IN THE HIGH COURT OF JUSTICE

1990 R No 860
1989 H No 3689

QUEEN'S BENCH DIVISION

ROYAL COURTS OF JUSTICE
THE STRAND
LONDON

Tuesday 24th November 1992

Before

THE HON. MR JUSTICE FRENCH

ELIZABETH REAY

Suing on her own behalf and as
Mother and Administratrix of the
Estate of DOROTHY REAY (deceased)
and as Widow and Administratrix of the Estate
of GEORGE REAY (deceased) (Plaintiff)

V.

BRITISH NUCLEAR FUELS plc (Defendants)

AND

VIVIEN JANE HOPE (Plaintiff)

V.

BRITISH NUCLEAR FUELS plc (Defendants)

APPEARANCES:

For the Plaintiffs: MR B A HYTNER QC
MR B F J LANGSTAFF
MR G S READ and MISS T GILL
(Instructed by Messrs Leigh, Day & Co. Solicitors, London)

For the Defendants: MR K S ROKISON QC
MR M G SPENCER QC
and MR C J BUTCHER
(Instructed by Messrs Freshfields, Solicitors, London)

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TWELFTH DAY'S PROCEEDINGS

TUESDAY, 24TH NOVEMBER, 1992

MR. HYTNER: My Lord, I call Prof. Greaves. My Lord, may I, first of all, make an apology that, through an administrative blunder, in respect of which I am wholly innocent, your Lordship's T-cell lineage has got mislaid between whoever took it from your Clerk last night and Prof. Greaves, so he has not seen it. My Lord, no doubt it can be put to him in the witness box if your Lordship has copies.

MR. JUSTICE FRENCH: It will be none the worse and none the better for that.

MR. HYTNER: My Lord, it has been agreed between Mr. Spencer and myself that, in respect of Prof. Greaves' report, only A and B should be dealt with today, C onwards being contentious.

MR. JUSTICE FRENCH: So it is pages 5-12.

MR. HYTNER: 1-5, my Lord, I think.

MR. JUSTICE FRENCH: 5-12, I think.

MR. HYTNER: Yes.

MR. SPENCER: My Lord, also on Prof. Greaves' second report, paragraphs 15, excluding the last phrase, and 16.

MR. JUSTICE FRENCH: So page 8, isn't that, if I remember rightly?

MR. SPENCER: The bottom of page 7, top of page 8.

MR. JUSTICE FRENCH: I have read that. So it is 5-12 of the first report....

MR. HYTNER: No, my Lord, 1-5 of the first report.

MR. JUSTICE FRENCH: That is dealing with biography and summary.

MR. HYTNER: My Lord, I have got a different pagination, I am sorry. That will be about right. My Lord, it is sections A and B.

MR. JUSTICE FRENCH: Yes, and that is 5-12.

MELVYN FRANCIS GREAVES Sworn:

Examined by MR. HYTNER:

Q. Will you give your full name, Prof. Greaves?
A. I am Prof. Melvyn Francis Greaves.

Q. Could you just, in a sentence, give your present occupation and appointments?
A. Yes, I am a research scientist and I am employed by the Institute of Cancer Research as the Director of the Leukaemia Research Fund Centre at the Institute for Cancer Research.

Q. I think it is probably more sensibly chronologically, before you deal with the diagnosis of Dorothy and Vivien, to go to section B in your report, which is - I am not sure what your page number is. It is page 3 in mine.
A. Yes.

MR. HYTNER: What I propose to do, my Lord, is just briefly ask him to go through this, really not reading it out, but if your Lordship requires any amplification, perhaps your Lordship would indicate:

Q. I think your report is written broadly in English, Prof. Greaves. I think it does not require very much translation.

Q. MR. JUSTICE FRENCH: Can I just ask something at the outset which has puzzled me, as to whether, when one is dealing with the initials ALL, one is speaking always of acute lymphatic leukaemia or whether one is also speaking of acute lymphoblastic leukaemia and whether there is any difference between the two if you are. Do you follow?
A. Could you repeat the beginning of the sentence, your Lordship?

Q. ALL is a series of initials with which we have become familiar and, no doubt, you have been familiar a long time. One sometimes sees it written out "acute lymphatic leukaemia". One sometimes sees it written out "acute lymphoblastic leukaemia". Is there any difference?
A. No, my Lord, there is no difference. They are interchangeable terms. Most people would use "lymphoblastic" but they are really the same.

Q. MR. HYTNER: While my Lord is asking that, which I am grateful for because it is something that has puzzled us from the start of these medical reports, could you just explain more fully what a blast is, what type of cell a blast is, because it is not just used for lymphoblastic. The term "blast" is used for all sorts of stem cells?
A. Yes, it is actually a very old-fashioned word to describe the physical appearance of a cell down a microscope and it simply means a large cell.

Q. Has it no connotation in relation to a cell which is a stem cell as opposed to a cell which does not proliferate?
A. The large cells are invariably dividing, so it is really a dividing, active, large cell but, other than that, there are no implications about where it sits in the developmental system of blood.

MR. JUSTICE FRENCH: I may have got this wrong and, no doubt, it will be proved very quickly if I have. I understood Prof. Catovsky to describe it as an immature cell.

MR. HYTNER: My Lord, that is why I was asking the question.

Q. MR. JUSTICE FRENCH: That is not how you would express it?
A. That is not how I see it, no. Mature cells, when they are dividing, have this blast-like appearance. It is a feature that many cells can take on when they are activated.

Q. What is a blast-like appearance?
A. It is simply a large cell and the nucleus, under the microscope, has a particular appearance characteristic of active cells. It is rather an anonymous appearance, as a matter of fact, but most people recognise it....

Q. MR. HYTNER: Since there may be a difference between yourself and Prof. Catovsky about this, could we actually explore this a little more? The term "immature" and "mature" cells, is the mature cell the cell after it has divided and differentiated and is then ready to perform its function in the body? Is that what is meant?
A. That is exactly correct, yes.

Q. That is correct?
A. Yes, it is a functional cell.

Q. MR. JUSTICE FRENCH: No matter of what kind?
A. That is correct.

Q. Whether it is pluripotent or differentiated?
A. The pluripotent cells are not functional. The mature functional cells have a single function, are a single cell type.

Q. I thought pluripotent cells had lots of functions?
A. Their function is to produce other cells that have functions, my Lord. May I make one other comment on this, that this is partly a historical anomaly, that large dividing blast cells were thought a few decades ago to be immature because people were used to this appearance being characteristic of immature cells, but when the biology of these cells was analysed, really in the '70s, it became apparent this morphology was actually

rather misleading in terms of whether cells were mature or immature and there are other criteria that are used in the laboratory to make that definition whether the cell is an immature or mature cell. A blast definition, purely cells, this is an active dividing cell and no more.

Q. Sorry, you used a word like "divided" and I am not sure whether I heard it correctly?
A. Cells that are proliferating. That is to say, they are dividing to make daughter cells.

Q. Dividing?
A. Dividing, yes.

Q. Blasts are mature cells....?
A. Blasts can be immature or mature cells.

Q. Blasts are large cells....?
A. But in the process of dividing to produce daughter cells.

Q. MR. HYTNER: Does it follow then that a fully mature cell, which has ceased proliferating or dividing and is now performing its sole function, would never be a blast?
A. No, it does not because, in the lymphoid system, uniquely in the whole body, these mature cells have the capacity to remain dormant for years or decades, but then become activated to become a blast, so uniquely in that cell system mature cells can become blastic.

Q. This is in the lymphoid system?
A. In the lymphoid system, yes.

Q. MR. JUSTICE FRENCH: Is this correct, Prof. Greaves? Uniquely in the lymphoid system, mature cells may remain dormant for years and then become active?
A. It is, my Lord.

Q. MR. HYTNER: That leads me to a question which I was going to put at some stage and it seems a convenient time to put it. It relates to an answer that Dr. Hylton Smith gave when he was giving a general exposition on the whole field of radiation and so forth. If one takes cells in the body other than in the blood system, once a cell becomes mature and is performing its function, has it then got a limited life span?
A. Outside of the lymphoid system?

Q. Outside of the lymphoid system?
A. Not necessarily. For example, muscle cells and nerve cells, which stop dividing when they become mature, can live for many, many years also, but unlike lymphoid cells, they cannot then be activated into division.

Q. If such a cell suffered a mutation of a gene for any reason, would that be in any way dangerous to the life or

limb of the individual, save that that particular cell might be killed?
A. I assume you are referring now specifically to those mature cells that cannot undergo or do not normally undergo further divisions.

Q. Yes?
A. The generally held view, which I subscribe to, is that those cells are not at risk of transformation and contributing to disease if they are not dividing or are unable to divide.

Q. Would that be so in the lymphoid system?
A. No, it would not.

MR. JUSTICE FRENCH: Is this something that sounds as though it may be rather important?

MR. HYTNER: Yes, my Lord, it is something that really is contrary to something that Dr. Hylton Smith said.

MR. JUSTICE FRENCH: That is what made my ears, as it were, prick up:

Q. Let us go back to square one. Some cells, e.g., muscle cells, may remain functional in the body for decades?
A. That is correct.

Q. MR. HYTNER: But they never divide? Once they are mature, they never again divide?
A. It is extremely unlikely.

Q. MR. JUSTICE FRENCH: "It is very unlikely that they will divide and, if there be DNA damage to such a cell, the general view, to which I subscribe, is that the surrounding tissue is not at risk", or will that not do?
A. Or the tissue itself that has been damaged, the muscle cell or the nerve cell.

Q. The tissue of which the cell is a part?
A. That is correct, yes.

Q. I think you said this does not apply to the lymphatic tissue?
A. That is correct, my Lord.

MR. HYTNER: My Lord, Prof. Greaves has just used the phrase that concerned us when Dr. Hylton Smith was giving evidence. It may be that, if Dr. Hylton Smith had been asked to expand on the phrase, there would not have been a conflict between them, but the phrase was "at risk". Prof. Greaves has added on to that phrase "at risk of further transformation" and, my Lord, that, I think, may be the clue to the real puzzle by Dr. Hylton Smith.

