Rothwell et al. v. Raes et al.*
Rothwell et al. v. Hall*
Rothwell et al. v. The Queen in right of Ontario et al.*

Indexed as: Rothwell v. Raes
(Ont. H.C.J.)

66 O.R. (2d) 449
[1988] O.J. No. 1847
Action Nos. 58624/80, 431/86 and 560/86

ONTARIO
High Court of Justice
Osler J.
November 18, 1988.

[Ed. note: Supplementary reasons for judgment, released June 1, 1989, are appended to this document.]

*Notice of appeal filed December 19, 1988.

Torts -- Negligence -- Causation -- Infant suffering serious neurological deficiency -- Condition diagnosed after vaccination against whooping cough -- Claim against physician, manufacturer and Crown as distributor -- Burden of proving on balance of probabilities that vaccine could cause, or did cause damage not discharged -- Consideration of methods of determining cause.

Torts -- Negligence -- Standard of care -- Common practice -- Physician recommending and administering vaccine against whooping cough -- No warning given of potential side-effects then believed to exist -- Following common practice -- Physician not negligent.

Torts -- Negligence -- Products liability -- Manufacturer of vaccine knowing of scientific opinion concerning risk of

adverse effects -- Failing to inform physicians using vaccine -- Manufacturer negligent notwithstanding subsequent change in scientific opinion.

Torts -- Negligence -- Vicarious liability -- Employers -- Physician agreeing to arrangement as locum tenens -- Exercising own professional skill and judgment -- Employing physician not vicariously liable.

Limitations -- Professions -- Action by infant against physicians -- Limitation period not commencing to run until minor of full age -- Nothing in health disciplines legislation restricting application of rule -- Limitation period in Health Disciplines Act, R.S.O. 1980, c. 196 inapplicable -- Limitations Act, R.S.O. 1980, c. 240, s. 47.

The infant plaintiff was one of twins the other of whom was stillborn and macerated. At approximately three, four and five months he received immunization doses of a multi-purpose vaccine (known as a quadrigen) to protect him against diphtheria, pertussis (whooping cough), tetanus and poliomyelitis. The vaccine was administered in the office of the defendant family practitioner, although two of the three shots were given by another physician who served from time to time as his locum tenens. A little over a month after the third shot it was suspected that the infant plaintiff was suffering from a developmental abnormality. A thorough examination by a number of physicians in hospital followed and according to the hospital discharge note signed by a paediatric neurologist, "... it was felt that on the basis of the results of the investigations and the history of the parents, the possible diagnosis was post pertussis encephalitis". Later, the neurologist wrote a letter expressing the opinion that the neurological condition was explicable in two ways: either it had existed since birth or it was a reaction to the inoculation, which produced "a diffuse encephalopathy with seizures. This is a well recognized entity likely due to the pertussis component and can produce severe brain damage." The infant plaintiff was blind, almost deaf and severely retarded, both physically and mentally. He was unlikely to improve and would require constant care.

The infant plaintiff and his parents commenced actions against: (1) the physician who had administered the vaccine, for negligence, especially in failing to warn of the alleged material risks of the vaccination; (2) the locum on the same basis; (3) the manufacturer, for negligence in the manufacture of a product it knew to be inherently dangerous which it had not made in accordance with current technological advances, and for failing to bring to the attention of the medical profession the inherent dangers; (4) the Crown, for negligence in distribution of the vaccine. A claim against the municipality was withdrawn. The actions were tried together, the trial lasting 74 days, the major issue being that of causation.

Held, the actions should be dismissed. The burden was on the plaintiffs to establish on a balance of probabilities that the brain damage was caused by the vaccine. They had failed to discharge the burden. It had not been shown that the vaccine could cause brain damage. Even if it had been established that brain damage might be due to the vaccine, the evidence suggested that the infant plaintiff suffered from neurological deficiencies from the beginning and that his condition was idiopathic. In any event, neither of the physicians nor the ministry had been negligent, although the manufacturer had been negligent in failing to bring the dangerous effects which current medical opinion believed to be present, to the attention of the physicians.

Even the plaintiffs' expert witnesses agreed that if a causal connection existed between pertussis vaccine and brain damage -- encephalopathy -- it was extremely rare. Thus the personal experience of such cases, even on the part of the most specialized consultants, was necessarily limited. The witnesses referred to many scientific publications in giving testimony and annexed them to their reports. The decision had to be based on the evidence of the witnesses including their reports, but articles and studies referred to could be used to assess the evidence where there was conflict. The question was difficult and complex.

It is easy to fall into the error of believing that because

there is a temporal association between brain damage and vaccine administration, the one is the cause of the other (the logical fallacy reflected in the proposition post hoc ergo propter hoc). Temporal association gives rise to a hypothesis that should be tested, no more. Some children are born with neurological deficiencies that go undetected until the age of six months because the deficiency relates to the type of complicated behavioural development which normally takes place at and after that age. Or defects may not show up until illness or an exterior stimulus such as vaccine brings them out or causes them to be observed by a more attentive observer. Thus temporal association could be coincidental. In the absence of a specific pathological condition or clinical syndrome that is associated only with the vaccine, the possibility of another cause cannot be ruled out. Another approach to the question is through epidemiological studies showing the frequency of occurrence of neurological reaction associated with vaccination, as compared with its frequency of occurrence in a population to whom the vaccine has not been administered. While not providing clear proof of causation, such studies may give rise to a useful inference. In drawing an inference there are other factors besides temporal association to be considered, including strength, consistency and specificity of the association, plausibility and coherence.

At the time the infant's deficiency was detected there was a widespread belief on the part of the medical profession that a causal connection existed between the pertussis vaccine and brain damage. This belief was causing considerable concern about the vaccination programme for whooping cough which itself carries a risk of brain damage. No particular pathology or clinical syndrome had been identified in cases of suspected pertussis vaccine damage and the opinion was based in large measure on literature arising from studies. By the time of the trial, however, considerable doubt about the validity of this opinion had been generated. Even the neurologist who had signed the hospital release note and whose letter may have been the basis on which the plaintiffs decided to launch their actions had changed his mind and concluded in giving evidence after being called by the plaintiff that the condition known as post-pertussis encephalopathy was "probably a myth".

A number of major investigations had been conducted in an attempt to determine definitively, the risk of encephalopathy from the vaccine. Most were British. Two well-known early studies consisted entirely of analyses of case reports -- descriptions of the circumstances and condition of particular children with encephalopathy who had also been vaccinated -- sometimes described as anecdotal episodes. They concluded that there was a risk of destructive encephalopathy arising from vaccination. However, as neither study involved a control for purposes of comparison, it was impossible to draw valid scientific conclusions as to probable causation. It could not be determined, statistically, how frequently encephalopathy occurred among those vaccinated as compared with a group which had not been vaccinated. An hypothesis only was suggested because of the possibility in every case that there was another cause of the deficiency. Case studies without control are the weakest form of epidemiological study.

For a study to give rise to a significant conclusion, it would be necessary to establish the possibility of chance as the explanation for the difference in the incidence of neurological injury between the study group and the control to be less than 5%. Even a retrospective case study involving a control -- a group of children who have been vaccinated is compared with a group who have not -- suffers from methodological flaws, although because of the fact that it may be the only practical option, it is a type of study often used. But a case study with a control would have difficulty ruling out chance, bias, the confounding of results by other conditions, and other problems which would tend to skew results.

A cohort study whereby a group of people it is desired to study is identified and periodic checks are made of them to see what happens, is a still more reliable type of study but would be virtually impossible in connection with pertussis vaccine because the expected rarity of the reaction would mean an enormous cohort would be needed and it would have to be observed over a long period. The most reliable type of study would be a randomized, prospective controlled trial. No study

of this variety had been undertaken.

A major study involving 130,000 children which reported 12 cases of impairment following the administration of a vaccine containing the pertussis element and only four cases following the administration of another vaccine immunizing only against diptheria and tetanus, had not been a true cohort study. In particular, it had relied on voluntary reports and had studied only children who had been immunized.

One case study which involved 134,000 children who were vaccinated for pertussis and 133,000 who were not, was by far the most complete and careful study and yet it had not managed to eliminate the possibility of bias and chance. Most of the participants in it thought that it disclosed no causal relationship. Some thought it proved that such a relationship did not exist. Its preliminary report concluded that most cases of damaging neurological illness were attributable to causes other than immunization, that they occurred within seven days and particularly within 72 hours of vaccination more frequently than would be expected by chance, and that taking account of possible alternative explanations, it seemed likely that permanent damage from pertussis vaccination was, if it occurred at all, a very rare event, much rarer than damage caused by whooping cough; attribution of a cause in individual cases was said to be "precarious". Some experts in North America thought it established a 1 in 330,000 risk of brain damage whereas two studies had indicated a 1 in 11,000 or 1 in 22,000 risk of such consequences of the disease.

The expert witnesses who favoured the view that a causal relationship existed relied in part on the literature, the studies and the conventional wisdom in reaching their conclusions. Furthermore, they were not as qualified or experienced as were the witnesses who favoured the view that no causal relationship could be established.

For all of these reasons, the court concluded that no such relationship had been proven.

Even if it had been proved that there was a rare possibility

that the pertussis vaccine could cause brain damage, the risk of such damage from whooping cough was much greater. Furthermore, the evidence of the infant plaintiff's condition from birth was such as to indicate possible neurological deficiency. One of twins, the other of whom was still-born and macerated, indicating that he had been dead for some time, the infant plaintiff's "jitteryness", his cyanosed appearance on several occasions as well as the results of a CAT scan and measurement of his head size at various intervals pointed to neurological deficiency from birth. The infant plaintiff's condition seemed to place him in the relatively large group of children whose condition is idiopathic.

Limitations defence

Section 47 of the Limitations Act, R.S.O. 1980, c. 240, provides that in the case of a minor the limitation period should not begin to run until he or she becomes of full age. Nothing in the Health Disciplines Act, R.S.O. 1980, c. 196, restricts the application of this section, hence the limitation period in the latter Act was inapplicable. Nor did the appointment of a litigation guardian affect the limitation period.

Negligence of the physician and his locum

The defendant physician was not negligent either in recommending the vaccination or in failing to warn of possible damaging effects. It was at the time the practice to recommend vaccination without reference to the rare possibility of harmful consequences. Three doses of the vaccine were administered, two of them by the locum, and no reaction which would have caused alarm occurred after either of the first two. Nor was the physician negligent in his choice of physicians to serve as locum tenens. No evidence of negligence on her part was offered.

