I
19 -- maybe I could just interject that since I've been
20 aware of this case, I have had discussions with the
21 company that manufactures gabapentin because
22 gabapentin, in a way, was the major unknown in this
23 case. We know a great deal about the other three drugs
24 and they have certainly shared with me some information
25 that they have about their drug and about deaths

1 occurring in people taking gabapentin, but they have
2 not indicated to me that they have any other studies
3 that have not been published. I didn't ask
4 specifically, so I can't guarantee that they don't.

5 Q. Fair enough. So to the extent there's a
6 bit of an unknown along those lines, it may be of
7 assistance for the jury to make some kind of
8 recommendation that further studies be done with
9 respect to the interaction between morphine and
10 gabapentin? Is that something that may be helpful in
11 assisting us in reviewing a case like this?

12 A. Yes. I don't think it would be helpful
13 any time in the immediate future, but it may be helpful
14 -- it may certainly be helpful in preventing further
15 deaths of this kind. Have the product monographs been
16 introduced into evidence?

17 THE CORONER: No.

18 THE WITNESS: This might be a good point to
19 mention that there is a difference between
20 the official prescribing information for this
21 drug in the United States and the official
22 prescribing information in Canada.

23 MS. POSNO: I have to confess that I'm not
24 sure which information you're speaking of.
25 I'm going to leave it in Mr. Coroner's

1 discretion whether he thinks this is
2 something we should get into at this time.

3 THE CORONER: I'm willing to go by Dr.
4 MacLeod's views.

5 THE WITNESS: It will be a very brief
6 comment, but given the question you have just
7 asked, I think that perhaps the jury should
8 be aware of the fact that in -- when this
9 drug, gabapentin, was approved in the United
10 States, the Food and Drug Administration in
11 the United States felt that it was necessary
12 to put a paragraph in the official
13 information, that is, the information that
14 goes to all health professionals, hospitals
15 and pharmacists and so forth. They wanted a
16 section put in on sudden and unexplained
17 deaths and the statement describes the death
18 of eight patients that occurred during the
19 initial studies of the drug and there were
20 2,203 patients in those initial studies, so
21 eight of 2,203 died suddenly.

22 The conclusion was that that number of
23 unexplained -- of sudden unexplained deaths
24 was not particularly unusual in an epileptic
25 population and this drug was being, as I said

1 before, was being developed for the treatment
2 of epileptics, so -- and it is a known fact
3 that epileptics sometimes suffer sudden
4 death, so the Food and Drug Administration
5 insisted that the paragraph be put in,
6 outlining this experience but then concluding
7 that this number of deaths was -- could not
8 be interpreted in view of the fact that they
9 were occurring in epileptics.

10 Now when the drug came to be approved in
11 Canada, where we also have our own similar
12 approval process and we also come around to
13 the same kind of an official approved product
14 information sheet, the Canadian government
15 Therapeutic Products Program did not insist
16 on the inclusion of that paragraph, so they
17 presumably believed that the observation was
18 unimportant or uninterpretable.

19
20 BY MS. POSNO:

21 Q. Do you know, just because this may be a
22 question in the jury's mind, whether those eight
23 deaths, then, and the study of the 2,200 people was
24 focused on a population of people suffering from
25 epilepsy?

1 A. They were all patients with epilepsy.

2 Q. Okay, and we're not dealing with that
3 situation here?

4 A. No, and of course we won't know until
5 such time as this drug is approved for use in patients
6 with pain syndromes, so at the moment, it is
7 experimental for that purpose. At some point, there
8 will be a product, an official product monograph which
9 describes its use in pain as well and it may or may not
10 include that statement about sudden death.

11 Q. And if I understand your earlier
12 testimony, the level of medication or the dose of
13 medication of gabapentin in pain treatment versus
14 epilepsy treatment is much higher in the pain treatment
15 situation?

16 A. Is much higher.

17 Q. Okay. But we don't have a study of
18 that ---

19 A. There are studies appearing in the
20 literature, but we haven't gone through the official
21 drug regulatory approval for that, and of the studies
22 that have appeared, I certainly have not seen any that
23 describe sudden, unexplained death as a feature.

24 Q. So we're at the beginning of learning
25 more and more about this drug?

1 A. That's really the conclusion I think has
2 to be drawn.

3 THE CORONER: That's why, Ms. Posno, we had
4 the debate whether it would be a red herring
5 to bring in the deaths since they were in an
6 epileptic population; that we know do die
7 suddenly and unexpectedly and the instance or
8 the rate of deaths, sudden and unexpected
9 deaths in epileptics on the drug and off the
10 drug were not in any way significantly
11 greater, so Dr. MacLeod debated this, we
12 brought it out, but it's hard to put a
13 significance on it for this particular set of
14 situations.

15 MS. POSNO: Absolutely, I understand what
16 you're saying. I hope we've made it clear
17 for the jury that we're drawing a distinction
18 there and the reason we are.

19
20 BY MS. POSNO:

21 Q. Moving on to a different area, then, Dr.
22 MacLeod, in your paper here, the letter, you have
23 indicated that just in a general statement that the
24 maximum pain relief following the administration of
25 morphine generally occurs within 10 to 20 minutes

1 following the administration of the drug?

2 A. That's correct.

3 Q. Okay, so if a patient is not experienced
4 or enjoying any pain relief following the 20 minutes, I
5 take it it's reasonable to give a little more morphine,
6 provided you're within reasonable limits?

7 A. Yes, that's the usual clinical approach.

8 Q. Okay. And there's a comment in here
9 about -- I'll direct you to where I'm looking, Dr.
10 MacLeod -- in paragraph 2, you just make a passing
11 comment about the administration of a further IV 2
12 milligrams of morphine 50 minutes after the first dose
13 of morphine and you queried whether or not pain relief
14 had been received by that time. I take it you're not
15 being critical of the fact that there was further pain
16 relief administered in the event pain relief had not
17 being achieved?