MR. JUSTICE FRENCH: Yes.

Q. MR. HYTNER: So that there is no doubt about this, if a cell in the lymphoid system mutates for whatever reason, would there then be a risk of further damage being caused to the tissues?
A. Yes.

Q. MR. JUSTICE FRENCH: To spell it out, a risk of further damage to the lymphoid tissue?
A. That is correct, my Lord.

MR. HYTNER: My Lord, I am asked to keep strictly to within A and B and and I shall do so:

Q. Could you now look at Figure 1 on page 4?

MR. JUSTICE FRENCH: Can I just interpose to say that you were quite right about the pagination. The index at the front of the report is wrong. Yes, page 4?

MR. HYTNER: And we come to Figure 1. My Lord, I am not sure whether anything on Figure 1 requires amplification for your Lordship.

MR. JUSTICE FRENCH: I regarded - I do not know if you remember - I regarded this as perhaps being complementary to the cell diagram that I handed down last night.

MR. HYTNER: Yes, my Lord.

MR. JUSTICE FRENCH: Have we got one?

MR. HYTNER: My Lord, the trouble is I have not. (Produced to witness)

Q. MR. JUSTICE FRENCH: Let me own up, Prof. Greaves. I caused that to be extracted from the Penguin Dictionary of Biology and it seemed to me, thinking purely as a layman, as though it might be a complement to yours and really I welcome any criticisms of that because I do not know how accurate it is?
A. Well, my Lord, on looking at it quickly, there really is no difference of any substance in the way this cellular family tree is drawn from the one that I have drawn. The only difference really is that I have added on to mine how these different types of cells can give rise to different types of leukaemia and lymphoma, but the general structure is essentially the same.

Q. It seems to me as though one has more B proliferation than the other. I may be wrong about that?
A. Well, no, I do not think there is, in effect, my Lord.

Q. Very well. Anyway, you regard that sheet as being a fairly useful mnemonic for....?
A. Yes, it is relatively simple and generally correct.

Q. If there is any important inaccuracy, would you please say?
A. I cannot see any inaccuracy, my Lord.

Q. MR. HYTNER: I think, going over again to the end of B, at the top of page 5, there does not seem again to be anything that requires explanation since, as I say, most of your report is written in English. Now, having done that, could you go back to the beginning of your report, which I had overlooked, and go back to the diagnosis of Dorothy and Vivien. Is a possible difficulty in relation to both these girls that, since they were diagnosed at a time when there was no litigation, the diagnosis was made on clinical grounds and not on a haematological examination?
A. It is not entirely true. I think the problem was, particularly with Dorothy Reay, that this diagnosis was many years ago before some of the additional useful tests we now have were available, plus there was not an adequate store of material that we could look at retrospectively to do the type of tests that one would normally do in the 1990s to look at these types of illnesses.

Q. MR. JUSTICE FRENCH: Tissue was not retained. Is that what you are saying?
A. There is a small amount of tissue, but insufficient tissue of adequate quality, as several people, including myself, have noted.

Q. I suppose the very fact of preserving it reduces the quality, does it?
A. Not necessarily. I think now there are probably better ways of preserving material, my Lord, but 20 years ago or so that was not the case perhaps.

Q. MR. HYTNER: But you have little doubt that she did have acute lymphoblastic leukaemia?
A. Dorothy Reay you are referring to?

Q. Dorothy Reay?
A. Yes, I think it is really extremely unlikely that there could be any other diagnosis other than acute lymphoblastic leukaemia in this case, based on the post mortem analysis primarily.

Q. There will, of course, be other evidence in relation to diagnosis, but turning to Vivien Hope, have you any doubts from what you have seen, from the data you have reviewed, that she suffered from non-Hodgkin's lymphoma?
A. No, I see no reason to doubt that.

Q. You speak of the expertise of the centre who diagnosed her and the fact that she was said to have a B-cell type lymphoma. Do you regard it as a possibility now to be certain as to what cell lineage her lymphoma was?
A. No, I do not. I think, unfortunately, that no information has been provided from Newcastle as to

whether this was, indeed, a B-cell or a T-cell type of disease, and I understand that subsequent tests that have been performed, I believe by Dr. MacLennan, that have sought to answer that question have proved equivocal and, in fact, there is no information on which we could base a decision as to whether it is a B-cell type or a T-cell type, so that remains unknown, I am afraid.

Q. MR. JUSTICE FRENCH: So there is no information from Newcastle and now no means of finding out, you would say?
A. That has been attempted, my Lord, but it was not successful on the material that was available, so I think it is unlikely we will be able to discover whether this was a B-cell or a T-cell type of non-Hodgkin's lymphoma.

Q. Was this Dr. Gatter who did a test?
A. Dr. Gatter, and I believe also probably Dr. MacLennan, attempted to look at some of the sections with immunological methods, but the results were equivocal, I think was the expression used.

Q. Dr. Gatter offered to have another go. I do not know whether anybody asked him to?
A. I am not sure, my Lord.

Q. MR. HYTNER: We can expand on this slightly because, if we go to your second report, paragraph 15 on page 7, it has been suggested you were considering a statement in another report that Dorothy Reay was more likely to have had "a null acute lymphatic leukaemia than a common acute lymphatic leukaemia or one of the acute non-lymphoblastic leukaemias that are relatively more common under one year of age than in the next decade." You agree with that, do you?
A. Could you just direct my attention to which paragraph that is? Did you say....?

Q. 15. It is the bottom of page 7 in your second report?
A. I do not think I have that here actually. I can answer the question, anyway, I think.

Q. I am told it is the back of your file.
A. Yes, thank you. Yes, page 7.

Q. At the bottom. You need not deal with the bit after the semi-colon because that will be dealt with later?
A. Yes, what is meant by that statement is that, in the great majority of cases of infants less than one year of age who have acute lymphoblastic leukaemia, at least 75 per cent of them, probably nearer to 90 per cent, have a form of acute lymphoblastic leukaemia that we have referred to as null acute lymphoblastic leukaemia. What it is, in effect, is a cancer of a very primitive B-cell type, more primitive than the type of cell that is seen in the more common form of ALL in older children.

Q. When you say "primitive", do you mean immature?
A. Yes.

Q. MR. JUSTICE FRENCH: Is "null" a synonym for "immature" or has it a separate meaning?
A. No, my Lord, it is a very bad term, used historically, coming from a time when we were not able to classify this cell so it was labelled "null", meaning it had no markers. This was 10 years ago or more. Subsequently, markers have become available to enable us to identify this type of cell in infant ALL as a very immature B-cell type.

Q. So, if I am making a note of this, if I am to write "immature B-cell type" and forget "null", that would be more helpful?
A. That would be much more helpful and appropriate, I think, my Lord.

Q. MR. JUSTICE FRENCH: Dorothy Reay is more likely to have had an immature B-cell acute lymphatic leukaemia or lymphoblastic leukaemia than common acute leukaemia?
A. That is correct, my Lord.

Q. MR. HYTNER: Now going to Vivien Hope, Prof. Catovsky commented on the "starry sky" appearance in her bone marrow. Could you first of all tell us what that means?
A. In lymphomas in which the cells are proliferating at a very high rate, which are often referred to as high grade malignant lymphomas, there are a great many macrophages, my Lord. These cells are activated in the tumour, they are eating and consuming debris, of which there is a great deal, and then when the lymphoma section is looked at down the microscope at low magnification, in between the actual lymphoma cells are large, pale macrophages containing small pieces of debris. It creates the celestial appearance of a sky, large numbers of macrophages in between the tumour cells, basically.
Q. If that appearance is observed what does it tell the diagnostician?
A. I think it is primarily an indication that it is a high grade malignant lymphoma, more often seen in certain sub-types of lymphoma than in others.

Q. MR. JUSTICE FRENCH: A high grade lymphoma?
A. Yes.

Q. Starry sky indicates a high grade lymphoma?
A. Yes. Almost invariably with a large number of proliferating cells.

Q. MR. HYTNER: High grade you have explained as meaning proliferating at a considerable rate?
A. Hyperactive, yes.

Q. That we understand. Does a starry sky appearance tell you anything of the cell lineage of the lymphoma?

A. Not unequivocally but in certain types of lymphomas of certain lineages this appearance is more frequently observed and, for example, I think I referred to the fact that in Burkitt's or Burkitt-like lymphoma this is almost invariably seen in sections.

Q. You also refer to the B-cell lineage?
A. Yes, Burkitt-like lymphomas are invariably B-cell and in that sub-type of lymphoma, I think because it is high grade and proliferating at a higher rate, there is almost invariably a starry sky appearance. I should add you can see that type of physical appearance occasionally in other types of high grade lymphomas that are not Burkitt-like. It is most commonly seen in the Burkitt-like lymphomas.

Q. MR. JUSTICE FRENCH: Let me see if I can summarise that. Starry sky indicates a high grade B-cell lymphoma, mostly Burkitt's?
A. I am not sure if that wording is quite correct, my Lord. In Burkitt-like lymphomas this starry sky appearance would almost invariably be present. The same appearance can be seen in other types ....

Q. Can I ask you to pause? In a high grade B-cell lymphoma it will almost always be present; it is a Burkitt-like lymphoma? No?
A. That is not quite what I was attempting to say, my Lord.

Q. The trouble is if you do not chop it up I forget where you started and cannot note the answer.
A. Shall I attempt to summarise again?

Q. Yes, please.
A. A starry sky appearance is characteristic of high grade lymphomas and I think we should add the sentence now that high grade lymphomas are those lymphomas in which cells are dividing at a high rate.

Q. Such lymphomas are those in which cells are dividing at a high rate?
A. Then I would add, and I think this is the point that was causing confusion, that this appearance is typical of Burkitt-like lymphoma but can also be seen in other types of non-Burkitt lymphomas.

Q. This is typical of Burkitt-like lymphoma but can also be seen in non Burkitt-like?
A. That is correct.

Q. The word or the capital letter "B" does not appear in that. Should it?
A. We could add that for clarification, I think, my Lord.