Liability for the locum tenens

Even if the locum had been negligent, she was exercising her own professional skill and judgment and the family physician

could not be vicariously liable.

Manufacturer's liability

The manufacturer's leading researchers were familiar with the literature postulating encephalopathy and grave brain damage as possible consequences of administration of the vaccine. Had the manufacturer warned the physician the court could not presume that he would have failed to discuss the possibilities or at least mention them. Therefore the manufacturer was negligent in this respect. It was not negligent in failing to manufacture the Japanese version of the vaccine since no tests had been done which would have led to its acceptance by the scientific community as superior to the product used.

The ministry's liability

The province reasonably relied on the federal government to license and monitor vaccines. The province's decision not to exercise the authority it had, and had at one time used, to regulate and monitor did not subject it to liability. No other province issued warnings at the time. Only one monitored drugs used. Hence no negligence could be found on the part of the ministry.

Damages

An appropriate sum for non-pecuniary damages for the infant would have been $209,000. His compensation for loss of future income should be based, according to the evidence, on a 30-year life expectancy. For the period 18 to 25 it should be calculated on the basis of 75% of the average industrial wage to allow for the "apprenticeship factor" and thereafter on the average industrial wage. The gross-up for tax should be 5%, the discount rate 21/2%.

The mother and father were each entitled to $50,000 for loss of guidance, care and companionship and the mother was entitled to special damages of $25,000.

Total damages, had the plaintiffs succeeded, would have

amounted to $2,000,000 or more.

Reflection

The cost and duration of proceedings and the strain it added to the plaintiffs' already heavy burden as well as the prospect that such problems would likely be litigated again with the possibility that different evidence or the different intellectual make-up of the judge might lead to a different result suggested that some other method of dealing with the problem would be attractive. For example, some jurisdictions have statutory compensation schemes for persons suffering neurological damage in close temporal association with vaccine administration.

Papamonolopoulos v. Board of Education for City of Toronto (1986), 56 O.R. (2d) 1, 30 D.L.R. (4th) 269, 38 C.C.L.T. 82, 10 C.P.C. (2d) 176; leave to appeal to S.C.C. refused 58 O.R. (2d) 528n, 35 D.L.R. (4th) 767n; Crits v. Sylvester, [1956] O.R. 132, 1 D.L.R. (2d) 502; affd 5 D.L.R. (2d) 601, [1956] S.C.R. 991; Davidson v. Connaught Laboratories (1980), 14 C.C.L.T. 251; Lambert v. Lastoplex Chemicals Co. Ltd. (1971), 25 D.L.R. (3d) 121, [1972] S.C.R. 569; Buchan v. Ortho Pharmaceutical (Canada) Ltd. (1984), 46 O.R. (2d) 113, 8 D.L.R. (4th) 373, 25 B.L.R. 225, 28 C.C.L.T. 233; affd 54 O.R. (2d) 92, 25 D.L.R. (4th) 658, 32 B.L.R. 285, 35 C.C.L.T. 1; City of Kamloops v. Neilsen (1984), 10 D.L.R. (4th) 641, [1984] 2 S.C.R. 2, [1984] 5 W.W.R. 1, 66 B.C.L.R. 273, 29 C.C.L.T. 97, 26 M.P.L.R. 81, 54 N.R. 1, apld

Kennedy v. CNA Ass'ce Co. (1978), 20 O.R. (2d) 674, 88 D.L.R. (3d) 592, 6 C.C.L.T. 201, [1979] I.L.R. Paragraph1-1092; affd 26 O.R. (2d) 352n, 116 D.L.R. (3d) 384n, distd

Other cases referred to

Wilsher v. Essex Area Health Authority, [1988] 1 All E.R. 871; Rogin v. Shannon (1986), 37 C.C.L.T. 181; Lawson v. Hospital for Sick Children (1988), 65 O.R. (2d) 132; Swain Estate v. Lake of the Woods District Hospital (1988), 64 O.R.

(2d) 206, 49 D.L.R. (4th) 447, 26 C.P.C. (2d) 152; Poulin v. Madon, [1950] O.R. 219, [1950] 2 D.L.R. 303; Hopp v. Lepp (1980), 112 D.L.R. (3d) 67, [1980] 2 S.C.R. 192, [1980] 4 W.W.R. 645, 22 A.R. 361, 13 C.C.L.T. 66, 32 N.R. 145; Reibl v. Hughes (1980), 114 D.L.R. (3d) 1, [1980] 2 S.C.R. 880, 14 C.C.L.T. 1, 33 N.R. 361; revg 21 O.R. (2d) 14, 89 D.L.R. (3d) 112, 6 C.C.L.T. 227; revg 16 O.R. (2d) 306, 78 D.L.R. (3d) 35; Videto v. Kennedy (1981), 33 O.R. (2d) 497, 125 D.L.R. (3d) 127, 17 C.C.L.T. 307; Kenny v. Lockwood, [1932] O.R. 141, [1932] 1 D.L.R. 507; Andrews v. Grand & Toy Alberta Ltd. (1978), 83 D.L.R. (3d) 452, [1978] 2 S.C.R. 229, [1975] 1 W.W.R. 577, 8 A.R. 182, 3 C.C.L.T. 225, 19 N.R. 50; Wipfli v. Britten (1984), 13 D.L.R. (4th) 169, [1984] 5 W.W.R. 385, 56 B.C.L.R. 273, 29 C.C.L.T. 240; Lindal v. Lindal (1981), 129 D.L.R. (3d) 263, [1981] 2 S.C.R. 629, [1982] 1 W.W.R. 433, 34 B.C.L.R. 273, 19 C.C.L.T. 1, 39 N.R. 361; MacIsaac v. Smith (1987), 58 O.R. (2d) 289, 35 D.L.R. (4th) 451, 39 C.C.L.T. 239, 19 C.P.C. (2d) 56; Fergus v. Hamilton Civic Hospitals (1983), 40 O.R. (2d) 577, 144 D.L.R. (3d) 214, 23 C.C.L.T. 254; affd 50 O.R. (2d) 754, 18 D.L.R. (4th) 638, 33 C.C.L.T. 56

Statutes referred to

Courts of Justice Act, 1984, S.O. 1984, c. 11, s. 90 (am. 1984, c. 64, s. 7)
Evidence Act, R.S.O. 1980, c. 145, s. 35
Food and Drugs Act, 1920, S.C. 1920, c. 27, s. 4 (am. 1927, c. 56, s. 2), Sch. B (enacted idem, s. 14)
Health Disciplines Act, R.S.O. 1980, c. 196, s. 17
Health Protection and Promotion Act, 1983, S.O. 1983, c. 10 (am. 1987, cc. 18, 32)
Limitations Act, R.S.O. 1980, c. 240, s. 47
Public Health Act, 1882, S.O. 1882, c. 29, s. 9 (rep. & sub. 1887, c. 35, s. 9)
Public Health Act, S.O. 1912, c. 58, s. 6(c)
Public Health Act, R.S.O. 1970, c. 377, s. 4(c) (am. 1972, c. 1, s. 1)
Public Health Act, R.S.O. 1980, c. 409, s. 7(c) (repealed 1983, c. 10, s. 111(1))

Rules and regulations referred to

Rules of Civil Procedure, O. Reg. 560/84, rules 7.01, 7.02, 7.05, 31.10
Rules of Practice, R.R.O. 1980, Reg. 540 EDITORIAL NOTE: These reasons for judgment are abridged starting at p. 507.

ACTIONS for damages for negligence causing personal injury.

W.D. Dunlop and John Cox, for plaintiffs.

C.L. Campbell, Q.C., F.P. Morrison and David Hamer, for defendant, Dr. Daniel E. Raes.

W.S. Wigle, Q.C., Pamela Stevens and Alan West, for defendant, Connaught Laboratories Limited.

Meredith Fleming, Q.C., and Howard Brown, for defendant, Dr. Sheila E. Hall.

D.S. Ferguson and Erin Coffey, for defendant, Her Majesty The Queen in right of Ontario.

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OSLER J.:-- On January 17, 1979, the minor plaintiff, Patrick Rothwell, was born at Joseph Brant Memorial Hospital in the City of Burlington. He was one of a pair of male twins, the other of which was stillborn and macerated. On April 20, 1979, May 25, 1979, and June 26, 1979, Patrick received immunization doses of "DPTP" vaccine in the office of Dr. Daniel E. Raes, a medical doctor with a family practice in the City of Burlington. The vaccine is known as a quadrigen and is intended to give protection against diphtheria, pertussis, tetanus and poliomyelitis. The disease pertussis is otherwise known as whooping cough. The vaccines were administered either by Dr. Raes, Dr. Sheila E. Hall, a family physician at that time filling in for Dr. Raes from time to time as a locum, or by a nurse in the office of Dr. Raes, acting under the instructions of one or other of the two physicians.

The plaintiff, Donna Frazer now Rothwell, is the mother of the minor plaintiff and Colin Rothwell is his father. Since the birth of Patrick, Colin Rothwell and Donna Frazer have intermarried and the latter will be referred to throughout by her present name, Donna Rothwell.

Subject to what will be said below, Patrick, prior to his vaccinations, had been considered to be a healthy, normal child. By August of 1979, serious developmental abnormality was suspected. He was examined by a series of physicians, and ultimately was hospitalized at the Hospital for Sick Children in the City of Toronto on October 8, 1979, at the suggestion of Dr. Douglas McGreal, a paediatric neurologist. Following his hospitalization, the discharge note was prepared by Dr. Judy Moyes and signed by Dr. McGreal. The conclusion stated was that "... it was felt that on the basis of the results of the investigations and the history of the parents, the possible diagnosis was post pertussis encephalitis".

At the request of the then solicitor for the Rothwells, Dr. McGreal furnished a letter on March 31, 1980, in which he expressed the opinion that Patrick's neurological condition was explicable in two possible ways: either that his condition had existed from birth or "... that he had a reaction to the DPTP inoculation producing a diffuse encephalopathy with seizures. This is a well recognized entity likely due to the pertussis component and can produce severe brain damage."

The writ of summons in the first of the present actions names Dr. Raes and Connaught Laboratories Limited as the defendants, and in the statement of claim, delivered January 4, 1982, it is alleged that "... as a result of this reaction" the infant plaintiff is blind and severely retarded both physically and mentally. The claim is against Dr. Raes for negligence in connection with the administration of the vaccine, mentioning especially his failure to warn of the alleged material risks which accompanied the vaccination.