18 A. No, I'm not being critical, it's simply
19 that once you've set up a self-controlled
20 administration device, it wasn't clear to me from the
21 record why the treating physician then chose to go back
22 and give an additional bolus instead of letting the
23 patient control her own analgesia.

24 Q. And to be fair to you, you didn't have
25 the whole chart?

1 A. No, no, I wasn't -- I simply didn't have
2 the information that would allow me to give ...

3 Q. From the nurses' records, for the
4 assistance of the jury on this point, this is in the
5 emergency department and Nurse Matthews maintains that
6 the pain score remained at 8 out of 10, it may have
7 gone down to 7 out of 10, but back up to 8 out of 10
8 around this time period. Moving onto a different area,
9 then, a lot of your report focuses on the concentration
10 level of morphine in blood and much of this is a little
11 confusing to a lay person when you hear it for the
12 first time. And what I'd like to do is try to begin at
13 first principles and explain what it is we're looking
14 at, why we're looking at it and how we get to your end
15 conclusion that, my understanding is, that the level of
16 morphine was probably appropriate given the 14.5
17 milligrams that was administered.

18 A. That's correct, except that the only
19 morphine measurements we have come several hours later.

20 Q. Right, so let's start with that. What
21 you have to work with only is a blood sample taken
22 during the autopsy and in that blood sample is a
23 percentage or concentration level of morphine, that's
24 what you have to work with?

25 A. That's correct. Do we know for certain

1 that it was taken during the autopsy?

2 Q. We just spoke to Dr. Smith this morning
3 to confirm that.

4 A. Okay, because I didn't know that,
5 actually, when I wrote this.

6 Q. Right. So what we have is a post-mortem
7 blood sample and that's all the information you have to
8 work with and what you're trying to find out as I'm
9 reading the report is well, I know the concentration of
10 morphine after death, what was the concentration at its
11 highest hours before, sometime within an hour or two
12 after the drug was administered, so we have to work
13 backwards. So you've got your current post-mortem
14 sample and then morphine, as I understand, eventually
15 breaks down and has a lower concentration over time.
16 Can you explain for the jury the half life of morphine
17 and how that works?

18 A. Mm-hmm, you mean in life?

19 Q. In life.

20 A. In life, yes. Sure, well, as with any
21 drug, once it's taken, it reaches a maximum
22 concentration in blood or in the organ where it's
23 having its action. Obviously something has to happen
24 at that point to either inactivate the drug or to have
25 the drug disappear, otherwise the action would go on

1 forever. So when we look at the concentration in
2 blood, we look at the weight of its decline and usually
3 we express that as something called a "half life" and
4 that's the time it takes to go down by 50 percent, so
5 to go from 10 to 5 to 2 and a half. And it's simply a
6 measure of how rapidly the drug is being removed from
7 the body and usually it is being removed by being made
8 more water soluble, I don't want to confuse you, so
9 that it can be -- so that it can leave the body in
10 urine or in sweat or in respiratory vapour or whatever,
11 but mostly in urine.

12 Q. So you start with the medication being
13 administered at one level, the concentration goes up in
14 your blood to a maximum point at an hour to two hours
15 after administration, sometime like that?

16 A. Or -- no, no, the maximum -- when you
17 give a drug intravenously like this, the maximum
18 concentration is almost immediate.

19 Q. Okay. And thereafter the concentration
20 in the blood slips down.

21 A. That's correct.

22 Q. Now in this case, we have the death
23 occurring and then you have your blood sample taken and
24 normally the concentration in the blood should be quite
25 low or depending on how much medication they have, but

1 should be lower at that level, and the difficulty as
2 I'm understanding is the concentration you have is
3 quite high.

4 A. It is quite high.

5 Q. Which would indicate that at the time
6 that the drug was administered, the concentration would
7 be much higher than we anticipate it would have been
8 following 14.5 milligrams of morphine?

9 A. That's correct.

10 Q. And you've explained that the reason
11 that probably happens is there is evidence that in
12 post-mortem samples of blood with morphine, the
13 concentration of the morphine can go higher. I don't
14 know if we need to get into the reasons why that
15 happens here, but your understanding is that may have
16 happened in this case because the 14.5 milligrams would
17 not give that excessively high concentration at that
18 time. Now, I also understand that there's a
19 concentration level measured from a urine sample?

20 A. Yes, that's correct.

21 Q. And that urine sample is consistent with
22 a lower concentration, is it, than the post-mortem
23 morphine sample would give you?

24 A. Yes, I mainly asked that that sample be
25 done just in case there had been some inadvertent

1 overdose of morphine. There are other kinds of
2 mistakes that can be made when you're dosing a patient
3 with morphine and so I wanted to be sure that the
4 concentration in the syringe was correct, that she
5 wasn't somehow getting two or three times as much as we
6 thought and that was correct and I also wanted to know
7 how much was in the urine which would give some
8 indication if there had been a massive overdose by
9 mistake and I'm certain that there was not.

10 Q. Okay, and that's the reason we're
11 looking back, isn't it, in terms of determining the
12 highest concentration level within the blood?

13 A. We want to make the best possible
14 estimation of what that maximum concentration was in
15 blood.

16 Q. And you're satisfied that there was no
17 inadvertent overdose or incorrect dosage of medication
18 within the syringe?

19 A. That's correct.

20 Q. So to the extent when the jury is
21 reviewing your letter, your report here, to the extent
22 there's references to concentrations post-mortem,
23 measuring back the half life, attempting to determine
24 at 1:45, they can rest assured that your end conclusion
25 is that the level of concentration appears to be

1 appropriate for the amount that was administered and
2 there was no overdose from your review of the records?