Q. Where do we put that in?
A. I think it might be helpful to emphasise that Burkitt is always a B type lymphoma.

Q. MR. HYTNER: Always?
A. Yes. Burkitt lymphoma is always a mature B cell disease.

Q. So if it is Burkitt-like it will be of "B" lineage?
A. Yes. If I might add to clarify the point further, I think my last sentence were words to the effect that this appearance can be seen in non-Burkitt lymphoma, and I think we should say it can be seen in non-Burkitt T or B lymphoma.

Q. It seems sensible now to carry on and just give a very brief description of the difference between a lymphoblastic lymphoma and a Burkitt-like lymphoma?
A. I have to say, my Lord, this is a subtle difference and we run here into the fact that lymphomologists and pathologists have not always agreed about the classification of these diseases, so it does depend somewhat on which national and international classification scheme one adheres to, but the majority of pathological, diagnostic schemes these days would distinguish lymphoblastic from Burkitt-like. That has not always been the case historically but now that is the case. Lymphoblastic would be again a large, as I said, blastic dividing cell. Burkitt cells tend to be rather smaller, more medium size, they have characteristic vacuoles in the cytoplasm of the cell. It is not always easy to distinguish the two which is why historically the two have often been put together.

Q. At the risk of being reprimanded for going outside "A" and "B" would it be sensible to bear in mind, as we go through the whole of this evidence, that until about ten years ago there had not been a great deal of development in the classifications of leukaemias and lymphomas, and that the developments have taken place in the last decade?
A. It is true in a sense that there have been an enormous number of attempts to classify these by morphological and microscopic criteria for decades, of course. What has changed from about ten years ago is the introduction of laboratory tests that greatly refine the precision of the diagnostic analyses, so we are no longer entirely reliant on rather crude features of cell size and shape, but can introduce more definitive tests.

Q. MR. JUSTICE FRENCH: Is this where immuno-phenotypes come in?
A. That is correct, my Lord.

Cross-Examined by MR. SPENCER

Q. Just so we know, Prof. Greaves, as I understand it you have been at the forefront of some of that work in developing the different immuno-phenotyping techniques particularly, I think, in relation to acute lymphoblastic leukaemia, is that correct?
A. That is correct.

Q. Just by way of background, you come to this subject not from a medical training but from a zoological training, would that be correct?
A. I think the zoology is almost irrelevant, with respect. I come to it from a laboratory based immunological training.

Q. I just wanted to be clear that you were not, in fact, a clinician, you are not medically qualified?
A. That is correct.

Q. One of the problems that has bedevilled this area is that it is looked at by so many different types of scientists, if I can use that word all-embracingly, who come to the subject from different points of view?
A. Correct.

Q. The clinician naturally enough is anxious to identify the disease as accurately as possible because that may assist him in his treatment of the disease, that is right, isn't it?
A. That is correct.

Q. So much of the efforts of the last ten years to identify the different diseases by type and sub-type, using as we now can monoclonal antibodies to provide immuno-phenotypes, has been generated by the desire of clinicians to finely hone their treatments?
A. That is true.

Q. Because if you can narrow down your diagnosis to as unambiguous a disease entity as possible, then you are better able to assess the efficacy of the treatment that you apply to it. It is really as simple as that, isn't it?
A. Yes.

Q. Just as a matter of background, I do not know whether you know that Vivien Hope's condition was treated by a treatment regime applied to it at random as part of a controlled trial?
A. I am not aware of how she was treated.

Q. Would that surprise you particularly?
A. Not particularly. I think the way these patients are treated does depend on when it happened, what part of the country they were in, what hospital they were seen at. It is not particularly surprising.

Q. Many patients get assigned to a particular treatment trial where the treatment is, as it were, drawn out of an envelope blind as part of an assessment of the efficacy of various treatments. You know about that?
A. That is very common, yes.

Q. Only in that way can the clinicians develop a feeling for the efficacy of one treatment compared to another, that is right, isn't it?
A. That is correct, yes.

Q. Can I start by asking you about the point of controversy. We had hoped to avoid controversy today and it may be we have, I don't know. It crept into your evidence right at the beginning, and that is where you and Prof. Catovsky appear to part company over the concept of what exactly a blast is. As we know Prof. Catovsky in his report - you have seen his report because you have commented upon it in your second report?
A. Yes.

Q. He does refer to the disease, acute lymphoblastic leukaemia, as a disease seen in the early immature lymphoblast, I think. That is right, isn't it?
A. I have not got it in front of me but that statement is correct.

Q. You have seen that he says that?
A. Yes, indeed.

Q. It is right too that is not something that you have commented upon at all in your second report, that statement, have you?
A. It is completely non-contentious.

Q. I thought you would say that.

MR. JUSTICE FRENCH: I think what is contentious, or may be contentious, is what a blast is.

MR. SPENCER: Yes:

Q. Can we explore that? He appears to be suggesting that a blast is an immature cell, or may be in this disease?
A. Catovsky is referring to the term blast in the context of acute lymphoblastic leukaemia and in that particular context it is indeed an immature cell.

Q. I am grateful, and we can marry that up with your statement, bottom of page 4, first report ....

Q. MR. JUSTICE FRENCH: Can I just write this down and see if it is right? In the context of acute lymphoblastic leukaemia the blast is an immature cell?
A. Yes.

Q. MR. SPENCER: If I can take you to your report where you appear to be saying the same thing, the bottom of page 4:

> "Thus, acute lymphoblastic leukaemia (ALL) is the result of malignancy in the precursor cells of the B or (to a lesser extent) T lineage."

A. Yes.

Q. And there you are referring to the same thing are you not?
A. That is correct.

Q. If Prof. Catovsky were to say that blasts generally are only the immature cell then you and he would part company?
A. We would, yes.

Q. It is far from clear that he says that but we will be able to find that out this afternoon. I am not going to ask you, Prof. Greaves, about the evidence that you have given about cells dividing and when a lymphoid system cell can mutate as a blast that has lain dormant, because we will come to that, I think, when we consider genetics - we are concerned with mutations when we come to genetics. What I want your help about if you would be so kind is considering the types of disease with which we are concerned. It is right, isn't it, that you would agree that the disease that in all probability Vivien Hope had was a distinct disease entity from acute lymphoblastic leukaemia?
A. That is very likely, yes.

MR. JUSTICE FRENCH: Could you repeat that?

MR. SPENCER: The disease Vivien Hope had was a distinct disease entity from acute lymphoblastic leukaemia:

Q. Just so we can try and understand the problem, the lymphomas, properly so called, arise from lymph cells coming from the lymphatic system?
A. That is correct, yes.

Q. The problem is that such cells are found in the bone marrow, that is right, isn't it?
A. Yes.

Q. And can indeed lead to disease in the bone marrow?
A. Yes.

Q. So again the diagnosticians are always anxious to try and see whether the disease, that I suppose may in some cases present simply as a bone marrow disease or leukaemia, is in fact a lymphoma, by looking very closely at the cells involved?
A. That is correct.

Q. MR. JUSTICE FRENCH: Can I intervene here? I have read somewhere that lymphomas while plainly coming from or concerning lymph cells, migrate from the lymph system to the bone marrow and then back again. Is that nonsense?
A. That is correct.

Q. So it is not that they originate in the bone marrow, it is that they come from somewhere else, go to the bone marrow and then out again?
A. Yes, these are cells that circulate round the body, my Lord, into bone marrow and indeed to other tissues to some extent, as part of their normal function of looking for infections and dealing with them.

Q. So when one reads that they migrate to the bone marrow, they could equally well migrate to the kidney?
A. They would be migrating through the kidney either in the lymphatic or the blood cell system, passing through, so to speak, trafficking through.

Q. MR. SPENCER: We have a lymphatic system that I think connects between one lymph node and the other, doesn't it?
A. That is true, yes.

Q. And we have a constant circulation of lymph cells through that circulatory system, all looking for disease?
A. Yes.

Q. But also the lymph nodes push lymph cells into the blood circulation as well, for the same purpose?
A. That is correct. The lymph node is not only a traffic zone but it is also a production site for those cells.

Q. Right, and so those cells go out of the lymph nodes into the blood system where they circulate quite happily in the blood system, again looking for disease?
A. Yes.

Q. Then they drain out of the blood system back into the lymph glands again as well?
A. Yes.

Q. Just so we can understand it, the lymph cells produced by the lymph system are the watchdog cells that identify disease, do they not?
A. They identify primarily infections.

Q. Infection is what I meant, the presence of a foreign infection?
A. Yes.

Q. Which will create an antigen/antibody response?
A. An immune response, that is correct.

Q. Sometimes called a humoral immunity or ....?
A. Yes, if they make antibodies as a response it is referred to as a humoral response.

Q. The lymph cells make antibodies?
A. That is correct.

Q. MR. JUSTICE FRENCH: They make antibodies as well as detect infection?
A. Yes.

Q. MR. SPENCER: Once they detect infection then a series of reactions are set up that result in other cells coming from different places, and the body begins the great fight. That is how it works, isn't it, very simply?
A. Yes, more or less.

Q. So if we can get back to where we were it is no surprise that one finds lymph cells in the blood and indeed in the bone marrow?
A. No surprise at all.

Q. As I was putting to you, and you agreed, the first presentation of what is truly a lymphoma in the sense that it is a disease of a lymph cell that has come from a lymph gland, may in fact appear as a leukaemia, that is, a disease in the bone marrow?
A. That is unusual but it can happen, yes.

Q. I accept entirely it would be unusual but it could happen?
A. Yes.

Q. MR. JUSTICE FRENCH: Presumably when diagnostic devices were rarer that could happen more often, in days gone by, that the mistake could be made?
A. That is probably correct as well, my Lord.

Q. Lymphomas can rarely be mistaken for leukaemias?
A. Infrequently, yes.

Q. Can infrequently ...?
A. They may infrequently present diagnostically as leukaemias for the reasons you have now outlined, that they may spread to the blood rather quickly.