As against the defendant, Connaught Laboratories Limited, it is claimed that the damages arise as the result of the defendant's negligence in manufacturing a product, DPTP, which it knew to be inherently dangerous and not in accordance with technological advances as at 1979, and in failing to bring to the attention of the medical profession the inherent dangers that existed in the use of DPTP, or the contra-indications to which regard should be paid in its administration.

On March 25, 1986, a second action was commenced against Dr. Sheila Hall. In an amended statement of claim dated May 15, 1986, it is claimed that Dr. Hall caused or contributed to the mental and physical injuries suffered by Patrick Rothwell by reason of the breach of a duty she owed to the plaintiffs to care for Patrick Rothwell and to advise of the risk involved in the administration of DPTP vaccine, as well as in numerous other ways.

On September 16, 1986, the third action was commenced against Her Majesty The Queen in right of Ontario and the Regional Municipality of Halton alleging negligence in a variety of

ways, including, principally, the establishment and encouragement of a system of immunization using DPTP and the storage and distribution of the vaccine. The claim was later withdrawn against the Regional Municipality of Halton when it was appreciated that distribution of DPTP was arranged entirely by provincial health authorities without the intervention of the regional municipality.

On April 8, 1987, Master Sandler made an order that the three actions should follow one another upon the list for trial, "... to be tried as the trial judge may direct". At the opening of the trial, upon consent of all counsel, I made an order that the trials would proceed together, with all relevant evidence adduced in connection with each action applicable to each of the other actions.

The minor plaintiff, Patrick Rothwell, has suffered very severe brain damage. He is, to all intents and purposes, blind and largely deaf. His purposeful movements are limited, he cannot speak and he must be assisted and cared for with respect to virtually every activity of life. It is unlikely that there will ever be substantial improvement. A more detailed assessment of this unfortunate boy's handicaps will be set out at a later stage.

The problem of causation

It is apparent that all three of the plaintiffs' actions depend for their success upon a finding that there was a causal relationship between the administration of DPTP vaccine and the severe brain damage or encephalopathy suffered by the minor plaintiff. If, on the balance of probabilities, it is found that the administration of DPTP can cause encephalopathy, or permanent, serious brain damage, the actions may succeed. If it is found, on a balance of probabilities, that such a causal relationship can exist, the plaintiffs have the burden of showing, again on the balance of probabilities, that it did exist with respect to Patrick. The issue of causation, or the etiology of Patrick's condition, occupied a major part of the trial. If it is more probable than not that there is no causal connection between the pertussis component and severe,

permanent brain damage, the actions must fail.

The first task before the court, therefore, is to determine whether it has been shown, on the balance of probability, that DPTP vaccine can cause severe, permanent brain damage such as Patrick has experienced.

It is not too much to state that medical opinion about the effect of the pertussis component of DPTP vaccine has been in a state of ferment for at least the past decade. It is probably safe to say that at the time of Patrick Rothwell's birth in 1979 the opinion of virtually all general or family practitioners in North America, and probably in the United Kingdom, as well as that of the vast majority of paediatricians and neurologists was to the effect that, upon rare occasions, severe, permanent brain damage resulted from the administration of the vaccine. In the intervening years, much has been written in medical journals about these alleged effects and a good deal of clinical experience has been recorded. Pathologists, neurologists, paediatricians and neonatologists have worked and written extensively in this field. A major contribution to the present state of opinion on this controversy in the medical profession has been made by the work of epidemiologists and statisticians.

It will be necessary to examine a good deal of the evidence about these undertakings that was presented to me in the course of a trial in which 64 days were occupied with the taking of evidence. It may be a useful illustration of the extreme swings of opinion that appear to have occurred and to be occurring to point once more to the opinion of Dr. Douglas McGreal, which may well have been the starting point for the development of the plaintiffs' claims. Upon Patrick's discharge from the Hospital for Sick Children on October 18, 1979, and again in his letter of March 31, 1980, Dr. McGreal referred to the probability that Patrick had had a reaction to the DPTP inoculation which produced a diffuse encephalopathy with seizures, "... a well recognized entity likely due to the pertussis component ..." which could produce severe brain damage.

In his evidence before me in October of 1987, Dr. McGreal stated his agreement with a view advanced by Dr. J.B.P. Stephenson, an eminent paediatric neurologist in Glasgow, Scotland, that the condition known as post-pertussis encephalopathy was a myth. On the next day, he modified this to state that, in his view, it was "probably" a myth.

The word "encephalopathy" was used extensively in the evidence. It is a somewhat unsatisfactory word in that, as used by many of the medical experts who testified, it has no very precise content. A very rough consensus would seem to indicate that it stands for a condition of neurological injury of a serious nature, not involving infection or inflammation. When the latter exists, the condition is more usually described as encephalitis. For my purposes, it is useful to have in mind the definition adopted in the guide-lines for notification sent out by the National Childhood Encephalopathy Study (N.C.E.S.), a major study in Great Britain to which further reference will be made. In those guide-lines, it was stated that:

> The term "encephalitis" is taken to indicate any infective or inflammatory cerebral disorder. The more general term "encephalopathy" is used when the cause of the cerebral disorder is not immediately obvious.

In accordance with the Rules of Practice, reports were delivered in advance of trial with respect to all the medical professionals who gave evidence. The defendants, Doctors Raes and Hall, were, of course, engaged in Patrick's treatment, as were Doctors Brody, Nicholson and, to a degree, McGreal. Almost all of the many other doctors who testified did so as experts in various fields whose study or experience could be expected to be of assistance to the court. Some of them, of course, examined Patrick for the sake of giving an opinion, but these were not directly concerned with his treatment.

In every case, the report was, of course, available to counsel and was referred to in the examinations and cross-examinations of the witnesses. One or two brief passages in a few of the reports were objected to as going beyond the expertise of the witnesses. Such passages were not relied upon

by me in considering and weighing the evidence of the respective witnesses. Otherwise, the reports and the viva voce testimony form part of the record and have been taken into consideration.

Causation in general

The central question of the etiology or cause of Patrick's condition involves an association, at least temporal, between pertussis vaccination and encephalopathy. Even those witnesses who came down strongly in favour of the view that there is a causal relationship readily acknowledged that the relationship is a rare one. As one would expect, therefore, the personal experience of even the most specialized and expert consultants was limited and there was much reference to the scientific literature on the subject. Many scientific publications were annexed to, or became associated with, the reports filed and I have referred and will refer freely to some of such publications.

In what follows, reference to the evidence of a particular expert witness may generally be taken as including the report filed.

To a large extent, the witnesses who concerned themselves with the etiology of Patrick's condition expressed the problem as one of determining when it would be proper to diagnose a post-pertussis encephalopathy. For purposes of this examination, I shall adopt the criteria advanced by two of the plaintiffs' witnesses.

Dr. Jerome Vincent Murphy is a highly trained physician, with specialist qualifications in paediatrics and neurology. He is presently a professor at the University of Missouri School of Medicine in Kansas City, and chief of staff of the section of neurology at the Children's Mercy Hospital in that city.

Dr. Mark Robin Geier is a medical doctor, with a Ph.D. in genetics, who has worked extensively in the fields of gynecology and obstetrics. He was at one time a researcher at the Laboratory of General and Comparative Biochemistry at the

National Institutes of Health, Bethesda, Maryland, and is an associate professor in the psychiatric department in the Uniform Services University of the Health Sciences, in Bethesda. In addition, as a private consultant, he sees several hundred patients a year for genetic counselling.

Dr. Murphy recognizes a clinical entity known as post-pertussis encephalopathy. At Tr. vol. 8, p. 958, line 18, he described it thus:

> It's a severe problem and, fortunately, extremely rare. It involves the sudden onset of a major neurologic deficit following within 72 hours an immunization with pertussis vaccine. The deficit can be seizures, or it can be a weakness of one side, a hemiparesis, or a sudden loss of previously acquired skills that the infant had.

Dr. Geier gave his personal criteria for diagnosis of post-pertussis vaccine encephalopathy in Tr. vol. 24, p. 2981, commencing at line 4, as follows:

> The first is that the child needs to be considered to be reasonably normal by his caretakers prior to the injection of the vaccine.
>
> The second is that there is an onset of neurologic symptoms in close proximity following the time when the pertussis vaccine is injected. I use generally 72 hours, although there are those who would allow up to one week following the injection.
>
> And third, that no other explanation for the symptoms that are seen is found, on further examination of the case.

Those three criteria describe with reasonable accuracy the conditions agreed upon by the experts as being necessary for the diagnosis -- prior normalcy, the development of symptoms within a time span of not more than 72 hours and the absence of other explanation.

In 1985, an ad hoc panel of the American Medical Association,

which was put together to explore the need for a compensation system for vaccine-injured patients, published a report in the Journal of the American Medical Association which appears as 73A in the binder identified as ex. 73. In establishing its criteria the committee added the requirement that:

> In these cases, the infant will be so demonstrably ill that any prudent parent will seek medical care during the acute encephalopathy.

Asked to comment on an excerpt, of which the above sentence formed part, Dr. Geier indicated, at p. 2986, that the panel's criteria were very similar to the ones he had mentioned as his personal criteria, and he pointed out that the panel drew the conclusion that, if those criteria were met, it was more likely than not that the problems that occurred were due to the vaccine and not to other causes.

By way of aside at this point, it should be pointed out that almost immediately following the sentence quoted, the A.M.A. panel stated that:

> It was the opinion of the panel that the probability of encephalopathy being considered a possible adverse reaction to pertussis vaccine is 100%. In any specific case of encephalopathy related to vaccine administration, there is about a 60% to 70% level of probability of vaccine causation; about one in three may have residual brain damage after one year.

Dr. Mortimer, a witness for the defendants, was a member of that panel and he stated in his evidence that between drafts of the report he had the benefit of access to some of the data provided by the N.C.E.S., as a result of which he urged that the figure of 100% be reduced to 90% or 95%. Dr. Mortimer's doubts are clearly documented in his evidence between pp. 4153 and 4158, Tr. vol. 31.