3 A. I think we can be certain that she got
4 14.5 milligrams of morphine, as the record shows.
5 There's no way that we can be certain about what the
6 maximum blood concentration was, but my best estimate
7 and it really is an estimate is that it would have been
8 probably in the range of 120 -- I forget what I said in
9 the letter -- between 120 and 150, which would be a
10 therapeutic concentration.

11 Q. Just moving on to one more area here, in
12 paragraph eight you indicate that the dose of morphine
13 is consistent with acceptable therapeutic norms?

14 A. Yes.

15 Q. So I take it there's no criticism here
16 that the 14.5 milligrams was an excessive dose to give
17 to a child in Lisa Shore's condition?

18 A. No, I think the dosing was appropriate.

19 Q. Okay. There's one last comment, just a
20 point on within that paragraph eight, you make a
21 statement there that Lisa Shore received a comparable
22 dosage of morphine back in March of 1998, so she had
23 received a dosage of morphine before at or around that
24 level, apparently without adverse effects and you
25 questioned whether or not gabapentin had been

1 prescribed at that time. Do you have any further
2 knowledge on whether Lisa Shore had gabapentin in her
3 system at the time she was on morphine back in March of
4 '98?

5 A. I'm not sure -- I don't think I ever
6 suggested that. I did question whether she had ever --
7 after the time when she went to the Boston Children's
8 Hospital, whether there had been any other occasion
9 when she received the combination of morphine and
10 gabapentin. I don't believe she received gabapentin
11 before going to Boston, but I could be incorrect in
12 that. I haven't examined the past records. I was
13 simply trying to point out that morphine alone in
14 relatively high dose had been tolerated by her well in
15 March of 1998.

16 Q. That's right, okay, so my understanding
17 of what you just said and it clarifies it for me, then,
18 is when she did have a comparable level of morphine
19 months earlier, she tolerated it and to your knowledge,
20 she didn't have gabapentin at that time?

21 A. I'm -- I'm relatively certain that she
22 did not.

23 MS. POSNO: If I may, Mr. Coroner, my
24 reviewing of some of the records may have
25 indicated that she was, but I don't want to

1 mislead anyone, I just don't know whether
2 this is an issue the jury may be interested
3 in knowing whether Lisa Shore had gabapentin
4 at the time when she had a comparable level
5 of morphine. Perhaps Mr. Gomberg could check
6 on that.

7 THE CORONER: Well, we need to have a 15
8 minute recess this afternoon anyway, so
9 perhaps if we have it at this time, you could
10 consult with Mr. Gomberg and we'll be in a
11 position to answer that after the recess.

12 MS. POSNO: Thank you.

13
14 --- A BRIEF RECESS

15
16 THE CORONER: Ms. Posno, did you still have
17 a few questions?

18
19 CONTINUED CROSS-EXAMINATION BY MS. POSNO:

20 Q. Dr. MacLeod, I've now learned through
21 the assistance of interpretation of earlier records
22 that it appears that Lisa Shore did have very low
23 levels of gabapentin prescribed at that time, but it
24 was after the morphine administration to which you were
25 referring in your letter, so it did not happen at the

1 same time.

2 A. So to the best of our knowledge, there
3 was never a prior occasion when she got both gabapentin
4 and morphine?

5 Q. That's right.

6 A. Yes, thank you.

7 Q. To my knowledge of the document. Those
8 are my questions, thank you, Doctor.

9 THE CORONER: Mr. Hawkins?

10 MR. HAWKINS: Dr. Cairns, I don't believe
11 that Dr. MacLeod's report has yet been made
12 an exhibit.

13 MS. BROWNE: No, I was just about to say
14 that. Ms. Posno had referred to it but the
15 jury were reading it and it has yet to be
16 marked.

17 THE CORONER: It certainly was the intention
18 to make it an exhibit.

19 MR. HAWKINS: Sorry, not the CV, I meant the
20 report.

21 MS. BROWNE: The report, yes. We hadn't
22 asked for that yet, but perhaps it could be
23 marked.

24 THE CORONER: Yes, it should be the next
25 exhibit, yes.

1 CONSTABLE CULLETON: 31.

2 THE WITNESS: Could I just ask that you make
3 sure that you enter one with the correction
4 on the -- are you going to take mine?

5 MS. BROWNE: That's the one that's going to
6 be entered, so maybe you could make the
7 correction?

8

9 EXHIBIT NO. 31: Report of Dr. MacLeod

10

11 CROSS-EXAMINATION BY MR. HAWKINS:

12 Q. I'd like to sort of work through some of
13 this report with you. I guess starting, you've done it
14 in numbered paragraphs and I guess I'd start with you
15 at number seven and I'd like to work through some of
16 the ones after that. Now, we heard from Dr. Mayers
17 earlier and you have talked about the variability in
18 morphine concentrations and in that paragraph what you
19 say is your best information or your interpretation is
20 that the likely peak concentration occurs from 1:00 to
21 1:30 which is at or about the time of the last morphine
22 administration.

23 A. Yes, that's correct.

24 Q. And the likely peak is 120 to 150
25 nanograms per millilitre?

1 A. That's correct.

2 Q. And then that's going to decline on a
3 gradual basis to what you think is immediately before
4 death of 40 to 50 nanograms per millilitre?

5 A. That's correct. And I'm assuming in
6 that -- that the half life in a patient like Lisa would
7 be about three hours.

8 Q. And that's how you sort of extrapolate
9 down from 120 to 40 or 50?

10 A. That's correct.

11 Q. Then going to number nine and flowing on
12 into paragraph ten where you're talking about the
13 respiratory rates and the heart rates, we've talked
14 about the respiratory rate drop to 8 to 10 at 2:50.
15 Thereafter as the respiration rate comes back up to 12
16 to 14 to 16 at various points, is that in your view
17 showing a sort of diminution or a decreasing morphine
18 effect as the hours progress?