Q. Present diagnostically as leukaemias; confusion between the two diseases was very likely more frequent 20 years ago?
A. Yes, sir, I think that is a fair comment.

Q. MR. SPENCER: Exactly the mirror image of that is leukaemia, again in leukaemia, acute lymphoblastic leukaemia, that is a disease of the bone marrow, isn't it?
A. Yes, it is.

Q. But in exactly the same way the cells can migrate via the blood system into the lymph nodes?
A. Indeed they do.

Q. And they do, and perhaps rarely again, 20 years ago a condition presented as a lymphoma when in fact it was in truth a leukaemia?
A. Yes. I must say this still happens today to some extent with respect to a particular type of ALL that can present as a lymphoma or an ALL, the T-cell type.

Q. Is that the T-cell type?
A. That is the T-cell type. It is there that there is still some confusion between whether the disease is truly a lymphoma or a leukaemia. I think Catovsky comments on that as well.

Q. Catovsky does comment on that and he makes that very point. Really what he appears to be saying is that nowadays, given our modern techniques, that is really the only area where that sort of mistake should now be made, given what I would call a full work-up?
A. Yes.

Q. You know what I mean by a full work-up?
A. Yes, of course.

Q. And you would agree with that?
A. Yes.

Q. MR. JUSTICE FRENCH: T-cell lymphomas are even today hard to distinguish?
A. No. Malignancy of a T-cell system can present either as, essentially the same disease, but can present either as a lymphoma or a leukaemia, depending on the stage when they are detected and quite often whether it is a pathologist or a haematologist who happens to look at the material.

Q. Yes. Cancer of the T-cell system can present either as a leukaemia or as a lymphoma. Diagnosis may depend on who makes it, a haemotologist or a pathologist?
A. Yes.

Q. MR. SPENCER: However, when we are dealing with T-cell disease there are other clues available to assist us in our diagnosis frequently, are there not?
A. There are laboratory tests with antibodies. The immunological tests I think you referred to earlier would help us to sort out the situation.

Q. Yes, and also presentation. As I understand it in half the cases of T-ALL there would be a thymic tumour as well?
A. Yes, we were talking about an origin from the bone marrow. The T-cell malignancies we are talking about actually originate in the thymus gland in the upper chest, and very often in these cases on X-ray there will be an enlarged thymic gland that can be seen, and this would be of diagnostic significance.

Q. You have identified absolutely correctly if I may say so, Prof. Greaves, the one area where there is room for diagnostic confusion, and I am really now just taking that on to identify how it is that the diagnostician can get round the difficulty that situation presents. One of the other clues, as you have just said, would be in the ALL, the T-ALL, you would often see, I think you agree 50%, there might be a thymic tumour?
A. Yes.

Q. And with the lymphoma, the T-ALL lymphoma, I understand from Prof. Catovsky's report that the thymic tumour would be there in 95% of cases?
A. Yes, that is probably right.

Q. Also Prof. Catovsky sets out - my Lord, it is page 15 and I do not think I need go through it with the witness because he has read it and as I understand his evidence I do not believe he disagrees with it - it is all set out on page 15 of Prof. Catovsky's report where he identifies various other subtle investigations that can be carried out to narrow down the diagnosis, and you would agree with what he there sets out?
A. Yes.

Q. Though the distinction between the diseases may, 20 years ago, have been a cause for confusion, to a very great extent nowadays that confusion should no longer exist? The diagnosis, the differential diagnosis can now be made as between the one disease entity and the other? That is right, isn't it?
A. That is correct. I would add that we have moved along from simply a distinction between lymphoma and leukaemia, into a more biological definition of the disease.

Q. Yes, but we are able to distinguish those two, and we are now looking at the different types of disease within those types? Is that what you are referring to?
A. That is right, yes.

Q. MR. JUSTICE FRENCH: What would you describe as the genus, of which these are species?
A. They are lymphoid cells, my Lord. We were talking specifically about the T-cell system within which one can have lymphoma or leukaemia, really of the same cell type. It is only by identifying the cell type in the laboratory that we can draw the conclusion that leukaemia and lymphoma are in fact malignancies of the same cell type.

Q. MR. SPENCER: To help my Lord, the genus is a malignancy of the T lymph cell?
A. Yes.

Q. MR. JUSTICE FRENCH: In each case?
A. Yes.

Q. MR. SPENCER: In each case, and we are now looking for sub-species in each case of the two diseases?

MR. JUSTICE FRENCH: In the case of each disease it is a cancer of the T-cells.

Q. MR. SPENCER: Obviously the same applies in respect of the B-cell lineage as well?
A. Yes.

Q. MR. JUSTICE FRENCH: The "T" in T-cells comes from the thymus?
A. Ultimately all of these cells come from the bone marrow...

Q. I am sorry, the "T"...
A. The letter "T" stands for thymus.

Q. What does the "B" stand for?
A. Well, I introduced that term 15 years ago and it now seems slightly anomalous, but it stood for bursa, derived because this system of cell production was sorted out first of all in the chicken and in the chicken the B-cells are produced in the bursa. Subsequently we discovered that these B-cells are produced in the bone marrow, which fortunately also begins with "B", so we can use it interchangeably for bursa in the chicken or "B" for bone marrow in ourselves and mammals.

Q. Is that one of the chicken bits that is not present in man because it is combined with something else?
A. That is correct.

Q. MR. SPENCER: The Bursa of Fabricius?
A. Yes.

Q. I only know that because it is in Prof. Catovsky's report, Prof. Greaves! Just to recap. we have with our B-cell lineage, two diseases, lymphoma and acute leukaemia. Similarly, with the T-cell lineage and we must not lose sight of, though we are not concerned with, acute myeloid leukaemia, which is quite a different disease concerned with the myeloid lineage cells, and also the range of chronic diseases which again are affecting different cells or cells at different stages of maturity and also constitute in themselves a different category of disease? That is right?
A. Yes, as illustrated in my Figure 1 on page 4 of my report.

Q. There is just one thing I wanted to ask you about...

A. MR. JUSTICE FRENCH: Before we go on, can we forget as far as Dorothy Reay and Vivien Hope are concerned, all about AML?
A. Yes, I believe we can.

MR. SPENCER: My Lord, I think that is common ground:

Q. I think we can forget about chronic disease too?
A. Yes.

MR. JUSTICE FRENCH: Yes.

Q. MR. SPENCER: Just before we come to your report, the extent to which these are now established as separate diseases, and I am talking specifically here about the difference between non-Hodgkin's lymphoma and acute lymphoblastic leukaemia. They may well be treated in different units in a hospital by different specialists? Would that be a fair generalisation?
A. I think that varies. In some hospitals both would be treated by the same physician. In other hospitals they may be treated by different individuals.

Q. In a District General Hospital you may have very little choice as to who treats you and the same man will treat both?
A. Yes, quite possibly.

Q. In what I might call a tertiary referral centre like the Royal Marsden you would have quite different specialists specialising in the one or the other?
A. Usually, yes.

Q. The specialist treating the leukaemia would be a haematologist, I think?
A. That is correct.

Q. Whereas the person treating the lymphoma could be an oncologist?
A. Yes, that is true.

Q. Someone who treats lumps.

MR. JUSTICE FRENCH: Prof. Fairley used to describe the onkos as the brain of an ass. I think he was joking!

MR. SPENCER: Yes. It's unfair on asses!

Q. Figure 1, Prof. Greaves. Just one thing I wanted to ask you about. At the top right hand corner you show the pluripotential stem cells giving rise to CML and AML, via the myeloid lineage for AML. Forgive me, I would have thought it was the other way round? If you transpose CML with AML, it might better represent what happens?
A. No, that is not correct. This is a very simplified diagram, of course. It may well be misleading, but what it is meant to indicate is that AML comes from a cell type which is derived from the pluripotential stem cell and is now in the myeloid section of the family tree. CML is also, of course, a myeloid cell. It comes from the transformation of the pluripotential stem cell, which is common to the lymphoid and myeloid system, but the cell has the appearance of a myeloid cell which is why the disease is called chronic myeloid leukaemia, but its origin is from a stem cell. It is a case where the morphology of the leukaemic cell that the haematologist would see is in fact misleading in terms of its origin. It is only by the biological investigations that we have been able to discover that that disease originates in the stem cell.

Q. The disease AML does as well, doesn't it?
A. It normally originates from a slightly less primitive cell which is not the pluripotential stem cell but an immature myeloid cell.

Q. That is why you put in the myeloid lineage to indicate that?
A. Yes. It is equivalent to ALL originating from immature lymphoid cells.

Q. Very well, I don't think we need trouble about that. Can I then ask you about the diagnosis that we have in these two cases? Starting with Dorothy Reay, you have already said in your evidence you agree with Prof. Doll's statement, which you refer to on page 7 of your second report, that Dorothy Reay is more likely to have had a null acute lymphatic leukaemia than a common acute lymphatic leukaemia. That caused me a slight concern because Prof. Catovsky appears to say in his report that in his view she had most probably an early B acute lymphoblastic leukaemia and I wondered whether in fact there was any difference between those two, but I think the answer is that for all intents and purposes there is not?

A. There is no difference at all between those two.

Q. Sometimes the null sub-divides into either "early" on the one hand or a pre pre-B? Is that right?

A. I think that level of detail is not important, with respect. It is a very immature B-cell. It can be called null. There is no difference of opinion between the experts on this point.

Q. Whether one calls it "early" or "null", there is no difference? You are ad idem? You agree?

A. Yes.

Q. MR. JUSTICE FRENCH: So you can use null and early B-cell interchangeably?

A. Yes.

Q. MR. SPENCER: It just so happens Prof. Doll used "null", and you have agreed with it. Prof. Catovsky uses "early". Can I then come to Vivien Hope? As far as this is concerned you appear to be agreeing with Prof. Catovsky, where he, in his report, refers to Vivien Hope's disease as more likely to have been a B-cell Birkitt-like lymphoma?