Pertussis -- the disease

In describing the pertussis or whooping cough disease and, to

some extent, the development of pertussis vaccine, I shall rely to a large extent upon the evidence of Dr. Edward A. Mortimer and that of Dr. John B.P. Stephenson. Dr. Mortimer is a professor of paediatrics and vice-chairman of the department of epidemiology and bio-statistics at Case Western Reserve University School of Medicine in Cleveland, Ohio. He has much interest and experience in epidemiology.

Dr. Stephenson is a consultant in paediatric neurology at the Royal Hospital for Sick Children, Glasgow, Scotland. He has had extensive experience and is one of approximately 20 senior consultants in paediatric neurology in the United Kingdom. He testified that he is mainly consulted by other consultant paediatricians, and that those on his level of paediatric neurology would probably be limited to about 10 or 12.

Pertussis, or whooping cough, is a dangerous disease, largely of early childhood, caused by infection with Bordetella pertussis, an organism named after one of the investigators who first identified it. The disease is characterized by sustained paroxysms of coughing, with a characteristic "whoop" marking the effort to inhale after prolonged exhalation during coughing spells. Before the widespread use of vaccine, it is said that almost every child in North America had whooping cough. The disease was sometimes complicated by seizures, perhaps both anoxic and epileptic, by encephalopathy of various kinds and by death.

Dr. Geraghty, one of the plaintiffs' witnesses, of whom more will be said, stated that there was universal agreement among scientists that the brain damage from whooping cough disease was due basically to a protein, pertussis toxin, in the pertussis organism. Dr. Mortimer is of the opinion that the prime, if not sole, cause of disease-produced brain damage is the lack of oxygen caused by the repeated coughing spells. He stated, at Tr. vol. 31, p. 4126, that:

> ... I find no reason to implicate anything further than anoxia. That isn't to say that there isn't, because I don't know. But clearly, lack of oxygen is a major, if not the sole contributor.

The opinion of Dr. Stephenson is somewhat similar. He feels that pertussis disease may be complicated by anoxic and epileptic seizures and that the encephalopathies that occur are thought to result indirectly, "... mediated by hypoxia and increased intracranial pressure due probably to the paroxysmal coughing associated with acute pertussis compounded by the effects of the secondary seizures".

Dr. Mortimer tells of two population-based estimates of the frequency of permanent brain damage from the disease. A study in the Borough of Brooklyn, New York City, in earlier years, suggested that about one in 22,000 cases displayed obvious, severe brain damage. Some of the data in the National Child Encephalopathy Study (N.C.E.S.) gave an estimate of about one in 11,000 children who developed pertussis-caused brain damage.

It obviously was desirable to develop an immunizing agent, if this could be done. Treatment of the disease lacks specifics. While antibiotics given early in its development may diminish severity, they are not satisfactory as a means of control because exposure is sometimes not recognized and early symptoms are indistinguishable from those of the common respiratory diseases. Prevention, therefore, is the preferred course.

The pertussis organism has been peculiarly resistant to the efforts of scientists to read its biological secrets. By the 1940s, trial-and-error methods had resulted in the production of a vaccine that is somewhat crude by the standards of the mid-twentieth century, but was demonstrated to be effective.

It is Dr. Mortimer's estimate that, in the United States, 80% to 90% of vaccinated children exposed to whooping cough are protected. From the public health standpoint, protection is even greater because of what is known as "herd immunity" resulting from the fact that, when the majority of a population is immune to a contagious disease, those who are not immune are protected to a degree because transmission of the disease in the community is much less likely to occur.

Pertussis -- the vaccine

As has been stated, the secrets of the pertussis organism have commenced to be discovered only recently, and even today there is only limited understanding of its composition and of those components which create adverse reactions in animals or humans exposed to them. In the earlier years, therefore, it seemed reasonable to produce a vaccine that contained all of the components of the organism, even though many of them would appear to be irrelevant to the question of immunity. Such a vaccine is known as a whole-cell vaccine for obvious reasons and in contrast to what have become known as acellular or sub-cellular vaccines. One of the latter was licensed and used in the United States during the 1960s by the Ely Lilly Company, and several varieties are now being produced by Japanese concerns and have recently been the object of an international study in Sweden.

There appears to be universal agreement among knowledgeable medical and scientific personnel that so-called "minor" reactions are very frequently associated with the administration of the whole-cell vaccine, now almost universally employed in combination with other vaccines, as with the DPTP. The pertussis component is known to be highly pyrogenic, meaning that it produces an area of inflammation in the vicinity of the vaccination site, and it frequently produces irritability and a moderate degree of fever and even febrile convulsions of short duration. These are considered to produce no long-term sequelae and are not a cause for concern.

Reactions to pertussis vaccine

Since the practice of vaccination with pertussis, alone or combined, has become widespread, many reports of devastating brain damage have been made. Medical and public authorities in many parts of the world became concerned because, in their view, the obvious advantages of immunization through vaccination were being seriously undermined by a falling off of acceptance by parents as a result of such reports. Public health authorities became greatly concerned that the disease itself would once more increase, as in fact it did in at least England, Japan and Sweden, and as a result various studies were

instituted with a view to determining in a definitive way the relationship between vaccine and the brain damage that was thought to follow.

In assessing this relationship, it had been easy and natural for lay persons, and probably the great majority of physicians, to conclude that, because there was sometimes a temporal association between vaccine administration and the development of devastating brain damage, the one was the cause of the other. The logical fallacy encompassed in the term post hoc ergo propter hoc is an error into which it is easy to fall. In studying the possible causative relationship between DPTP and brain damage, a number of considerations must be kept in mind. To begin with, DPTP is generally given in North America and in most parts of Europe within the first six months of life, an age when disastrous events, such as S.I.D.S. (sudden infant death syndrome) and seizure disorders such as infantile spasm, are most likely to occur. It has been said that, statistically, within any large group of the population, the chances of a number of encephalopathies developing within three days of virtually any observable event are very great.

Dr. Thomas Millar Pollock, sometime director of the Epidemiological Research Laboratory, Public Health Laboratory Service, London (retired in June, 1983), and author of some 98 publications, including 48 on vaccination, immunization and clinical trials, at p. 11 of his report, ex. 69-7, puts it this way:

> The types of permanent neurological disorder attributed to pertussis vaccine, e.g., epilepsy or physical and mental deterioration, tend to become evident in children at an age when pertussis vaccine is being given. Moreover, they occur in unvaccinated as well as vaccinated children. Thus in any child population in which most children are vaccinated, neurological disorder is bound to occur by chance in some children who have been recently vaccinated. The appearance of cases of neurological disorder soon after vaccination does not in itself prove that the vaccination was responsible, any more than the occurrence of a neurological disorder in a child who has recently been christened proves the existence

of a causal relationship between these two events.

Next, an infant who fails to develop normally because of problems later found to have been present from birth or before, frequently appears to be normal for the first few months of life. Neurological defects can be very difficult to observe during the early months because so little is expected of an infant. A very primitive central nervous system may well be capable of supporting the normal activities, confined mainly to sleeping and eating, masking the fact that there may be little or no development of the portions of the brain associated with more complicated activities. For example, as some of the experts say was the case with Patrick, it may well be that a primitive form of vision can be sustained by the area of brain stem alone but in later months of development genetic imperatives compel this function to be passed to other parts of the brain, and it may then become apparent for the first time that such parts have not developed or are defective.

Dr. Mortimer testified that in the United States three of every 1,000 infants born alive ultimately turn out to be moderately or severely retarded, and in about 40% of those no cause is ever recognized. Another way of stating it in medical terms is that perhaps 40% of cases of moderate or severe retardation are idiopathic in origin.

A third consideration is that it is possible for children with pre-existing central nervous system defects to show no signs obvious to parents or even to family physicians of such defects until illness or an exterior stimulus such as vaccine brings them out or causes them to be observed by an observer made more attentive by the obvious illness or "minor" reaction.

As a result of the reappearance of whooping cough in disturbing proportions, at least partly because of public fear of brain disorders resulting from the vaccine, steps were taken by certain countries to allay public fear and to increase immunization rates.

In Japan, it was sought to increase the rate of immunization by delaying administration of the vaccine until two years of

age as it was believed that older children were less likely to incur severe reactions. The rate of immunization continued to be poor and, as a second step, a new acellular form of pertussis vaccine was licensed in 1981. The type of tests and studies that would be required in North America, or in the United Kingdom, were not carried out and, in addition, several varieties of acellular vaccine were licensed. Consequently, as may be relevant in another section of my judgment, no real comparison of effectiveness and of reaction rates between the Japanese acellular and the western whole-cell vaccines, has, until very recently, been possible.

In the United Kingdom, several major attempts at definitive studies were made with a view to determining, on a scientific basis, the risk of damage from pertussis vaccination.

Epidemiology in medicine

It is necessary to digress to consider the various types of study that are sometimes performed, the results of which may be considered acceptable by the scientific community. The design, organization and interpretation of such studies are the province of epidemiology and they involve, to some degree, the discipline or science of statistics. The evidence most helpful in these matters was given by Dr. Pollock, Dr. Stephenson, Dr. James D. Cherry and Dr. Kenneth Duncan MacRae. Dr. Cherry is professor of paediatrics at the University of California, Los Angeles, and chief of the division of infectious diseases at that university's medical centre. For over 20 years he has been engaged in research concerning vaccines, experimental vaccines and new vaccines, and he has been the designer and director of a number of epidemiological studies, including one on pertussis vaccine.

Dr. MacRae, a Ph.D. in psychology and statistics and a Fellow of the Institute of Statisticians in Great Britain, is intimately familiar with the N.C.E.S., described below.

Epidemiology may be described as the study, control and prevention of disease with respect to the population as a whole, or to defined groups thereof, as distinguished from

disease in individuals. Clinical epidemiological studies can be carried out for the purpose of investigating the relationship between a particular condition existing in the environment, or population, and a particular disease or condition of health. A clinical epidemiological study cannot in itself prove causation but it may justify an inference that a statistical association reflects a causal link.

Dr. MacRae, founding himself upon a paper delivered by Sir Austin Bradford Hill in 1965 in connection with the founding of the industrial medicine section of the Royal Society of Medicine, refers to nine guide-lines for drawing an inference about causality. These guide-lines are said to be widely respected and adopted, and are briefly listed here as strength of the association, consistency of the association, specificity of the association, temporality of the association, biological gradients, plausability, coherence, experiment, and analogy. Elaboration with respect to some of these headings may later be necessary.