19 A. Well, at the very least, it shows some
20 compensation for the morphine effect, so the -- you can
21 overcome the morphine effect in various ways, perhaps
22 by other kinds of respiratory drives that bring the
23 rate up. But the net result is that the effect of
24 morphine is diminishing.

25 Q. And over that time, the body is

1 compensating for the morphine and also the morphine is
2 getting flushed out of the system?

3 A. That's what we would assume, yes.

4 Q. And then as we go through 3:20, 4:00,
5 down to 6:00, we see respirations in the range of 12 to
6 16, with the one reading of 10 that was pointed out to
7 you earlier. Are those normal respirations?

8 A. Those are certainly in the -- I would
9 say normal would be about 14, so they're in the
10 ballpark.

11 Q. Yeah, okay. So after 2:50, then, it
12 would not appear from the notes that we have that Lisa
13 was suffering from respiratory depression?

14 A. That's correct. I mean, the only place
15 where you might be concerned is that figure we
16 concentrated on before at 04:15, which was 10.

17 Q. Okay, and in this case you mentioned the
18 nurse came back five minutes later, rechecked it and it
19 was 16 and that's satisfactory?

20 A. That's correct.

21 Q. You comment in paragraph 10 and as we
22 look at the flow sheet, that at 5:00 the nurse takes an
23 oral temperature and you say:

24 "... It is notable that the patient was
25 able to co-operate at 05:00 with the

1 measurement of an oral temperature ..."

2 What's the significance of that?

3 A. Well, to my mind, it shows that the
4 patient was rousable and was, once roused, was able to
5 co-operate with something that does require a bit of
6 patient involvement in holding a thermometer under the
7 tongue.

8 Q. And so does that again suggest to you
9 that the patient has by that point compensated or
10 flushed out a lot of the morphine effect?

11 A. I think that might be over-
12 interpretation of what I'm saying. It certainly shows
13 that she wasn't comatose, you know, she wasn't ---

14 Q. She wasn't in a depressed state.

15 A. --- deeply incapacitated by morphine.

16 Q. Okay.

17 A. I mean, morphine given to an extreme is
18 an anesthetic, really.

19 Q. Right.

20 A. You know, these drugs are called
21 narcotics because they put you to sleep.

22 Q. Okay, but you don't see morphine given
23 to extreme here?

24 A. No, I think this is evident -- it
25 doesn't tell you how much morphine effect there was,

1 but it tells you that it wasn't extreme at that point.

2 Q. Okay. And then looking at the
3 gabapentin, you've referred to a paper, which I thought
4 I'd lost but now I've found.

5 A. It's your lucky day.

6 Q. I actually tried to read through it and
7 found it rather difficult. Just a couple of points
8 that I wanted to bring out in that paper; when you
9 wrote your first report of November 5th, you indicated
10 that you had done a literature search to search for
11 help to clarify the cause of death but at that point,
12 you couldn't find anything.

13 A. That's correct.

14 Q. And subsequently, in further research
15 you come up or you located the one paper that talks
16 about an experimental study in rats?

17 A. That's correct.

18 Q. That paper, and if I look at the first
19 page in the second column where it says

20 "... Gabapentin is a novel anti-
21 convulsant that anecdotal case reports
22 suggest has analgesic effects in both
23 host hepatic (ph.) neuralgia and reflex
24 sympathetic dystrophy ..."

25 Would I be correct in interpreting that

1 that gabapentin is not fully proven or we don't fully
2 know why gabapentin works with RSD, it's just some case
3 reports say that does.

4 A. Yes, I think that's a reasonable
5 interpretation. We certainly will point out to you
6 that this paper was submitted on the 5th of May, 1997
7 and we certainly -- there's certainly more information
8 in the literature now than there was at that time about
9 gabapentin, but this is a new drug and in honesty, it
10 is not fully known how it works in epilepsy either and
11 it's been approved for several years for the treatment
12 of epilepsy, so this is a complicated drug that works
13 in some unusual ways.

14 Q. Okay, and we're still in the process or
15 people such as yourself are still in the process of
16 researching how and why it works and how best to use
17 it.

18 A. Absolutely, and there are -- there's an
19 active investigation program right now of its use in
20 these complex pain syndromes.

21 Q. And that article concludes with the
22 statement,

23 "... The clinical safety of the
24 combinations of gabapentin and morphine
25 needs to be determined ..."

1 I take it you'd agree with that
2 statement?

3 A. I'm sorry, oh, yes, it's not the last,
4 the paragraph above. Yes. No, absolutely, I believe
5 that this case and probably others suggest that we
6 should be asking the company, the manufacturer, to do
7 some additional studies of the safety of gabapentin in
8 combination with morphine. I should emphasize that all
9 of the evidence suggested it's an extremely safe drug
10 when given by itself.

11 Q. Okay. And then in the first page of
12 your report, I take it as I read your report, you sort
13 of state your conclusions up front.

14 "... On review of all of the available
15 pharmacologic and toxicologic
16 information, I am unable to reach any
17 definitive conclusion on the cause of
18 death in this case ..."

19 Is that still your opinion or that is
20 your opinion?

21 A. I would still stick by that, that I am
22 not able to say with absolute certainty what the cause
23 of death was.

24 Q. And what you say at the bottom was

25 "... Although it cannot be proven with

1 certainty, there is a strong possibility
2 that the death may be explained by an
3 interaction of therapeutic drugs ..."

4 You put there and underlined "viral
5 infection," but that's not the case anymore, so just an
6 interaction of therapeutic drugs to cause some change
7 in cardiac conduction?