A. Yes. I think the only secure conclusion here is that it is a lymphoblastic lymphoma. I said, and I still believe, that it could be Birkitt-like because of the starry-sky appearance, but it seems to be the secure conclusion is that it is a lymphoblastic non-Hodgkin's lymphoma on which the different experts agree.

Q. Prof. Greaves, the law distinguishes between what something could be and what something is more likely to be. You very helpfully in paragraph 16 of your report said that you too believe from the starry-sky appearance of Vivien Hope's bone marrow cells, that Vivien Hope's disease is more likely to have been a B-cell Birkitt-like lymphoma. We find that written there?

A. Yes, but based on that one particular characteristic, the starry-sky...

Q. Yes, I understand. We are only concerned here with, as I have said, what is the most likely diagnosis in her case. I appreciate that nowadays a scientist, pathologist or

oncologist approaching her condition would like to have a greater degree of certainty than we can now obtain from the pathologist's reports of some years ago. Doing the best we can, that is the most likely diagnosis in her case, is it?
A. Yes.

Q. Though I think you have observed in your evidence today that the T-cell lymphoma can produce the starry-sky appearance, it is very, very unlikely that Vivien Hope had a T-cell lymphoma?
A. I think that is very unlikely, yes.

Q. Just so we can be clear, and I don't want to over complicate things but I think it is right we should just look at this for a moment together. The phrase "Birkitt-like" has been used. The reason for that is that there may be two forms of the same disease called Birkitt's lymphoma? Is that something you would agree with as a general proposition?
A. Yes, that is correct.

Q. One disease is what is called endemic Birkitt's lymphoma, that Dr. Burkitt identified in Africa?
A. Yes.

Q. That disease sometimes is seen in countries outside Africa?
A. That is correct.

Q. One of the features of that disease is the presence of the Epstein-Barr virus?
A. Of endemic Birkitt's lymphoma.

Q. But Birkitt's is seen without the presence of Epstein-Barr virus as well?
A. That is true.

Q. When that is the case then it is called sometimes non-endemic Birkitt's?
A. That is correct.

Q. If we are not sure as to which of the two categories it falls in but we are sure it is Birkitt's, we refer to it as Birkitt-like?
A. That is true.

Q. MR. JUSTICE FRENCH: So Birkitt-like is without necessarily the presence of EBV?
A. Yes. Usually, my Lord, with specific reference to the disease presenting outside the endemic regions, which means outside of Africa and south-east Asia. In this case we would refer to it as Birkitt-like because of its Birkitt-like appearance and the fact that the patient is obviously not in Africa.

Q. I think I read somewhere that 80% of the population of this country show signs of the Epstein-Barr virus?
A. That is true, my Lord.

Q. Why is it then not endemic here?
A. The endemic term refers to the disease, not the virus. The virus itself is indeed endemic throughout the world. The disease, Birkitt's lymphoma, in which the virus plays a critical role is only endemic in regions where there is malaria as a critical co-factor. Burkitt discovered it in tropical Africa and it is seen in south-east Asia. Most of us take care of this virus through the immune system and it is rare for it to contribute to lymphoma, for that reason, outside of Africa.

Q. Birkitt-like is an expression used for cases arising outside Africa and Japan too?
A. South-east Asia, my Lord.

Q. Arising outside Africa and south-east Asia.

Q. MR. SPENCER: Just so we can understand it, as my Lordship has observed, 80% of the population have been exposed to the Epstein-Barr virus in the sense that we would present with antibodies to that virus showing that at some stage we had been in touch with it?
A. Yes.

Q. We might never have had the disease as it happens?
A. The vast majority of people don't have diseases associated with infection.

Q. In the endemic form of the disease, as you have observed, malaria is present and would this be right, that it is thought that the malaria damages the immune system and the Epstein-Barr virus is then able to get a hold and establish itself as a disease in that individual?
A. Yes, that is correct.

Q. Of course, the same thing could happen with another disease other than malaria that has the same effect of damaging the immune system?
A. Yes, it could.

Q. AIDS, if I can call it that, springs immediately to mind?
A. Yes, AIDS in particular.

Q. Where we refer to the endemic disease that is really where Birkitt's was principally identified in that particular population?
A. Yes, it is geographic.

Q. The same disease is seen elsewhere?
A. It is.

Q. In its non-endemic form?
A. Yes.

Q. Just so we can understand it, I think one of the markers of the disease is a chromosomal change?
A. Yes, that is correct.

Q. Which would be seen in both forms of the disease?
A. That is correct. It is shared. It is a common chromosome chain. It is shared by endemic and non-endemic Birkitt's lymphoma.

Q. Just finally on this, just because you have the disease outside the endemic area it does not follow from that necessarily that you have not had the endemic disease?
A. In the sense that the virus is playing a critical role?

Q. Could have played a role.
A. That is clearly a possibility but it requires very special circumstances which one should be able to identify.

Q. The way one would hope to identify it is by identifying the presence of the virus in the lymphoma cells, or remnants of the virus in the cells?
A. Yes, that is correct, with the caveat that since 80% of the people carry the virus the tests would have to be performed in such a way they would indicate the virus was in the cell, and a particular form which is characteristic of the transforming activity of that virus. We all carry the virus, obviously. There are tests which should be able to distinguish whether the virus is simply a carrier - it just happens to be there in the individual, which is common - or whether it is there in a special form which could contribute to lymphoma formation.

Q. I see. I think that is as far as I want to go in relation to that. I think I am probably already in somewhat deep water, Prof. Greaves. Just to complete it, I haven't taken you to all the parts of Prof. Catovsky's report that he is going to be giving in evidence today because as I discern it there is really no difference between the two of you on this aspect of the case?
A. I think that is right.

Q. Prof. Catovsky will be here this afternoon and you will be able to hear his evidence this afternoon. I am grateful, Professor.

MR. HYTNER: My Lord, there are two areas, and I only say this out of caution, which I do not propose to re-examine on because whilst the cross-examination has elicited non-contentious broad statements, exploration of the broad statements in re-examination would certainly lead us into contention. Those two areas are the statement that Vivien and Dorothy have distinct diseases. I reserve further re-examination or cross-examination on that because it would lead to controversy. The second area is what else other than AIDS can do the job that malaria does in Africa? I think again if that were explored in detail would lead us into controversy and those areas I don't re-examine on.

Thank you, Prof. Greaves.

MR. JUSTICE FRENCH: Now if I have got it right this is as far as we can get this morning?

MR. SPENCER: My Lord, I am not going to call Dr. Ray Powles and so it is just Prof. Catovsky who will be here this afternoon. My Lord, at two o'clock we will be able to start again.

MR. JUSTICE FRENCH: Very well, two o'clock.

(Luncheon adjournment)

MR. SPENCER: My Lord, I will call Prof. Catovsky.

MR. JUSTICE FRENCH: Yes.

DANIEL CATOVSKY Sworn:

Examined by MR. SPENCER:

Q. Prof. Catovsky, is your full name Prof. Daniel Catovsky?
A. Yes.

Q. And you live at 12 Dell Way, St. Stephen's Road, London W13?
A. Yes.

Q. I think you are the holder of the Chair of Haematology at the Institute of Cancer Research. Is that right?
A. Yes, correct.

Q. And you are an Honorary Consultant at the Royal Marsden Hospital?
A. Yes.

Q. You, I think, have written for the assistance of the Court two reports. The first report is dated 1st June of this year. Is that right?
A. Yes.

Q. And there is a second report also, dated 10th September, 1992?
A. Yes, correct.

Q. And you produce both those reports as your evidence in this case, but it is right to say that we are not concerned today with anything contained in your second report. We are concerned only with your first report and parts of it. I think, in your first report, you set out your qualifications and your experience and I am not going to take you through that because it is there set out and it is plain that, in summary, much of your life's work has been related to the leukaemic diseases. Is that right?
A. Yes.

Q. Lymphomas as well?
A. Yes, indeed.

Q. From the point of view of a haematologist. Is that right?
A. Yes.

Q. Then, at page 3, you set out the overview of leukaemias and lymphomas.

MR. SPENCER: My Lord, I am not going to go through it line by line. I know that your Lordship will stop if there is any particular part that your Lordship wishes to have clarified:

Q. In "Overview of leukaemias and lymphomas" you describe that leukaemias are malignant disorders that arise primarily from the bone marrow cells, but can invade other organs of the body, most particularly the spleen and lymph nodes. Is that right?
A. Yes.

Q. MR. JUSTICE FRENCH: I was just wondering, Professor, about your use of the words "primarily" and "secondarily". You could really leave those out, could you not? You could say, "Disorders arising from bone marrow cells and affecting the blood and other haemopoietic tissues"?
A. Yes, I think you could.

Q. Thank you. I just wondered quite why there was a first and a second?
A. Too many words, yes.

Q. MR. SPENCER: It has just been brought to my attention that you do not, in fact, have in front of you, a copy of your report?
A. I have got it in.....

Q. I think you should have a copy. While that is being brought to you, I think just to assist my Lord, when considering cancer, Professor, the clinician concerned is always concerned to know whether the cancer he is considering is a primary or a secondary lesion. That is right, is it not?
A. Yes, in the context of cancer, it usually starts, for example, in the lung or whatever and then you get metastasis in other tissues.

Q. The reason for that is that, if you are, in fact, treating a secondary cancer but you do not know that it is one, you might miss out on the primary cancer elsewhere and not treat that?
A. Yes.

Q. That is the real concern, is it not?
A. Yes.

Q. So where you refer to "primarily" and "secondarily", it is almost second nature, I suppose. Would that be a fair comment to make?

MR. JUSTICE FRENCH: Yes, I see now why it is there. Thank you.

Q. MR. SPENCER: And you say, in respect of....

Q. MR. JUSTICE FRENCH: Sorry, in the same sentence, is blood itself a haemopoietic tissue? I will tell you why I ask it?
A. Yes.

Q. Because you refer to "the blood and other...."?
A. Haemopoietic tissues. I mean, it should be considered a tissue, I think, yes. It should be considered a tissue.