Temporality is probably the most obvious and common association to give rise to concern about the safety of vaccination, and indeed what is claimed to be the close association in time between one or more of Patrick Rothwell's vaccinations and the onset of serious neurological disorder is a major part of the foundation of the plaintiffs' claims. However, the epidemiologists acknowledge only that an association in time gives rise to an hypothesis and ways of testing the hypothesis that one event causes another, e.g., that vaccination causes severe, permanent brain damage, must be found. As indicated, no epidemiological study can conclusively prove a cause-and-effect hypothesis. Nevertheless, evidence of varying weight can be found in various types of study.

Dr. MacRae describes four kinds of epidemiological studies that may be helpful in investigating alleged relationships of cause and effect. In his view, the weakest are known as case reports, sometimes described as anecdotal episodes. It was a series of articles in learned journals giving such case reports that first gave rise to the concern among physicians that pertussis vaccine might be responsible for serious neurological

damage, and that led to further, more sophisticated studies such as will be later described. One of the best known of such series of case reports, and one referred to by virtually every epidemiological or neurological expert who testified, was that described in the journal, Paediatrics, in April of 1948 by Doctors Randolph K. Byers and Frederic C. Moll, entitled "Encephalopathies Following Prophylactic Pertussis Vaccine", hereinafter referred to simply as Byers and Moll. (Exhibit 73C.) That was a series of case reports of 15 children who developed acute neurological symptoms after pertussis vaccination, and it concluded, at p. 444, that "... an important risk of encephalopathy attends the use of prophylactic pertussis vaccine. ... Efforts to diminish the hazard by modification of the vaccine or new methods of administration seem indicated."

A second article frequently cited by witnesses was published in the British Medical Journal in 1967 by Dr. Justus Strom, of the Hospital for Infectious Diseases, Stockholm, Sweden. (Exhibit 73D.) The reported condition was the appearance of neurological symptoms within seven days of vaccination in one case per 3,600 cases examined, and three cases of destructive encephalopathy in the seven years covered by the survey, that is, one per 170,000 cases.

A further study involving case reports was made by Dr. Kulenkampff and others, from the Hospital for Sick Children, Great Ormond Street, London, England, and published in the Archives of Disease in Childhood in 1974. (Exhibit 73E.) The authors examined 36 children seen over a period of 11 years "... who are believed to have suffered from neurological complications of pertussis inoculation (given as triple vaccine)".

While at least one of the plaintiffs' witnesses, Dr. Mark Geier, relied heavily on these articles as evidence for the statement that there was a causal relationship between pertussis vaccine and encephalopathy, in none of them was there a control group so that the background of the study could be assessed. In other words, only vaccinated children were looked at and no comparison with unvaccinated children was possible.

Furthermore, in the case of the Kulenkampff article, the authors recognized the problem in the following sentence, commencing on p. 48:

> We do not think that data from our study are of direct help for the debate on the merits of pertussis inoculation because we do not know either the prevalence of natural infection or the frequency of inoculation encephalopathy in the population we serve.

They went on to state that other authorities had reached different conclusions and acknowledged that "... the differences between our two views may be due to differences in selection, and the conflict can only be resolved by a careful prospective study of the frequency and circumstances of possible complications".

So much for the case reports -- an hypothesis is suggested but the absence of controls for comparison makes it impossible to draw conclusions as to probable causation. As Dr. MacRae put it,

> ... and a case report is the weakest form of evidence -- in fact it's logically invalid. And all it actually can ever do is suggest to a doctor that there might be a problem that he should study. [Tr. vol. 38, p. 5041.]

Going up the reliability scale, Dr. MacRae expressed the view that the next most dependable is the case control study, usually described as "retrospective". This is a study in which a group of "cases" is identified, that is to say, persons with the form of injury or illness whose cause is being investigated are grouped together and they are compared with persons who do not have the injury or illness, known as the controls. This type of study is denoted retrospective because it commences with the fact that the injury or illness exists and it looks backwards into the history of the cases and compares them with the history of members of a control group.

Dr. MacRae stated that such a study is subject to many methodological flaws, which may be examined subsequently, but

it is a form widely used because it may be the only practical option available in the circumstances.

Stronger still, in statistical evidentiary value is the cohort study in which the group of people it is desired to study is identified and recorded and then periodic checks are made for as long as may be necessary into the future to see what happens to them. The example given by Dr. MacRae as the classic cohort study was one in Britain wherein a questionnaire was sent to all doctors in the United Kingdom asking them to detail their smoking habits. Subsequently, the death certificates of all the doctors recorded were collected as the deaths occurred and, in Dr. MacRae's words, "[t]hey found the death certificates of the doctors who smoked made a taller pile than the death certificates of those who didn't". One of the problems with the cohort, of course, is that it may be necessary to wait for a very long time for significant events to emerge and the study to be completed.

At the top of the list of reliability compiled by Dr. MacRae is what he calls the gold standard, that is, the randomized prospective controlled trial. The example given by Dr. MacRae concerns a study of breast cancer in women in Great Britain designed so as to make certain that equivalent groups of patients receive different treatments so that differences in results can only be attributed to difference in treatment, there being as nearly as possible no other differences between the patients.

In Dr. MacRae's view, the randomized trial overcomes all the problems associated with the case control and cohort techniques save the problem of chance, to be examined in more detail subsequently.

Before proceeding to examine individual studies, and in particular the National Child Encephalopathy Study (N.C.E.S.), something should be said of other statistical concepts that may warp or skew results if not taken into consideration. For my understanding of these concepts, I rely, again, on the evidence of Dr. MacRae, whose evidence in this respect was not seriously questioned.

The first of these concepts is chance. The possibility that two events may coincide by pure chance and without the intervention of any necessarily causal effect can never be entirely eliminated. The effort of those who design statistical and epidemiological studies is always directed to minimizing the probability of chance and the effect that it will have upon the results of the study.

The importance of chance in a particular study may vary with the size of the study and hence chance is a consideration in deciding on how large a study need be in order to be reliable.

A homely example given in the course of the evidence concerned the case of a barrel containing 10,000 marbles, 5,000 of which were, in fact, black and 5,000 of which were white. If one were to withdraw blindly, say 50 marbles, it could well be that something like 30 of these would be black and 20 white. If the composition of the contents of the barrel were to be reported on the basis of such a sample, it would, of course, be erroneous, given the known fact that 50% of the entire contents was composed of each colour of marble.

It would be difficult, and it is unnecessary, to go into the methods by which statisticians have determined how to calculate the probability that chance is the explanation for a particular result. It must suffice to say, and I do not believe this assumption was challenged by any witness or by counsel, that medical and biological science has adopted what is called the 5% level of statistical significance as the criterion by which to judge the possible effects of chance. If the probability that chance accounts for the result is less than 5%, the result of a study is said to have statistical significance, meaning that chance is considered to be an unlikely explanation of the result.

At p. 11 of his report, ex. 124, tab 2, Dr. MacRae points out that one aim of the analysis of a study is "... to quantify the probability that any difference found (between cases and controls, for example) could have occurred by chance alone ...". He states that a study comparing 100 cases and 100

controls which found that 85% of the cases and 75% of the controls had had a certain exposure, can be shown by a commonly acceptable formula, or statistical test, to have a probability of 7.7% of such a difference arising by chance alone. If the study had been twice as large, namely 200 cases and 200 controls, and the same difference had been observed, the probability of that occurrence happening by chance would be much lower, namely, 1.2%.

There are two points to bear in mind with respect to the adoption of the 5% level. First, it is a criterion by which the question of whether chance is a possible explanation can be considered. Second, it must always be remembered that one may reject chance by virtue of the 5% custom, but it is still possible that the unlikely may have happened. Concluding that there is a difference, when in fact the finding is merely due to chance, is one type of error known as a type 1 error, and the figure of 5%, or whatever the probability is, is merely a measure of the probability of making a type 1 error when in fact there is no real difference between the two groups.

By an appropriate calculation which involves a statistic known as the "standard error" of the difference between two groups, the accuracy or precision of the result of a study can be estimated. A common way of expressing the accuracy of a study's result is to calculate an interval which states the range of possible "true" differences likely to give rise to the result found in the study. This is known as a "confidence interval". In line with the use of 5% as the level of statistical significance, it is common to use what is called a 95% confidence interval which gives the range of possible true differences all of which have a probability of more than 5% of giving rise to the result found by the study. A value lying outside the confidence interval has a probability of less than 5% of giving rise to whatever difference is found in the study. If zero is inside the confidence interval this means that a true difference of zero is more than 5% likely to give rise to the study result, or, in other words, the difference given by the study is not statistically significant. On the other hand, if zero is outside the confidence interval it means that a true difference of zero has a probability of less than 5% of giving

rise to the study result, and the difference is, therefore, statistically significant. That is to say, there is a smaller than 5% probability that a difference such as shown in the study will appear if in fact there is no real difference.

The other side of this part of the problem is that, contrary to the case where a spurious difference is shown where no real difference exists, a study may for reasons of design weakness or otherwise fail to detect quite a large difference, an error known as a type 2 error.

The probability of the existence of a type 2 error varies with the size of the study. If an effect or difference is thought to be relatively rare, a very large study is more likely to return a true result than is a small one. The term "power" is used to describe the probability that a study will indeed find an effect or difference if it is there to find. With 95% power there is just a 5% chance that the effect looked for will be missed if it is indeed there to find.

In calculating the appropriate size for a study, the desired power is a factor to be considered -- the smaller the study the lower the power.

Another consideration that must be taken into account in the design of a study is the question of bias. Bias in this connection is not the same as the subjective prejudice that is sometimes spoken of as legal bias. Bias in statistical terms is a systematic tendency in the design, conduct or analysis of a study that results in overestimating or underestimating the association between an exposure and any disease. Dr. MacRae gives some potential sources of bias that may be of importance when the results of various studies with which we are concerned are looked at, including that of the N.C.E.S. What he calls "exposure suspicion bias" refers to the probable tendency to look more rigorously for the suspected cause when an individual is known to be a "case". Correspondingly, the examination may be less rigorous if the examiner knows that the individual is a control rather than a case.

There is then the "diagnostic suspicion bias" which may come

about when the examiner knows that the subject or individual has been exposed to the suspected cause.

Another circumstance to be avoided is any that may give rise to "confounding". This term refers to the fact that a third variable may be responsible, in part or in whole, for the apparent association between a case and the factor being investigated as a possible cause or, on the other hand, that a third factor has masked a real association between the risk factor and the case and prevented such association from being found.