8 A. I believe that's the most probable
9 explanation of the death.

10 Q. Okay. Thank you, those are my
11 questions.

12 THE CORONER: Mr. Gomberg?

13

14 CROSS-EXAMINATION BY MR. GOMBERG:

15 Q. Dr. MacLeod, I'm Frank Gomberg, I'm the
16 lawyer for the family. I want to thank you for coming
17 today. I have a few questions to ask you and I think
18 that it will be helpful for you to look at the flow
19 sheet as I do that. First of all, am I correct that,
20 and I don't think this came up earlier during your CV
21 or during the presentation of your CV, but you were
22 also the Dean of Medicine at McMaster?

23 A. I was from 1987 to 1992.

24 Q. All right. And therefore you have some
25 familiarity with clinical medicine, if I can put it

1 that way, is that correct?

2 A. I'm qualified as a clinical practitioner
3 and as a pharmacologist.

4 Q. All right. So this isn't a situation
5 like before where with Mr. Mayers or Dr. Mayers who has
6 a PhD, as I understand it, in pharmacology, but is not
7 a medical doctor; you're both?

8 A. I am both.

9 Q. All right. Now, I'd like to talk to you
10 about the blood pressure reading of 90 over 60 at 1:45
11 in the morning, all right? First of all, I take it
12 that you would agree with me that it's better that we
13 have that reading than if we didn't have that reading?

14 A. I think it's helpful. It gives us at
15 least a milestone that we can look at.

16 Q. All right. So it's useful in the sense
17 that that's information which is written down and we,
18 14 or 15 months later, can look at it and figure out
19 that the blood pressure as you put it was low at 1:45
20 in the morning, right?

21 A. That's correct.

22 Q. All right. And if it wasn't written
23 down, we wouldn't know what it was?

24 A. No.

25 Q. And we wouldn't know that it was low?

1 A. Right.

2 Q. All right. Now, at 2:30 in the morning
3 -- by the way, the pulse of 72 at 1:45, as a clinician,
4 that's a perfectly reasonable pulse, isn't it?

5 A. That seems -- the only thing that's a
6 little bit surprising about both the pulse and the
7 blood pressure is that these measurements are taken
8 after she has been in the emergency room for almost two
9 hours, I think.

10 Q. Right.

11 A. She's been through, I think, a great
12 deal and she comes up to the ward and most people under
13 those circumstances would be somewhat stimulated, their
14 sympathetic nervous system would be active and normally
15 that would put the blood pressure up a little bit, put
16 the pulse rate up a little bit.

17 Q. All right.

18 A. But the other hand, she has also been
19 given morphine which is a sedative, so it may be it --
20 these figures are not particularly surprising, and
21 although that's low, it's not dangerously low.

22 Q. The blood pressure?

23 A. The blood pressure.

24 Q. All right. And first of all, in terms
25 of things like orders being made in the emergency

1 department and those orders getting up to the ward,
2 you're aware of the fact that there were orders made in
3 this case that didn't make it to the orthopedic ward?

4 A. I'm aware of that.

5 Q. All right. And as a clinician and as a
6 dean of medicine, I take it we can agree that that's
7 not a very good thing?

8 A. That's certainly not acceptable, no.

9 Q. All right, it's completely unacceptable?

10 A. Unacceptable.

11 Q. Shocking.

12 A. Shocking.

13 Q. Well, there are varying degrees of
14 unacceptability, I just wanted to make sure that the
15 jury got it and that I understand it, too, so that's
16 why I phrased it like that.

17 A. I appreciate that.

18 Q. Now, at 2:30 in the morning given the
19 fact that the blood pressure was at least marginally
20 low at 1:45, I take it you'd agree with me that it
21 would have been a good thing to know what the blood
22 pressure was then.

23 A. Yes, it would.

24 Q. And the same thing with the pulse?

25 A. And with the pulse, as well.

1 Q. And I take it given the fact that an
2 order was given that a sedation scale be taken, that it
3 would have been a good thing to know what the sedation
4 scale was?

5 A. It would have -- it would certainly have
6 been useful.

7 Q. And the same thing with the pain scale?

8 A. And with the pain scale.

9 Q. All right. Now, 2:45 I'm going to
10 leave, because that's not that much after 2:30 except
11 for the fact that the respiration is going down, right?

12 A. Yes. I'm not sure that, again, it's not
13 clear to me whether Lisa was monitored or not
14 monitored, but in clinical monitoring, by observation,
15 the difference between 14 and 12 would not normally be
16 considered significant.

17 Q. All right. In any event, there was no
18 blood pressure taken at 2:45 or at 2:50 or throughout
19 the rest of the night?

20 A. That's correct.

21 Q. All right. And that's completely
22 unacceptable, too, isn't it, given the proposition that
23 her pulse rate goes up from 72 at 1:45 to 120 less than
24 two hours later?

25 A. Well, there's no doubt that anybody

1 looking at this chart would like to know a great deal
2 more about what was happening at 2:50 in the morning
3 and thereafter.

4 Q. All right. And by "what was happening,"
5 you mean a pulse rate, right, for all of those times?

6 A. You'd certainly want to know the heart
7 rate and blood pressure.

8 Q. All right. Now, in terms of measuring
9 respiration, we don't know and there's going to be some
10 controversy about whether those numbers were taken from
11 a machine or were taken manually, but I take it that in
12 terms of doing those respirations, there are other
13 things other than numbers that are important and I'm
14 talking now specifically about the depth of breathing.

15 A. Yes.

16 Q. All right, and that's important as well,
17 isn't it?

18 A. It is.

19 Q. To measure that. And by that I mean the
20 sufficiency of the breathing as shallow breathing will
21 not introduce as much oxygen into the bloodstream as a
22 regular deep breathing?

23 A. Yes, it's commonly expected that you
24 will describe the character of the respiration as well
25 as count the rate.