Q. And a haemopoietic tissue?
A. Haemopoietic, yes.

Q. MR. SPENCER: We seem to think of tissues, Prof. Catovsky, as the solid structures of the body?
A. Yes.

Q. Rather than the liquid structures?
A. The bone marrow is not very solid either. I mean, it is solid, but inside it is not....

Q. Anyway, if we go on, you also deal with lymphomas. Again malignant proliferations of cells and, likewise, you say, though they arise usually in the lymph nodes, sometimes the spleen or the thymus, they too can spread to other tissues such as the bone marrow, liver, lungs, skin, etc. You then go on, I think, to consider the normal bone marrow and blood cells and you describe the bone marrow as the "central organ of haemopoiesis". You set out there the development of the B-lineage cells from the bone marrow stem cells and describe how they subsequently migrate to peripheral lymph nodes and spleen. You describe then the development of the haemopoietic system and the involvement of the thymus gland and, at the bottom of page 5, you say that:

> "Abnormalities in this system of growth factors, as a result of mutations of deletions or their respective genes .... may be important in the pathogenesis of myeloid leukaemia."

We are not going into the pathogenesis of leukaemia today at all, Prof. Catovsky, just to be clear about that. You say:

> "The precursors of B-lymphoid cells in the bone marrow can only be identified by sophisticated immunological analysis."

We heard about that this morning from Prof. Greaves, who described how, in the last 10 years, much work has been done on the immunophenotyping of the different disease forms. I think you have been involved in that work, have you not?
A. Yes.

Q. Then, at paragraph 2.2, you describe the lymphoid tissue and the lymphatic system. Just briefly, could you explain what exactly the lymphatic system is so that we can understand it, Prof. Catovsky?
A. The lymphatic tissues are concerned with the responses of the body, immunological responses, so you get mainly lymphocytes and.....

Q. MR. JUSTICE FRENCH: I would rather like to make a note of this if it is important and, if you go too fast, I shall miss it. Lymphatic tissue....
A. Lymphatic tissue is concerned with immunological responses and it is constituted mainly by lymphoid cells. It is a system of cells, which we call lymphoid cells. They are lymphocytes, plasma cells and some other cells who help perform the immunological function.

Q. They consist mainly of lymphoid substances?
A. Lymphoid cells.

Q. Lymphocytes, lymphoid cells and other....?
A. Other cells who help in that function, like macrophages and so on. They have different.....

Q. And other cells which aid the lymphoid cells?
A. Yes.

Q. E.g., macrophages.

MR. JUSTICE FRENCH: Yes?

Q. MR. SPENCER: Which is the principal organ of the lymph system?
A. In adults they are not one organ. They are all the lymph nodes. The lymph nodes is the main organ, if you have to have one major organ.

Q. What do the lymph nodes do?
A. I think the lymph nodes can be viewed as small factories in which the cells circulate through, make the antibodies when necessary, produce also the immunological responses, so it is like small factories in which all the cells are performing these functions in response to antigens or foreign bodies or whatever.

Q. MR. JUSTICE FRENCH: Small factories in which the lymph cells perform their function.

Q. MR. SPENCER: We know because, of course, Prof. Greaves told us this morning that the lymph cells are found not just in the lymph system, but also in the blood and in the bone marrow. Why do the lymph cells get put into the blood circulation?
A. I think that they interact with other cells. The blood can be viewed as a sort of circulation system which the cells go through different parts of the body and some sort of surveillance as well. There are some of these cells are seen sort of carrying memory and going around,

as it were, when necessary. There is a very active circulation between lymph nodes, blood and marrow and other organs.

Q. MR. JUSTICE FRENCH: When you say "memory", is that rather like if you have an immunisation against a disease?
A. Yes.

Q. Then they will remember the invasive injection?
A. Yes, they have special signals and some of the cells remain, have a very long life in the body.

Q. They have a surveillance. Would that be a good word to use?
A. Yes, immuno-surveillance, technically.

Q. A surveillance and memory factor.

Q. MR. SPENCER: And the cells which are responsible for that memory function my Lord has referred to are the B-lymphocytes, are they not?
A. There is one type. I think the T-lymphocytes as well are involved in the memory, but there is one particular form which is called the B-cell, memory B-cell.

Q. And that is involved in the system that is referred to in your report as "humoral immunity", is it not?
A. Yes, because eventually they make antibodies.

Q. MR. JUSTICE FRENCH: T-cells but mainly B....
A. Memory cells.

Q. B memory cells carry the memory function.

Q. MR. SPENCER: You mentioned when I asked you that the principal organ of the lymph system was the lymph node in adults. What about the position of children?
A. In children there is this important organ which is the thymus, early in life. Once the cells mature and they come out of the thymus and they do not return to the thymus, the thymus eventually become atrophic.

Q. What does that mean?
A. It does not have any function and I do not think there is evidence that you can actually find much of thymus in an adult, if you do a post mortem, for example. There is very little left.

Q. It withers away?
A. Yes.

Q. After it has performed its function, which it does in early life. Is that right?
A. Early life.

Q. The function of that is, we see again in your report, bottom of page 6, to generate T-cells. Is that right?

A. Yes, the function of the thymus is more concerned with T-cells.

A Q. Yes, as one might expect, and those cells are concerned with a form of immunity which you call cell mediated immunity, which I do not think we need go into, need we, Prof. Catovsky, but you observe that that is, in fact, the case. On page 7 you describe how those two immune systems collaborate in the development of what is called the immune response. In the middle of that page:

B "Both B and T cells are heterogeneous relating to the specialised function they perform in the lymph nodes. The latter are distributed throughout the body and are connected by lymphatic vessels."

Where you say "the latter" you are referring to the lymph nodes there, I think, are you not?

C A. Yes.

Q. Then, at page 8, you refer to "Immunological markers" and here you describe the developments that have occurred in recent years in relation to the development through "monoclonal antibodies" of immunophenotyping of cells. Can we go over the page then to the "Nature of leukaemias and lymphomas", where you expand upon your overview that we had at the beginning of your report. At paragraph 3 you observed that:

D "Leukaemias derive from bone marrow precursors and lymphomas from B and T lymphocytes found in the lymphatic system."

You then consider both the B-lymphoid cells and the

E T-lymphoid cells. You observe that:

"Leukaemia and lymphomas are monoclonal malignancies, that is they derive from a single cell."

Then you say this:

F "Acute leukaemias affect early cells, called blasts, whilst chronic leukaemias affect late (mature) leucocytes."

Prof. Greaves observed this morning that if, Prof. Catovsky, you confine blasts as a type of cell to the early cells, then he would disagree with you because he

G considers that blasts can also be mature cells as well. What do you say about that?

A. I think the definition is a semantic definition. I think classically it has been used for very immature cells, but we know that you can have....

Q. Sorry, did you say very....?

A. Immature, early cells, but you can have mature cells

H under appropriate conditions, make them look like blast

cells, and because blast cells is a term which is used mainly morphologically means what they look like. It does not necessarily imply what they are actually doing. It could be used either way, whether for immature or for mature cells, because a pathologist who looks at tissues can only guess what they might do normally. They look alike and it is very difficult to tell them apart sometimes.

Q. So it is a descriptive word rather than a definitive word?
A. Oh, yes, very descriptive.

Q. MR. SPENCER: Then I think that there is not any disagreement between you and Prof. Greaves over that. You then observe that, in relation to non-Hodgkin's lymphoma, it involves differentiated lymphoid cells and you describe how NHL is of high or low grade, depending on the degree of malignancy shown by their microscopic appearances. Where you refer to the degree of malignancy of a lymphoma, what is the characteristic of it which makes it malignant?
A. I mean, in simple terms, often it is the size of the cells and you have lymphomas where you get very large cells and we know they grow very fast and they are very malignant, and you have, in the other extreme, lymphomas of very small cells which look like small lymphocytes and sometimes they stay without major changes. I mean, the lymph nodes will grow up very, very slowly over a matter of months or years. Sometimes even they do not grow very fast, but if you have a lymphoma usually with large cells, it grows very fast, divides, so there is an interpretation based on what the cells look like on the degree, and that is the classification of lymphomas. It has a practical application for what the clinician has to decide on treatment. If he sees a high grade lymphoma, it is going to grow very fast. He knows that he has to use a particular type of treatment or approach, while in the low grade lymphoma sometimes you can just do nothing, perhaps even watch, for a long time.

Q. So really the degree of malignancy relates to the speed at which it grows?
A. Yes.

Q. As you have mentioned the significance of this from the clinician's point of view, it was Prof. Greaves' evidence today, and I think it would be your evidence, that much of the recent work to identify by genus and sub-genus and type and sub-type the different diseases has been encouraged by the needs of the clinicians more accurately to treat the diseases that they are seeing. Would that be a fair summary of the position?
A. Yes, absolutely right.

Q. I am grateful. You observe on page 9:

"To characterise acute leukaemias or high grade lymphomas nowadays it would be regarded as essential to have information derived from the immunophenotype because conventional .... techniques (that is, a histopathologist looking down a microscope) are not adequate."

Is that right?

A. Yes, they are not complete.

Q. Whereas, with the chronic leukaemias and low grade lymphomas, though immunology is very helpful, it would not be regarded as essential to the same degree?

A. Yes.

Q. Then, at page 10, you deal with the different types of leukaemia and we have that outlined for us in Table 1, which we find at page 28 of your report. Just in summary, looking at page 28, Table 1, you set out the acute leukaemia at the top. You observe that, in relation to acute myeloid leukaemia, there are at least eight sub-types. I do not think we need be concerned about those. In relation to lymphoblastic leukaemia of B-lineage, there are three types, according to differentiation - early-B, common-ALL and pre-B. Then, in relation to the T-lineage, thymic cell precursors, one major type and that is T acute lymphoblastic leukaemia. You then consider too the chronic forms of leukaemia. Three types of myeloid and four types of lymphoid, three again B-cell and one T-cell. I do not think we need trouble about what we find on page 10 beyond that.