An example given by Dr. MacRae is that of a case control study of the association between cirrhosis of the liver and cigarette smoking when, as is known to be the case, smoking and alcohol consumption are frequently found together, and there is a known association between cirrhosis of the liver and the drinking of alcohol.

Another problem in connection with case control studies is that of matching. This is the most common way of trying to deal with confounding. If, in the example given above, it was desirable to eliminate the confounding issue of alcohol consumption, one could match the smokers and the non-smokers for alcohol consumption before determining whether there was a difference which could be accounted for by smoking or non-smoking. In practice this is often very difficult.

It will next be necessary to look at the term "risk" as used in epidemiology. The term "absolute risk" refers to the rate at which an occurrence may be found in an entire population or group. Statisticians have worked up tables for the various risks which occur in life together. As an example, the chance of being murdered during a two-day stay in New York is one in one million. There is a similar chance of being killed in an automobile accident if one drives 140 miles, and likewise, a journey of 7,000 miles in a jet aircraft carries a one in one million chance of death. An example closer to the field of our consideration would be if within a particular country it was a fact that 2% of live births resulted in some form of abnormality, the absolute risk of being born abnormal would be

two in one hundred.

The term "relative risk" represents a ratio between two absolute risks. The example given by Dr. MacRae in his report is a hypothetical one. Suppose 5% of babies born to mothers who do not smoke weigh less than the normal weight for their gestation at the time of birth, but 15% of the babies of mothers who do smoke are underweight. The relative risk of being light weight at birth for the infants of smoking mothers is 15% over 5% or 3. In other words, an infant whose mother smokes has three times the absolute risk of being underweight when born than the infant has whose mother does not smoke.

In a case control study a formula known as the "odds ratio" can be used to calculate relative risk.

Another term sometimes used is that of "excess risk". This is the difference between the absolute risk for the exposed and the absolute risk for the unexposed, sometimes called attributable risk. If, for example, the exposed population have an absolute risk of three per thousand and the unexposed have an absolute risk of two per thousand, this produces a relative risk that is one and one-half times greater for the exposed, and an excess risk of one per thousand.

One of the criticisms that was made by some of the witnesses, and particularly by Dr. MacRae, is the way in which the term "attributable risk" is used in the N.C.E.S. The definition of "attributable risk", as found in what has been referred to as "the Blue Book", filed in this trial as ex. 27, is found at the foot of p. 97 in these terms:

> This is that part of the incidence of a defined condition in a population which can be attributed to a particular causal agent (in this case, the incidence of serious neurological illnesses in young children attributable to pertussis vaccine). It is the difference between the incidence of the condition in exposed (i.e. immunized) children and that in non-exposed (i.e. unimmunized) children.

Used in that sense, "attributable risk" is indistinguishable

from "excess risk".

The report goes on to state that "... the attributable risk can usually only be estimated from the results of cohort studies". Nevertheless, the report does attempt to state an attributable risk.

As we consider the N.C.E.S. in detail, we shall examine the criticisms. Here, I content myself with referring to Dr. MacRae's criticisms, substantially elaborated in his report and outlined in detail in his evidence. It is perhaps wise only to state at this point that, in Dr. MacRae's view, there are so many possible types of bias in the study it would be unwise to place any dependence upon an estimate of "attributable risk" to which the whole population is exposed by reason of the effect of DPTP vaccination.

It was necessary to conduct the above elementary examination of some of the concepts and methods of the discipline of epidemiology, as it is one of the methods or tools used by scientists when a possible causal relationship between two phenomena is examined, and many of the witnesses referred to epidemiological studies as authorities for or against their opinions.

The principal value of the studies, and of the various articles and learned papers to which reference was made in the course of the trial, is to act as touchstones which may be used to test the opinions of the witnesses who gave viva voce evidence and filed their reports before the court. While my conclusions must be based upon the evidence, and that of course means that I must assess and choose between the evidence of the experts where they are not in agreement, I may use the articles and reports as one of my means of assessment. While in most cases the reports are not evidence of the truth of the facts or the validity of the opinions stated therein, they are evidence, when such is acknowledged by the appropriate witnesses, of the fact that they were published, they were circulated and they were part of what has been referred to as "... the general corpus of medical and scientific learning on the subject and can be relied upon and adopted by suitably qualified experts":

Loveday v. Renton and Wellcome Foundation Ltd., unreported but delivered by Stuart-Smith L.J., in the Queen's Bench Division, High Court of Justice, England, March 29, 1988.

The distinction just made is important for at least one reason that may not be immediately obvious. When the specific claims against the defendant, Connaught Laboratories, come to be examined, it will be seen to be an important part of the plaintiffs' case that Connaught was aware of the existence of many reports indicating the possibility and even the probability that serious brain damage could sometimes result from the administration of DPTP vaccine, and that the actions they took or failed to take in connection with the manufacture of their vaccine and the warnings given or not given to prospective users demonstrate negligence. In this connection, the publication of the reports is important evidence but, without more, that is not evidence of the truth of their contents. The conventional wisdom existed; whether it was founded in fact may be another matter.

Onus and standard of proof

On the issue of whether or not DPTP vaccine can cause serious lasting brain damage, as indeed on all issues in the case, the onus is on the plaintiffs throughout. As to the degree of proof required, it is the normal civil standard of the balance of probabilities. Is it more likely than not that DPTP can cause such effects?

Proof of causation

Causation in scientific and medical matters may be easy to assign or may be extremely difficult. Causation may be taken as proved, for all practical purposes, in many diseases when a specific organism is invariably found in association with a specific physical condition of disease and other possible causal agents can be eliminated. Causation can be assigned when it has been shown that a specific group of symptoms, characteristic only of a specific agent or disease, is present. Causation can be assigned when a specific pathological condition, characteristic only of a specific causal agent, is

shown to exist in a patient, in life or at post-mortem examination.

Reverting once more to the guide-lines proposed by Sir Austin Bradford Hill and endorsed by Dr. MacRae, the specificity of the association between pertussis vaccine and major permanent brain damage can be investigated with respect to a possible clinical syndrome and with respect to specific pathology.

Specific clinical syndrome

If a causal relationship in fact exists, it would seem likely that the cause, allegedly pertussis vaccine, will produce the same sort of damage, i.e., a specific syndrome, whenever it operates to bring about an effect. The strongest proponent of the view that it does was probably Dr. Kevin Geraghty, called on behalf of the plaintiffs. For the moment I leave aside the question of credibility and state only that Dr. Geraghty is a physician of 14 years' experience, including his residency. He has recognized specialist qualifications in paediatrics, with a degree in bacteriology and immunology, and his specialty is in allergy and immunology. In his present practice he sees patients on referral for problems arising out of possible allergies or immunological or toxicological problems. His interest and knowledge in questions involving pertussis vaccine have been acquired and fostered mainly by reviews of the literature on the subject.

Dr. Geraghty considered that an unusual, high-pitched type of cry immediately following a pertussis vaccination would constitute a distinct syndrome. He went on to say, however (Tr. vol. 16, p. 2080) that:

> We know, from other neurological conditions, that is the nature of the cry associated with meningitis, cerebritis. Certain syndromes are well described with similar high pitched cries, the common denominator being involvement to the neurological system ... in common parlance, the brain.

Dr. Geraghty relied upon a paper (ex. 58, tab 1465), produced from the records of the defendant Connaught, in support of the

assertion that there is a recognizable clinical entity called post-pertussis vaccine encephalopathy.

With respect to that paper, however, Dr. Jack Cameron, the author, refers at p. 3 to three types of reaction as possibly due to a pertussis vaccine injection, which does not seem to me consistent with one unique syndrome. At Tr. vol. 18, commencing at p. 2299, Dr. Geraghty was unable to disagree with several statements taken from the report of the N.C.E.S. (ex. 28) as follows:

> The questions, does pertussis vaccine cause brain damage? and, if so, how often?, are difficult to answer because the neurological disorders allegedly caused by pertussis vaccine are apparently most uncommon and have no unique clinical features.

Similarly, at p. 2300, he did not disagree with the statement that:

> ... the similarity of the clinical features associated with different aetiologies, all conspire to create special difficulties in any attempt to demonstrate that pertussis vaccine rather than some other agent causes these conditions in some cases.

Finally, at p. 2301, he agreed that post-pertussis encephalopathy does not have any unique clinical features and that the features that have been claimed as indications of such a disorder are shared with other neurological disorders.

Dr. Murphy, called on behalf of the plaintiffs, agreed that there was no clinical picture, laboratory test or pathology that is distinctive for a post-pertussis reaction.

Dr. Curtis is a consultant in paediatric neurology at the North York General Hospital with appointments at other institutions in the area. It was her opinion that "... this child likely has a pertussis vaccination encephalopathy" (Tr. vol. 9, p. 1115). This opinion will be referred to again when dealing with the question of the specific aetiology in Patrick

Rothwell's case. On cross-examination, Dr. Curtis, whose knowledge comes to a large extent from a review of the literature as she has seen no actual case diagnosed as post-pertussis encephalopathy in her practice, testified, at vol. 9, p. 1168, as follows:

> Q. (By Mr. Campbell) And would you agree, from your review of the literature, that there is no typical reaction to pertussis so that it can be easily and conclusively identified?
>
> A. I think, yes, I would agree with that.
>
> Q. And would you also agree that there is no typical clinical picture of the manifestation of the encephalopathy?
>
> A. No typical one, no.

Dr. Mark Geier expressed the view that high-pitched unusual screaming, coupled with convulsions, presented "... about as classical description as you can have with the scream recognized as a neurological irritation", but he was unable to indicate that such reactions were unique to pertussis vaccination.

Dr. McGreal, as has already been indicated, was of the opinion by the time of trial that the syndrome of post-pertussis encephalopathy was probably a myth.

Dr. MacRae, in connection with his analysis of the N.C.E.S., and particularly the table on p. 167 of ex. 27, stated that:

> The concept that there is a specific type of illness uniquely associated with the vaccine is patent nonsense on the basis of this table. So the criterion of specificity does not apply to this area.

Dr. Stephenson, when asked if there was such a thing as a syndrome associated with encephalopathy following pertussis vaccination, stated:

> No, I think there is not. And nor could -- the National Child Encephalopathy Study in the United Kingdom couldn't find it. And I don't think there's any good evidence that it exists at all.