1 Q. All right. And the reason for that is
2 -- I may not have phrased it as elegantly as ---

3 A. No, you were right.

4 Q. That it's a question of oxygen profusion
5 in the blood, right?

6 A. That's correct, it's the question of
7 oxygenation of the blood.

8 Q. All right. And I take it that -- this
9 is pretty basic, but that that's what oximetry is
10 designed to measure, as well?

11 A. Oximetry would give you an indication of
12 the amount of oxygen being carried in the blood at a
13 particular moment in time.

14 Q. All right. So, for example, if oximetry
15 was taken, readings were taken all the way through, one
16 could tell whether the oxygen that was being carried in
17 the blood was, in a relative way, was going up or going
18 down from time to time?

19 A. Yes, that's correct.

20 Q. All right. And not only is the absolute
21 number important, but the relativity is important as
22 well, isn't it?

23 A. The direction in which it is moving.

24 Q. Sure, if it's moving up, that means that
25 your oxygen is getting better, and if it's moving down,

1 then that might sound an alarm in some clinician's mind
2 that they should try and figure out why it's moving
3 down, right?

4 A. Yes, you're absolutely correct.

5 Q. All right. But in terms of that type of
6 information, that too is markedly missing from the flow
7 sheet?

8 A. It is missing.

9 Q. And that's a problem, isn't it?

10 A. It's certainly a problem for anybody
11 trying to reconstruct the events of that night.

12 Q. Well, you raised exactly where I was
13 going and that is this: it's a two-pronged problem, I
14 suggest. It's a problem for treatment, right?

15 A. Yes, certainly anybody who was
16 monitoring the treatment, the analgesic treatment would
17 want to know some of those physical measurements in
18 order to decide what should be done.

19 Q. Well, sure, and in terms of treatment or
20 the ability to save this young child when she got into
21 trouble, it's also important, isn't it?

22 A. Yes, it is.

23 Q. In other words, if the blood pressure is
24 going down, all right, and the respirations are going
25 down and the pulse is going up, that may cry out for

1 the administration of some anti-morphine agent like
2 Naloxalone (sic), right?

3 A. Naloxone.

4 Q. Okay, I mispronounced it.

5 A. Yes, you're absolutely right, and I
6 think that was the prime question at 2:50 in the
7 morning and at that point, I believe there should have
8 been some reference made to the treating physician,
9 there should have been some discussion as to whether or
10 not Naloxone should be administered.

11 Q. All right. And, of course, assuming
12 that the treating physician was called at 2:50 in the
13 morning and was given information and there's an issue
14 about whether he was called, but there's no issue about
15 whether he got information, right, at 2:50 in the
16 morning?

17 A. Yes.

18 Q. The more information that he's given at
19 2:50 in the morning, the better it is, right?

20 A. That's correct.

21 Q. All right, because his ability to
22 respond to the situation is only as good as the
23 information which is communicated to him.

24 A. I agree with that.

25 Q. All right. And clearly he couldn't have

1 been told what the blood pressure was if he was told
2 anything at 2:50 in the morning because it wasn't
3 taken, right?

4 A. That's my assumption.

5 Q. The same thing with the sedation score.

6 A. That's correct.

7 Q. The same thing with the pain scale?

8 A. Correct.

9 Q. All right. The same thing with the
10 pulse at 2:50 in the morning?

11 A. Oh, yeah, it's not recorded here.

12 Q. All right. Now you indicated that
13 morphine causes depression in the blood pressure and
14 that it can even be used for that purpose. I take it
15 that if the blood pressures had been going down, then
16 one of the things that that might have suggested to the
17 clinicians, and we don't know, because we don't know
18 what the blood pressures were, was, that morphine was a
19 potential cause of that problem.

20 A. Yes, I think that -- I mean, that would
21 have been the interpretation. If the blood pressure
22 was, in fact, low or even when it was recorded here at
23 90 over 60, I think one would -- certainly I would
24 attribute that to morphine effect.

25 Q. All right. Now at 4:15 in the morning,

1 there's a pulse rate of 134 and I think that I wrote
2 your description down correctly; you said that that was
3 extraordinary, is that right?

4 A. It is certainly very rapid.

5 Q. And a respiration of 10 -- you referred
6 earlier I think in response to Mr. Hawkins' question
7 that normal is about 14; 10 may not be that far off
8 normal, but it is low and it's lower than 14?

9 A. I think 10 would be considered by almost
10 all observers to be abnormal.

11 Q. Abnormal?

12 A. Abnormal.

13 Q. All right. And I think you've --
14 sufficiently abnormal and you may not know this, but
15 that the doctor in his orders which never made it to
16 the floor indicated that he wanted to be advised if the
17 respirations went down to 11, right?

18 A. Right.

19 Q. I'm not sure whether you were aware of
20 that.

21 A. No, I wasn't aware of that.

22 Q. All right. But 11 is even higher than
23 10, obviously, so 10 would at least require some
24 consideration, right, particularly in conjunction with
25 what you've called an extraordinary heart rate?

1 A. Yes.

2 Q. All right. Now the question that I want
3 to ask you now I'm asking, I suppose, more as a
4 clinical pharmacologist than as a doctor, but there may
5 be some medical aspects to it as well. Let's assume
6 that one wanted to counteract the effects of morphine
7 at 4:15 in the morning, all right?

8 A. Yes.

9 Q. Could that have been done sufficiently
10 that the child would have been salvageable, keeping in
11 mind that she ---

12 A. Well ---

13 Q. --- let me finish -- it's my fault, I
14 didn't phrase it properly -- keeping in mind that it
15 looks like the time of death is somewhere between 7:00
16 and 7:15 or 7:30?