Then "Types of lymphoma", bottom of page 11. They, as you say, constitute a heterogeneous group of disorders by analogy with the leukaemias and they, as you have said, derive from the lymphoid cells and we find again, at Table 2, a summary of the different types of lymphoma. First of all, you deal with Hodgkin's Disease and, apart from observing the fact that it exists, I do not think we are concerned with that in relation to this case?

A. Yes.

Q. Then you refer to non-Hodgkin's lymphoma. Just help me about this, Prof. Catovsky. Is it right to say that when this distinction was originally made, what happened was that Hodgkin's Disease was identified presumably by Dr. Hodgkin and characterised by him and any lymphoma that did not, as it were, match up to his description was simply designated a non-Hodgkin's lymphoma. Is that how it happened?

A. Not exactly but roughly, because Hodgkin was describing very much earlier and the term was introduced. There is a tendency mainly for American doctors, who use the word "non" for something just to separate something. They call non-lymphoblastic leukaemia anything which is non-lymphoblastic. It has been established in practice over the last few years. It is not particularly useful, but it has been accepted widely.

Q. It is historical and we have to live with it?
A. It is historical, yes.

Q. If one was approaching this subject with, as it were, a clean sheet of paper, we would not talk about Hodgkin's and non-Hodgkin's, would we?
A. Probably not.

Q. We would talk about very much more well categorised diseases. Is that right?
A. Yes.

Q. While considering classification, you refer, of course, to the Kiel classification. That is one of a number of classifications, is it not?
A. Yes, I think it is probably the one who is more solid and has a more scientific basis compared with the others. The other widely used classification, the American working formulation we use, it is good in practice. It is mainly to give simple guidelines to physicians to know what to do, but it does not often address the question about the nature of the lymphoma, which is a very heterogeneous group of diseases, and the Kiel classification is more precise and this is why people like it.

Q. There is a third one. Is that the Rappaport?
A. Yes, but that has been superseded many years ago.

Q. Forgive me. You, anyway, refer to the Kiel classification and where you then set out in your table the grade of malignancy with B-cell and T-cell, that is the Kiel classification?
A. Yes.

Q. Probably a bit simplified, is that right?
A. It is simplified. All the categories are included here.

Q. If we look at the asterisks at the bottom, you say that children under 15 years of age have only high grade tumours, and adults have both high and low grade lymphomas?
A. Yes, that is right.

Q. You set above the line the low grade adults only, and I do not think we need look at those in detail, then high grade, adults and children, centroblastic, lymphoblastic, (non-Burkitt's) then Burkitt's, and the asterisks tell us that it is also described as lymphoblastic -

> "this disease is strongly linked with the Epstein-Barr virus in its endemic (African) form".

and we have heard today that it has too a non-endemic form, sometimes described as Burkitt-like?
A. Yes.

MR. JUSTICE FRENCH: I thought it was a little more subtle than that, wasn't it, that the virus is endemic but the disease is not?

MR. SPENCER: I will let Prof. Catovsky answer that, my Lord.

THE WITNESS: Yes, that is right. The disease has been associated strongly with a virus in Africa so when people use the term Burkitt's lymphoma they refer to the African or endemic form, but it was apparent that a similar looking disease occurs outside Africa and is called non-endemic because it is less frequent as well.

Q. MR. JUSTICE FRENCH: We are told that 80% of the population of the UK has the Epstein-Barr virus?
A. Yes.

Q. So you could call the virus endemic because almost everybody has it?
A. Yes.

Q. But it does not always express itself in the form of the disease, isn't that right?
A. Yes, you are absolutely right. I think in Burkitt lymphoma you have a number of factors which come together in Africa to cause that disease.

Q. MR. SPENCER: But when one refers to endemic Burkitt's one is referring to that disease in Africa that has all its constituent parts that are observed in Africa, is that right, and in its non-endemic form it would be the same disease, sporadic?
A. Yes, I think it is better to use the word sporadic, meaning that it is not so frequent.

Q. Prof. Greaves I think agreed today that the endemic disease is seen outside Africa but somewhat rarely?
A. Yes.

Q. MR. JUSTICE FRENCH: South-east Asia, you told us?
A. Yes.

Q. MR. SPENCER: And could be seen in this country as well, I think, is that right?
A. Yes, rarely, but it does occur.

Q. But also its non-endemic form is seen as well?
A. Yes, that is right.

Q. And Prof. Greaves agreed that it was the same disease but without necessarily the African features like the Epstein-Barr virus, would you agree with that?
A. Yes.

Q. Then immunoblastic is your last category there. Is that the same as large cell?

A. It is a form of large cell. Most of the high grade are large cells but this is a special type, very large perhaps.

Q. Then in the T-cell list, I do not think we need look at the low grade adult only form, in high grade you identify the first category, pleomorphic, medium and large cell, with which the retrovirus HTLV-I is involved. Then you have lymphoblastic, T-cell lymphoma - is that common in children?

A. Lymphoblastic T-cell, yes, in teenagers.

Q. Then two other categories I do not think we need trouble about. Page 12, about two-thirds of the way down the page, you say within the high grade B-cell non-Hodgkin's lymphoma:

> "... lymphoblastic (non-Burkitt) is rare and Burkitt's lymphoma, which can also be described as lymphoblastic, is more common. The high grade T-cell NHL T-lymphoblastic lymphoma is by far the most common form of lymphoblastic lymphoma (considering both B and T cell types). Without immunological analysis it is not possible to distinguish B or T lymphoblasts; only Burkitt's lymphoma can be recognised, by good pathologists and constitutes a distinct disease entity."

That is right, is it?

A. Yes.

Q. That is why, as you say, you list it separately in Table 2. Where you say it is a "distinct disease entity", distinct from other forms of NHL, Prof. Catovsky?

A. Yes. I think when you say "distinct disease entity" you refer to the clinical features, the immunological features on the cells and the appearances, by these two pathologists.

Q. MR. JUSTICE FRENCH: Could I just ask one question? You say about eight lines from the bottom of page 12:

> "The high grade T-cell NHL T-lymphoblastic lymphoma is by far the most common form of lymphoblastic lymphoma (considering both B and T cell types)."

Can you express that in a percentage?

A. Yes, I would say 80% perhaps, if you take everything which people will call lymphoblastic lymphoma.

Q. So I will write in about 80%?

A. Yes.

Q. MR. SPENCER: Coming over the page onto "Relationship and differences between leukaemias and lymphomas", you observe:

"The area which requires clarification is the relationship of lymphoblastic tumours (leukaemias and lymphomas) in children and young adults."

- because as you correctly observe it is that with which my Lord is concerned in this case -

"Because both ALL and lymphoblastic NHL are infrequent in adults and common in children, it is on the latter group that the discussion should centre. In children the NHL fall into three main types."

and you there set them out:

"i) Lymphoblastic lymphoma ... the majority of cases are of T-cell type.

ii) Burkitt's lymphoma, which has a mature B-cell immuno-phenotype.

iii) Large cell or immunoblastic ...

There are few-well documented cases of lymphoblastic lymphomas in which the cells have a B-cell precursor phenotype as seen in ALL: 80% of lymphoblastic lymphomas are T ...."

- this is, I think, the point you have just made -

"... 15% are non-B, non-T ...."

does that mean that you simply cannot say which they are?

A. That is true, yes.

Q. "... 5% have a B-cell immunophenotype. The immunophenotype of the most common form of ALL in childhood, common-ALL is only rarely represented in NHL ...."

and you discuss Burkitt's lymphoma - we have already, I think, discussed that - and you set the position out there. You refer at page 14, about seven lines down, to Burkitt's lymphoma having a unique chromosome abnormality, and we heard about that from Prof. Greaves this morning. It is an abnormality that is common to both the endemic and the non-endemic or sporadic forms of the disease. At the end of that paragraph, just to observe but not to deal with it, you reflect upon the initiation of lymphoma by Epstein-Barr virus in its endemic form but as we are not today concerned with the etiology of leukaemia or lymphoma we are not pursuing that today, Prof. Catovsky.

At the bottom of that page you deal with the overlap between the two disorders involved, T-lymphoblasts, T-cell, ALL and T-lymphoblastic lymphoma, and we again heard from Prof. Greaves today, and you agree, that this is the one area where there may still be room for error as to the precise categorisation.

Going over the page you observe this:

"The presentation, in 50% of cases of T-ALL, with a thymic tumour, also supports the argument that it is there that the disease started ...."

So for thymus ALL 50% have a thymic tumour, and then you say:

"... on the other hand, 95% cases of T-lymphoblastic lymphoma also present with a thymic mass."

A statistic with which Prof. Greaves agreed and he accepted that was an important consideration in making the differential diagnosis. That would be right, would it?

A. Yes.

Q. So when we came to discuss with Prof. Greaves the likely diagnosis of the lymphoma in Vivien Hope's case it was, I think, that statistic which enabled Prof. Greaves to say that the suggestion, or any suggestion that Vivien Hope suffered from a T-cell non-Hodgkin's lymphoma was very, very unlikely, and you would agree with that, I think?

A. Yes, I agree with that.

Q. I do not think we need dwell any further on T-cell disease. We can, I think, go over the page, where you deal with the "Relevance of the diagnosis of lymphoblastic leukaemia or lymphoma to the two cases under analysis". You observe:

"... the diagnosis made in both cases, Reay and Hope, was based exclusively on morphological analysis of histological sections."

That is looking down a microscope at slides prepared from the tissue involved, is that right?

A. Yes.

Q. You say:

"Because of the time when the diagnoses were made it was not possible to establish more precisely whether the lymphoblastic process involved B or T cell precursors. This is critical because, as discussed above, B-lineage ALL is a primary bone marrow leukaemia whilst T-lymphoblastic lymphoma (and T-cell ALL) and one of the B-lymphoblastic lymphomas (Burkitt's lymphoma) arise, respectively, in the thymus or in peripheral lymph nodes."