Dr. Mortimer stated that he had always been bothered by the fact that there is no characteristic syndrome alleged to be related to DTP:

> If a vaccine is going to produce a particular problem, such as occurred with rabies vaccine in the past, it's usually the same disorder, of one sort or another. It was often, for example, a form of transverse myelitis, an inflammation of the cord, with rabies vaccine. This just has not been reported with these temporally associated problems.

Finally, at Tr. vol. 32, p. 4255, in explaining why he does not believe that pertussis vaccine encephalopathy exists, Dr. Mortimer stated:

> And accordingly, I believe, with my colleagues, it is reasonable to expect that if there were pertussis vaccine encephalopathy that one would find a characteristic syndrome.

Dr. James D. Cherry, professor of paediatrics at the University of California and chief of the division of infectious diseases at the U.C.L.A. Medical Centre, was of the opinion that there was no evidence of a unique syndrome. He founded himself principally upon the study carried out by himself and another doctor upon the Meade Panel established by the British Committee on Safety of Medicines, and the statement in the N.C.E.S. report that pertussis vaccine-induced brain damage is "... certainly not a specific syndrome".

Dr. Thomas Millar Pollock, described above, one of the designers of the North-West Thames Study, a major study in Great Britain, made the following statement at vol. 22, p. 2848 of the evidence:

> Well, first of all, we didn't find any syndrome that could be attributed to DTP vaccine. We didn't find any collection of

symptoms which would -- to which anyone could point and say, "That is a DTP vaccine disorder."

That was the first thing.

Now, it has been claimed by Stewart and widely booted around that such a syndrome did exist. And we couldn't find it. And we thought we probably would have found it if it had been present.

Dr. Euan Ross testified that the Dudgeon Panel was not able to identify a specific syndrome. Finally, Dr. Ross, at vol. 20, p. 2594, in connection with the work of the N.C.E.S. stated:

And we were particularly eager to see if we could find this syndrome [in the N.C.E.S.]. And we failed.

The report of the N.C.E.S. itself (ex. 28), at p. 138, contains the following:

> The cases show a very considerable range of clinical manifestations, all of which are seen in unimmunized children. Nothing distinctive about illnesses which closely followed pertussis immunization was observed. In short, no evidence was found for the existence of a defined syndrome with neurological sequelae after pertussis immunization.

While certain criticisms of the N.C.E.S. were made by various witnesses and will be referred to below, the evidence of the experts was overwhelming in the conviction that the study was the latest and most comprehensive that has been made.

On all of the evidence, therefore, I am of the opinion that it is very much more likely than otherwise that there is no identifiable clinical syndrome of post-pertussis encephalopathy or, to be a little more specific, of serious permanent brain damage caused by pertussis vaccine.

Specific pathology

The case for the existence of pertussis vaccine as a

causative agent of severe permanent brain damage would be greatly strengthened if post-mortem or other examination were to disclose a characteristic pathological feature.

I have no recollection of a specific statement by a witness, or by the author of any authoritative article referred to, that a specific pathology peculiar to pertussis vaccine damage exists.

Dr. Arthur Zahalsky, called by counsel for the plaintiffs, was really qualified, if at all, in the field of immunology and had no expertise in pathology. He nevertheless, at Tr. vol. 13, p. 1825, appeared to approach a statement that there was histological evidence of causation "... ultimately leading to an array of damage which is corroborated histologically when one takes a look". He went on, however, as follows:

> There is, however, my lord, no defined picture that would represent a well described, highly refined, cellular histologic or pathologic picture of exactly what such damage would produce in every case.
>
> HIS LORDSHIP: Would you just go over that again. That last statement.
>
> THE WITNESS: Yes, my lord. I did not want to leave his lordship with the view that there is a defined pathologic picture, or a certain pathologic state defined by microscopic examination of tissues or by microscopic examination of sections of organs which are taken at autopsy in the unfortunate event of children who come to autopsy for a variety of reasons, where such events are temporally related to the injection of DTP vaccine.

On the question of Dr. Zahalsky's qualifications, I took the view, as evidenced in Tr. vol. 13, p. 1826 at line 29, that he was not talking about pathology per se, as he was not qualified to do, but about the appearance of cells on occasion when they are examined. This, if anything, places him even further from being able to state that there was a unique pathological picture that supported the hypothesis of post-pertussis

encephalopathy.

The plaintiffs' witness, Dr. Murphy, stated clearly that in his view, "[t]here's no clinical picture, laboratory test or pathology that's distinctive for this reaction".

Dr. Stephenson, about whose qualifications I have something to say in another place, was of the view that central nervous system diseases generally have a characteristic pathology and that, "... it doesn't make sense to me that you can have a disorder that can be like anything, that has no particular features that differentiated in any way from any other disorder. That doesn't make sense."

On reference to the literature, Dr. Stephenson's view was that what is known as the Corsellis and Janota paper, entitled "Immunization Against Whooping Cough: A Neuropathological Review", published in Neuropathology and Applied Neurobiology, Volume 9 (1983) (ex. 129-30 and ex. 111-10), was the best paper on the subject, and he concluded that though the very good neuropathologists who authored the paper were looking to see what sort of pathology resulted from pertussis vaccine,

> They didn't find any particular features. They found the sort of things people get when they have acute illnesses with fever, which are -- we now think are probably virus infections.

Dr. Euan Ross stated in his report, ex. 69-2, that no characteristic histological post-immunization syndrome was found and stated, with reference to Professor Corsellis' report that, "... usually if there is a clear-cut entity, you would expect the majority of specimens to look the same, or to show similar changes. And here, Professor Corsellis was not able to find consistent changes in these brains' sections that he looked at."

Professor Wigglesworth, whose qualifications are dealt with elsewhere, is a pre-eminent pathologist, but he acknowledged little first-hand experience,

> ... because at no time have I been referred, for autopsy, an infant whose brain damage was alleged to have been caused by pertussis vaccine. And so, coming new to the subject in relation to this particular case (Patrick Rothwell), I carried out a computer survey of the literature; and I was not only surprised, actually I was rather shocked to find that there was virtually no information on the subject.

Professor Wigglesworth went on to state that the only paper on the subject apparent in the literature was the review by Corsellis et al., and he stated his conclusions about that in Tr. vol. 42 at p. 5474, as follows:

> You can see that there is no pattern which could be regarded as specific, and in particular no change which one could recognize and either acute cases or chronic cases, which you could say was typical of this whole group related to pertussis immunization.
>
> And this group of workers have followed up every case that they could find in England and Wales, I think it was ... since 1960, up to the time at which they made their study. I think this is up to about 1981, probably, when they were collecting their material. It was published in '83.
>
> So it's at least twenty years' experience of every single case they could find, in Britain.

There is no evidence that a unique pathological condition has been observed and evidence of some weight that no such condition has been found to exist. I must conclude, therefore, on a clear balance of probability that there is no specific pathology associated with post-pertussis brain damage of a serious nature.

We must look, then, at the question of temporal association and at the epidemiological studies that have been made and that are recognized, in the opinion of any of the experts whose evidence I heard, as being valuable or authoritative.

Epidemiological studies

In the absence of a specific syndrome and specific pathology, one turns to reports and studies.

Although Dr. Geier pointed to a number of the early studies, such as those mentioned above and referred to as Byers and Moll, Strom and Kulenkampff et al., as being strong evidence of a causal relationship between pertussis vaccine and encephalopathy, Dr. Geier is not an epidemiologist nor is he a statistician, although he has done some studies in those fields. The majority of the experts whose testimony I received agreed with Dr. MacRae's statement that case reports, however extensive, without controls can do no more than raise an hypothesis for further investigation. Dr. Cherry, for example, pointed out that of the 15 children found by Byers and Moll over a period of 10 years to have had neurologic disease shortly after immunization, any or all could have been due to other causes. No controls were studied for comparison.

Similarly, Dr. Cherry holds the view that the Strom study, which indicated an apparent risk of about one in 80,000 vaccinated children, or one in half a million vaccinations, produced a relatively small number and, again, the absence of a control group meant that other causes, including chance, could not be eliminated. Similarly with Kulenkampff -- no controls and hence no dependable results.

Dr. Cherry was one of the designers and participants in the study known under the name of Cody and Baraff, undertaken for the U.C.L.A. School of Medicine in conjunction with the Bureau of Biologics, Food and Drug Administration, in Bethesda, Maryland. The report is entitled, "Nature and Rates of Adverse Reactions Associated with DTP and DT Immunizations In Infants and Children", published in the journal, Paediatrics, Volume 68, November 5, 1981, having been accepted February 3, 1980. The report is filed as ex. 73F and contains an extensive review of the earlier work done by others, as well as a description of the study design.

It is categorically stated, at p. 657 of the article, that,

> ... no encephalopathy, permanent neurologic damage or death was experienced within 48 hours of immunization in this project.

The report also states that its results were in agreement with previous reports that simple convulsions, especially febrile convulsions, following DTP immunization are not followed by neurological sequelae in the majority of cases. Dr. Geier agreed with this statement.

Dr. Geier further testified that, after the conclusion of the Cody and Baraff study and the publication of the report, further follow-ups indicated that two deaths had in fact occurred in the group studied. There was no follow-up to this statement before me and I am left with no evidence whatever regarding the cause of those deaths.

I can only be guided by the opinions of the majority of those experts whom I find credible and treat the Cody and Baraff study as another inconclusive examination.

Dr. Geier pointed to certain of these studies as indicating that a clustering effect occurred. In other words, more reactions were reported within a short period following immunization than would be expected if chance alone were responsible. Again, the problem with trying to draw conclusions from such reports is that problems of size, problems of control and problems of bias were not addressed and the figures cannot be relied on as doing anything more than giving some support to the hypothesis raised by the case reports themselves, demanding further investigation.

Well-designed case control studies

As a result of well-publicized studies, such as those that have been discussed above, anxiety grew in Great Britain and elsewhere about the supposed devastating consequences of immunization with pertussis and in fact in the United Kingdom and elsewhere tribunals were established for the purpose of analyzing and, if found eligible, paying claims for vaccine-related damage. However useful they may be as social

instruments, the experience of such tribunals can be of little help to a judicial determination of probable cause, as arbitrary criteria were selected and payment was made if a certain degree of handicap was shown to have occurred within a certain period of time following immunization.

The fact that alarm was prevalent and many claims were made gave impetus to the idea that well-designed studies should be undertaken for the purpose of proving or disproving, if possible, a causal relationship so as to satisfy not only the medical profession but the public on the question of the relationship between the pertussis component of vaccines and serious, lasting brain damage.