17 A. Yes, well, let me separate your question
18 out a little bit. I mean, there's no question that a
19 morphine antagonist, given at 4:15, would still be
20 pharmacologically effective in opposing the actions of
21 morphine, so that -- there's no question of that.
22 Would that have prevented Lisa's death, given the fact
23 that we don't know with certainty what the cause of
24 death was, can't be sure, but there's certainly a
25 probability of that being correct.

1 Q. Probably a high probability?

2 A. I think a high probability, yes.

3 Q. Of all of the monitoring that could have
4 been done or that was ordered to be done and that
5 wasn't done, is blood saturation monitoring -- oxygen
6 saturation monitoring important in this situation?

7 A. Well, I'm not sure that it was important
8 -- and as I say, I'm a little out of my field of
9 expertise, but I wouldn't say that it was especially
10 important at the time when she went to the ward, but at
11 the time when her heart rate started to go up and had
12 we known as we expect to be true that her blood
13 pressure went down, at that point, it became very
14 important to know what the state of her oxygenation
15 was.

16 Q. All right. And I think I'm being
17 repetitious, but that wasn't done?

18 A. It was not done.

19 Q. All right. Now the only other issue
20 that I wanted to raise with you relates to the -- and I
21 suppose in your capacity as a teacher of medicine would
22 be to answer this question: if a doctor makes an
23 order, then that order is supposed to -- and let me be
24 specific, now; an order that blood pressure be taken,
25 all right, hourly, let's say.

1 Q. Yes.

2 Q. I take it that the doctor wants that
3 blood pressure to be taken hourly regardless of whether
4 or not the patient is sleeping?

5 A. That's correct.

6 Q. All right. There's no question about
7 that, there's no confusion about that and I take it
8 you'd agree with me that it's not up to the nurse to
9 say well, I'm not going to take that blood pressure
10 because that patient is sleeping and I don't want to
11 wake her up.

12 A. I think your interpretation is correct.

13 Physicians writing orders sometimes write "do such and
14 such when awake."

15 Q. Right.

16 A. So it is -- it's not unusual for one to
17 qualify orders, but if you write the order, something
18 like "blood pressure to be done at hourly intervals,"
19 that's not ---

20 Q. Well certainly looking at that flow
21 chart, it would not be appropriate and would be
22 medically contra-indicated if I can put it that way,
23 not to take the blood pressure for all of those times,
24 just because she was sleeping?

25 A. Well, certainly the figures that are

1 here argue very strongly for a blood pressure
2 measurement.

3 Q. All right. And ---

4 A. If not every time, frequently anyway.

5 Q. All right, and that one would not
6 refrain from taking the blood pressure just because the
7 child is sleeping?

8 A. Not at all.

9 Q. And the reason for that and I think we
10 dealt with this with Dr. Schily earlier on is that
11 you're better off with a grouchy awakened child --
12 you're smiling, but, like, I'm serious about this --
13 you're better off with a grouchy child who has been
14 awakened a few times than with a child who doesn't have
15 blood pressure taken?

16 A. Well, this child was sick enough to be
17 admitted to the hospital in the middle of the night;
18 clearly her physical well-being is more important than
19 her sleep.

20 Q. All right, now, in terms of the heart
21 rate, and I promise to end here, in terms of the heart
22 rate, I'd take it that you would want to know if she
23 was monitored for heart rate, you'd want to know long
24 before that heart rate hit 160 beats per minute?

25 A. You certainly would.

1 Q. All right. And if you were setting a
2 machine which would deal with that issue, you'd want to
3 be alarmed or advised long before the heart rate hit
4 160?

5 A. I would.

6 Q. And, in fact, based on what you said
7 earlier, I would have thought that you would want to
8 know about 130, because you said that 134 was extra-
9 ordinary.

10 A. Yes. Extraordinary, I don't want to
11 live and die by this adjective; it's very -- a rate of
12 134 is very high in the circumstances and it is extra-
13 ordinary but, you know, the rate can go up from 134,
14 but, I mean -- no, I'm sorry, I lost my point.

15 Q. The question, just to get back to the
16 question is if I was setting a monitor to ring and I
17 wanted to be alerted at a certain number of beats per
18 minute given this girl's clinical history, the number
19 that you would set it at would be far, far less than
20 160 beats per minute?

21 A. Oh, absolutely. Probably ---

22 Q. Sorry, no question about that?

23 A. No question at all. The point I was
24 going to make before is the most important thing here
25 is not the absolute rate but the fact that it had gone

1 from 72 to 120, so there's clearly been a major change
2 and, you know, of course, any of us can have a heart
3 rate of 120 momentarily ---

4 Q. Right.

5 A. --- for some reason, but this was 120,
6 then 130, then 130, of course, this was a consistent
7 pattern and it's the magnitude of the change that is
8 extraordinary, not the absolute numbers.

9 Q. So if you're watching what's going on,
10 at least as far as the heart rate is concerned, it's
11 giving you a message?

12 A. Yes.

13 Q. And it's a powerful message, isn't it?

14 A. I think it is.

15 Q. And the power of the message is keep an
16 eye on this patient, because there may be a problem.

17 A. I agree with you.

18 Q. Those are my questions.

19 THE CORONER: Does the jury have questions
20 for Dr. MacLeod?

21
22 CROSS-EXAMINATION BY THE JURY:

23 BY JUROR #5:

24 Q. The morphine, she took 14.5 in two
25 hours; is that too much for a child?

1 A. No, I don't think so. It's a relatively
2 high dose. If it had just been given once as an
3 injection, you know, all at once, that would be quite a
4 high dose.

5 Q. Yes.

6 A. You wouldn't normally see that kind of
7 dosing outside of a very controlled setting like an
8 operating room, but 14.5 milligrams over a period of an
9 hour and half given in small doses repetitively, it's
10 not -- it's hard, but not out of the ordinary.