You then describe Dorothy Reay's onset of illness at age 10 months and you say:

"Because of the very young age of presentation and accepting the description as lymphoblastic, it is likely that she had an acute leukaemia involving B-cell precursors (early B-ALL)."

and with that Prof. Greaves agreed. There was a small moment of doubt because he described it as null rather than early, but that confusion was put right when he said that there is no difference between null and early.

Then the diagnosis in the case of Vivien Hope, you say:

> "... the disease was classified correctly as lymphoma as there was no evidence at any stage of her illness of involvement of the bone marrow."

and just to make that point we know, do we not, that for her condition, her own bone marrow was used to treat her?

A. Yes.

Q. In other words, a bone marrow sample was aspirated from her ....

MR. JUSTICE FRENCH: I think I understand the point.

MR. SPENCER: Your Lordship understands that, so I won't deal with that:

Q. You refer at the bottom of that page to some of the features described in Vivien Hope's case as the high mitotic rate and the "starry sky" appearance ... would be consistent with Burkitt's lymphoma. This diagnosis may have further support on ...."

various immunological grounds. Prof. Greaves concluded that the likely diagnosis in Vivien Hope's case was a Burkitt's lymphoma. What is your conclusion, Prof. Catovsky?

A. I would agree with that, yes, it is more likely.

Q. MR. JUSTICE FRENCH: What is more likely?

A. To be a diagnosis of Burkitt's lymphoma.

Q. MR. SPENCER: Prof. Greaves accepted that NHL and acute lymphoblastic leukaemia were distinct disease entities. I think you say as much in the last paragraph on page 18, is that right?

A. Yes.

Q. Where, Prof. Catovsky, you refer in that paragraph to the classification having a bearing on possible causation, and you refer to pathogenetic mechanisms, again that aspect of this part of your report is not being dealt with today; we are dealing with that at a later stage in the case, just to be clear. You then consider, at page 19, the "Overall incidence of leukaemias and lymphomas by type and age", and you refer to your Table 3, where you set out the incidence of leukaemias and lymphomas using, I think, fairly general categorisation, is that right?

A. Yes.

Q. So lymphomas we have, in all ages, 2-3 per 100,000 population per year, is that right?
A. Yes.

Q. Non-Hodgkin's, 4-5 per 100,000 per year, and then non-Hodgkin's in persons under 15 years of age, very much rarer, 0.2-0.4 per 100,000?
A. Yes.

Q. Of course, in Vivien Hope's case the onset of the disease in her was at an age when she was well over 15?
A. Yes.

Q. Then acute leukaemia, you set out the incidence for myeloid and I do not think we need to concern ourselves with that, except to observe that it is obviously more common in those over 55. In lymphoblastic acute leukaemia it is most common aged 0-4 years, with a rate of about 5 per 100,000 per year?
A. Yes.

Q. Then it gets less common as we get older and perhaps a slight increase over 55 but still ten-fold less common than in childhood at that age group, is that right?
A. Yes.

Q. Then we get on to etiology and causal mechanisms and as I have said, we are not caused with that, Prof. Catovsky, nor with hereditary factors. If we can come to your conclusion you have set out for us at page 27 in your first report and just to read the part of your conclusion that we are dealing with today:

> "My study of the two cases under consideration, Reay and Hope, led me to conclude, based on the available clinical and laboratory data, that they were suffering from two different forms of lymphoid malignancy. In Reay's case the most likely diagnosis was ALL of early B subtype, a disease arising in the bone marrow. In Hope's case, the agreed diagnosis was lymphoblastic lymphoma, a disease which in the majority of individuals does not start in the bone marrow and which, furthermore, was not involved in this case."

I think that is as far as we need go, but you would add in the case of Vivien Hope that the likely diagnosis was a Burkitt's lymphoma?
A. Yes.

Cross-Examined by MR. HYTNER:

Q. One small point only, Professor. You refer to, as was also asked of Prof. Greaves, the difference between the two diseases from which the two girls suffered. You said, and it will no doubt be explored in detail later on, that non-Hodgkin's lymphoma and acute lymphoblastic leukaemia are two different diseases?
A. Roughly, yes.

Q. Of course they are both malignancies of the lymphoid system?
A. Yes.

Q. Similarly you would say that CML is a different disease to ALL?
A. Yes.

Q. Indeed, it is a malignancy of a different system as well?
A. Yes. I think the haemopoietic system could be over-simplified and it has various constituents. The lymphomas usually arise from a different tissue. Now they obviously are connected, as they could be different, for example, a tumour from the head or the pancreas. Those are much more different, so there are some similarities. We pointed out in the report there are aspects in which you cannot separate sometimes where is the separation, where one calls it leukaemia or one calls it lymphoma. There are extremes within that grey area and in a way I think the two cases discussed here are, in a way, quite extremes from the way in which the disease evolved. Of course they do involve lymphoid cells in a way.

Q. And malignancies of lymphoid cells?
A. Malignancies of lymphoid cells, yes.

MR. SPENCER: My Lord, I have no re-examination of Prof. Catovsky. Your Lordship will see Prof. Catovsky again sometime in the New Year.

MR. JUSTICE FRENCH: Well, now, the evidence I have just heard is directed to diagnosis. What diagnosis - I suppose it is for the Plaintiffs to go first? What do you contend for, Mr. Hytner?

MR. HYTNER: My Lord, I think that happily in this area, as in occupational dose, there is no room now for disagreement. Dorothy Reay, acute lymphoblastic leukaemia - early B. My Lord, I suppose for total accuracy it is a malignancy of an early B cell.

MR. JUSTICE FRENCH: Yes. The "early B" comes in front of the "acute"?

MR. HYTNER: Yes. For Vivien Hope a non-Hodgkin's lymphoma, being probably a B-cell, Burkitt-like lymphoma.

MR. SPENCER: My Lord, I would agree with both of those. I don't know whether we need the "like" in Burkitt-like, but I don't think it matters. I think both agreed it was a Burkitt's lymphoma.

MR. HYTNER: My Lord, we think it is critical.

MR. JUSTICE FRENCH: Burkitt-like, rather than...?

MR. HYTNER: Burkitt-like, my Lord.

MR. JUSTICE FRENCH: So you agree, save that you would strike out the "like"?

A

MR. SPENCER: Yes. I don't think the "like", on the evidence, is necessary, or, indeed, critical.

MR. JUSTICE FRENCH: But you would like it out?

MR. SPENCER: I would prefer it out.

B

MR. JUSTICE FRENCH: Yes. We cannot go any further today, so we meet again on Thursday.

MR. HYTNER: Thursday, my Lord, when horns will be well and truly locked!

MR. JUSTICE FRENCH: Is the order of witnesses as given...

C

MR. HYTNER: The only technical alteration to the order of witnesses is that I understand from Mr. Langstaff that before Prof. Evans goes into the witnesses box he wishes to put in under the Civil Evidence Act the statement of Prof. Gardner, which was obtained by the Treasury Solicitor. My Lord, we haven't had a counter notice under the Civil Evidence Act, which is not surprising. However, my Lord, that not having been served we think that will simply be a formality, to put his statement in.

D

MR. JUSTICE FRENCH: Yes. Have you seen it, Mr. Spencer?

MR. SPENCER: My Lord, I have seen it. My Lord, we haven't finally considered our position in relation to it, but its timing, I don't think, is in any way critical as far as the evidence of Prof. Evans is concerned, but we are actively considering our position in relation to it and as soon as we are able to...

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MR. JUSTICE FRENCH: You don't want me to see it yet?

F

MR. SPENCER: My Lord, not at this stage. I anticipate that we will be able to say by Thursday morning whether or not we are serving a counter notice. My Lord, of course we can only serve a counter notice if we dispute the circumstances in which it is said that it is unreasonable to expect the Plaintiffs to call the Professor, and so, my Lord, it is that we are considering.

G

MR. JUSTICE FRENCH: Yes. So we wait and see about Prof. Gardner's Civil Evidence Act statement.

MR. SPENCER: My Lord, I don't know whether I can reiterate what Mr. Rokison said yesterday, but I am sure my learned friends have it well in mind, and that is our

H

concern about the position of Prof. Thomas and his view of the recent figures and their impact on Gardner as re-worked by Prof. Evans.

MR. HYTNER: My Lord, since that has been said again, since Mr. Rokison made that observation and I remained sensibly silent, I do know a little more about it and as I understand it there is correspondence now between solicitors. It is not quite as straightforward as I think Mr. Rokison felt yesterday, and rather than matters brought before your Lordship at this stage I think it is best left for the moment for the correspondence to mature.

MR. SPENCER: My Lord, that does cause us some concern because quite obviously the views that Prof. Thomas may adopt in relation to it may well affect us in our cross-examination of Prof. Evans.

MR. JUSTICE FRENCH: It may, of course.

MR. SPENCER: That is why, my Lord, we have been at pains to put a marker down about it.

MR. JUSTICE FRENCH: Is there anything additional from Prof. Evans, having regard to the extension of the Gardner cases and controls?

MR. SPENCER: My Lord, we have his results set out in Table 4. I am told there has come to us now something additional as well.

MR. HYTNER: My Lord, his report, as requested by Mr. Rokison, was delivered last night to Freshfields, and they have it.

MR. JUSTICE FRENCH: Yes. That is the document which I think has arrived but I have not yet looked at.

MR. HYTNER: Yes. It may be that Mr. Spencer has not had an opportunity to see it, but, my Lord, neither have I, but it has certainly been delivered and is there.

MR. JUSTICE FRENCH: Is there more mathematical work to be done?

MR. HYTNER: My Lord, I don't think so.

MR. JUSTICE FRENCH: No. That is what I think...

MR. HYTNER: Not as far as we know, those of us in court.

MR. JUSTICE FRENCH: I suppose there may be criticisms of the mathematical work that has been done?

MR. HYTNER: Bearing in mind the co-operation between Prof. Evans and Dr. Wakeford, it doesn't seem

likely there will be mathematical problems, but I cannot be certain about that at this stage.

MR. JUSTICE FRENCH: Very well, we can only wait and see. Yes, 10.30 on Thursday.

(Court was adjourned until 10.30 am on Thursday, 26th November, 1992)