11 Q. How about four drugs that were mixed in
12 the body, would that be un-normal (sic)?

13 A. The fact that she was receiving four
14 drugs? Well, she had a very unusual syndrome, and
15 you've undoubtedly heard, so she had a pain condition
16 for which there is no simple treatment. I mean, in the
17 minds of most of us, simple is always better than
18 complicated. If this could be controlled with one
19 drug, that would be the ideal, but it's not unusual
20 when you start to deal with some of these very
21 complicated conditions to try a recipe, you know, to
22 add some different drugs and she was treated by people
23 who are expert in these conditions and there's no doubt
24 that this was to some degree ---

25 Q. In two hours, they gave her four

1 different drugs. As a doctor, would you have done
2 that?

3 A. No, no, I'm sorry, I don't think they
4 gave -- she was on four drugs.

5 Q. Yes.

6 A. She was receiving those before she came
7 to the hospital; three of the drugs she was receiving
8 before she came to the hospital. The fourth one was
9 added in the hospital, the morphine, so I don't find
10 anything unusual in that. She had three drugs that
11 were intended to control her pain, but her pain was not
12 controlled and she came to the emergency department.
13 The people who saw her in the emergency department
14 obviously felt compelled to add an additional
15 treatment, really, the traditional treatment for pain,
16 and in fact I think there is evidence that it did
17 relieve her pain. It may have caused other
18 complications, but it did relieve her pain.

19 Q. That's what I was asking, did it cause
20 any complications, that's what I was asking.

21 A. Yes. No, well, you know, I think ---

22 Q. You would bet there was?

23 A. The conclusion that I would draw at the
24 end of this is that somehow those four drugs caused her
25 death.

1 Q. Thank you.

2 THE CORONER: Any further questions of Dr.
3 MacLeod?

4

5 BY JUROR #1:

6 Q. Well, when we speak about the four
7 drugs, wasn't there just a very small trace amount of
8 amitriptyline in the blood samples, so do we include
9 that as a fourth drug?

10 A. Oh, I think you have to consider it as
11 part of the equation. Bear in mind that the amount
12 that's in the blood is not necessarily what's
13 important; it may be the amount that's in her heart or
14 in her brain or in some other location, so that drugs
15 differ in how they distribute themselves in the body,
16 so they don't always circulate in the blood. The dose
17 of amitriptyline that she received was not a high one,
18 but it's not an insignificant one, either, and
19 amitriptyline is certainly a drug that does have the
20 ability to affect the heart as well as some other
21 organs. So I don't think you can dismiss amitriptyline
22 as a factor in this, but I think it's relatively less
23 likely that it played an important role.

24 Q. Less likely than the gabapentin?

25 A. I think that the two most likely

1 interacting drugs are gabapentin and morphine.

2
3 BY JUROR #5:

4 Q. Would you know exactly which part of the
5 body that each drug went to?

6 A. Oh, this is known. There are studies
7 that -- whenever drugs are introduced for human use,
8 there's a process of studying them ---

9 Q. Where it goes?

10 A. --- that looks as much as possible at
11 how they distribute to different organs and what
12 effects they have in different organs and because your
13 heart is so critical to your whole well-being, almost
14 every drug that comes on the market is studied with
15 respect to its effect on the heart. You still can't
16 say absolutely this is how this drug will affect that
17 particular patient, because we all differ. I mean, our
18 hearts are different as well as ---

19 Q. But the majority will go to the heart?

20 A. No, not necessarily, but -- oh, you mean
21 the majority of drugs will go to the ---

22 Q. Yes.

23 A. Yes, almost all drugs circulate and, of
24 course, much of the circulation passes through the
25 heart so many of them have effects on the heart.

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BY JUROR #3:

Q. In addition to his question, since you indicated that most of the morphine goes to the heart, then can I assume then at 2:50 a.m. when the respiration is at that lowest level, 8 and 10, can I assume then that there was -- there could have been a damage in the heart?

A. No, I think you have misunderstood something that I said. The effect of morphine on the respiration is actually mediated in the brain and so when you breathe, we all breathe unconsciously but we breathe because our lungs are getting messages from our brain that say, you know, inhale/exhale, we're not aware of it because we have been doing it since birth, but that's what's going on, and morphine stops that respiratory drive by an action in the brain, it's not acting in the lungs, it's acting in the brain. So I can't -- but morphine does have some effect directly in the heart and on blood vessels and so that may have contributed to the picture that you see here, but it's major effects are in the brain. That's why it's used for pain relief, because that's where we sense pain, as well. Have I confused you?

1 Q. No.
2 A. Okay.
3 Q. Thank you.

4
5 BY JUROR #5:

6 Q. Was that -- the swelling of the brain,
7 was that caused by the drugs?

8 A. I'm sorry, I don't know about the
9 swelling of the brain. The autopsy report that I had I
10 thought said the brain was normal.

11 THE CORONER: Dr. Smith commented that there
12 was slight swelling of the brain which he
13 felt was related to terminal events in terms
14 of whether she died over a five-minute period
15 or a ten-minute period, but he was relating
16 it to that as opposed to anything else.

17 THE WITNESS: I mean, this is something that
18 happens in death in anybody under any
19 circumstances. As the brain is deprived of
20 oxygen, it swells a little bit, so I don't
21 think you could attribute that to drugs
22 directly.

23 THE CORONER: Any other questions? Thank
24 you very much, Dr. MacLeod, for coming and
25 giving us the value of your expertise.

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THE WITNESS: You're very welcome.

THE CORONER: We'll adjourn until 9:30
tomorrow morning.

--- ADJOURNMENT.

THIS IS TO CERTIFY that the foregoing
is a true and accurate transcription
of my recordings and notes, to the
best of my skill and ability.

Barbara A. Pollard
Certified Court Reporter

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signature of Barbara Pollard, and accordingly are in direct
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Act, January 1, 1990.