A major study involving large numbers was carried out by Doctors T.M. Pollock and Jean Morris, Public Health Laboratory Service, Epidemiological Research Laboratory, London, and reported in the Lancet of April 2, 1983, under the title, "A Seven-Year Survey of Disorders Attributed to Vaccination in Northwest Thames Region". Dr. Pollock, one of the authors, testified before me. Dr. Ross discussed this report, ex. 69-8, in his survey of the literature.

Commonly known as the Northwest Thames Study, the summary states:

> Voluntary reporting of vaccine reactions was intensified in a single large region for seven years. Anaphylaxis and collapse, convulsion, and neurological disorder were reported most frequently after diphtheria/tetanus/pertussis [DTP]. The greater frequency of recorded reactions after DTP than after DT could have been due to bias caused by the adverse publicity accorded to pertussis vaccine, since no major difference was found when the immunization histories of children admitted to hospital with such conditions were compared. No convincing evidence that DTP caused major neurological damage emerged from this large and lengthy study.

Dr. Pollock, in his report, ex. 69-7, made the following statements about that study at p. 16:

> No single syndrome was found in DTP vaccinated children;
>
> . . . . .
>
> Temporary or permanent neurological impairment was reported [voluntarily] three times more often after DTP than DT.

The cases, out of approximately 130,000 children, were twelve and four respectively. "However, study of the individual reports of these twelve cases did not provide suggestive evidence that the vaccine caused these symptoms." Five cases concerned infantile spasms, a condition since demonstrated by others not to be due to pertussis vaccine, and other explanations appear to be possible with respect to the remaining five.

Reports of febrile convulsions inconsistent with the known background rate in infants made the authors suggest that febrile convulsions were reasonably well reported after DTP but not after DT. These findings suggested that the reports of neurological disorder might be biased, an explanation which seemed probable in view of the publicity given to the presumed dangers of DTP.

The authors of the study therefore switched to an objective method of comparison rather than relying on the original voluntary reports of physicians, and the hospital records of all children in the region in the age group eligible for primary immunization and admitted for neurological disorder were examined. The immunization records of those children were then compared.

> Of 64 children admitted to hospital with convulsions within 28 days of immunization, 16 had received DTP and 18 DT. [Diphtheria and tetanus components but no pertussis component.] The admissions rates for convulsion in children of the same age in both groups were 5.6 and 5.3 per 10,000 for a 28-day period. These rates are the same as the background rate experienced by unvaccinated children viz. 5.2 per 10,000.

Dr. Pollock concluded, at ex. 69-7, p. 18, that:

> ... when objective methods are employed for the comparison there is no difference in the incidence of convulsions and neurological disorder after DTP and DT vaccine. The pertussis component of DTP is not, therefore, a cause of these symptoms.

Dr. Ross' comment on the Northwest Thames Region study was that it was not a cohort study in the strict sense, as only those who were immunized were included.

As we have seen, a case-control study is an alternative to a cohort study and is sometimes the only practical method available.

As a preface to his account of the National Childhood Encephalopathy Study, Dr. Ross stated that such case-control studies are particularly valuable where relative risk is to be calculated, "... though the expected small number of possible cases present difficulties in determining attributable risk".

The National Child Encephalopathy Study (N.C.E.S.)

Dr. Thomas Pollock testified after Dr. Ross and acknowledged the weakness in the Northwest Thames Region study and confirmed that it was not a true cohort study. Because of the rarity of the suspected reactions and hence the necessity for an enormous cohort and a long period of time, a true cohort study would be practically impossible. He pointed out that the alternative is a case-control study.

An introduction to the N.C.E.S. may conveniently be found in the evidence of Dr. Ross, Tr. vol. 20, p. 2576, commencing at line 22, as follows:

> Q. Can you just describe for us what is a case control study?
>
> A. Yes. This is a study where an individual is recognized because something has happened to them.

> And in our case, we studied children with a serious neurological disease that had presented to a paediatrician. So these were the cases: children with serious neurological diseases. And the controls are two children -- and in our case, we decided to have children of the same health district, of the same sex, and born either on the same day or the next child afterwards.
>
> So they were controls. And so we have cases and controls.
>
> Children in England, Scotland and Wales who have come to hospital with a serious, acute brain illness. And for every case, two controls of the same sex, date of birth, and health district.

Thus, the National Child Encephalopathy Study.

The full genesis of that study is set out in the preliminary report, commencing at p. 79 of ex. 27, known to all as "the Blue Book'', which contains a number of reports from the Committee on Safety of Medicines and the Joint Committee on Vaccination and Immunization in the United Kingdom.

In its statement, which precedes that preliminary report, at p. 77 of "the Blue Book", the Joint Committee made the following cautious general conclusion which, it should be pointed out, referred to the preliminary N.C.E.S. study which included only the first 1,000 cases analyzed because of government pressure for an early report:

> IV.4. Serious neurological illnesses of the kind studied in the NCES are very rare events and brain damage resulting from them is even rarer. In the great majority of the children reported to the Study the onset of their illness had no close time relationship to immunization making a causal relationship unlikely. During the 3 years of the NCES, from the 1000 cases analysed a total of 35 children were found whose illness began within 7 days of immunization with triple vaccine (DTP). Three of these children were known to have had neurological problems previously, leaving 32 who were

apparently healthy at the time they were immunized. Most of these children when examined about a year later appeared to be completely recovered and were developing normally. Some of them probably contracted their illness due to one of the many other causes of such illness. As in previous reports it was not possible to identify a distinctive pattern of clinical features associated with whooping cough vaccine. However, having taken into account the possibility of chance association between immunization and onset of illness due to other causes, the results of the NCES confirm that their appears to be a very small risk of serious neurological reactions occurring within 7 days of immunization with DTP. It can be calculated that these reactions following DTP may occur after about 1 in 110,000 injections. Serious neurological illness can occasionally lead to brain damage and a few of these children, as with some of those whose illnesses were not associated with DTP, did show evidence of sequelae, but the rate at which this occurred was only about 1 in 310,000 injections. An estimated risk rate to a child given a full course of 3 injections might be of the order of 1 in 100,000.

The report itself, in Chapter 3, outlines the choice of study design available, describing the cohort approach and the case-control approach, the latter being described thus at p. 97:

(b) The case-control approach.

The case-control approach involves the collection of a series of individuals with a particular disease and comparing their history of exposure to the suspected agent with that of an appropriately selected group of individuals who do not have the disease.

Then follows a number of particulars which it is stated must be rigorously defined. The report goes on, still at p. 97:

The case-control method has the advantage of simplicity and speed. Its main disadvantage is that unknown factors related to the way in which controls are selected may influence their likelihood of being exposed to risk. For this reason the

> results of case-control studies must be interpreted with caution and their significance considered in the light of all relevant information. However, this was considered to be the only practical approach to the question of the suspected causal role of pertussis immunization in serious neurological illnesses.

Chapter 5 of the report outlines the method adopted, as does the report of Dr. Ross, ex. 69-2, at pp. 17-20. The cases were made up of the total of all children between the ages of 2 and 36 months admitted to hospital under the care of paediatricians, infectious disease physicians or neurosurgeons, as reported by the physicians in accordance with the guide-lines set out as Appendix 5 to the report at p. 157 of the Blue Book. They were instructed to notify the study of all possible cases of acute or sub-acute encephalitis/ encephalomyelitis/encephalopathy, defined as indicated earlier in these reasons, all unexplained cases of loss of consciousness, convulsions with a total duration of more than about one-half hour, or followed by coma lasting for two hours or more, or followed by paralysis or other neurological signs not previously present, lasting 24 hours or more, infantile spasms (West's syndrome), or Reye's syndrome (acute encephalopathy with abnormal liver function tests).

After the definitions of encephalitis and encephalopathy were given, the form sent to the doctors indicated that:

> ... the clinical features of both types of illness may include altered level of consciousness; confusion; irritability; changes in behaviour; screaming attacks; neck stiffness; convulsions; visual, auditory and speech disturbances; motor and sensory deficit.

To try to avoid overlooking any case, every participating clinician was sent a monthly reminder requesting the return of a card confirming that all children admitted under his care, who were suitable for inclusion in the study, had been notified (to the study) or that there had been no suitable case admitted during the preceding month.

The clinician responsible for a notified case, if the case appeared to satisfy the study criteria, was sent a clinical questionnaire on which to record the child's past history and clinical condition on admission, the results of investigations, and the clinical progress or condition of the patient on discharge or 15 days after admissions, whichever was sooner. Other steps were taken to ensure, so far as possible, that all cases that met the criteria within England, Scotland and Wales, were included in the study.

To eliminate possible variations in reporting practice, and in the method of assigning a date to the onset of illness, all case reports and clinical histories were reviewed by an epidemiologist and a paediatrician who, together, assigned for each case a date of onset which took account of all available information. The onset of illness was taken to be the date on which acute neurological symptoms or signs related to the current illness first developed.

The cases were divided into four categories: those apparently neurologically normal before the onset of the illness that had led to their admission who had, (a) complete clinical recovery or, (b) evidence of neurological damage; and those who had shown evidence of neurological abnormality before onset of the illness leading to their admission, and who showed, (c) no clinical deterioration or, (d) evidence of further neurological damage at the time of their assessment.

The initial report supplied by the hospital doctor was used to assess the neurological status of the case before the onset of illness and a child was considered to have been neurologically abnormal if there had been reported the presence of congenital defects with central nervous system involvement, a past history of non-febrile convulsions, neurological problems persisting beyond the first month of life, or retarded motor and/or intellectual development.

The eventual neurological condition was determined by a series of steps involving an assessment by the hospital doctor and, subsequently, either by postal inquiries or by a personal visit from a paediatrician member of the study team. The

hospital doctor recorded the apparent neurological condition of the child at 15 days after admission, or at discharge, under certain defined headings. Children who were reported not to show any of the symptoms or signs so defined after 15 days or at discharge were classed as "non-residual" and an inquiry about the progress of that child was sent to the relevant consultant and to the general practitioner concerned after one month, six months and one year following admission.

The group of children who did show any of the defined symptoms after 15 days or on discharge were classified as "residual" cases. It was presumed that such a group would include most of those likely to have suffered irreversible neurological damage and, in addition, all children with West's syndrome were included in the residual group because of the known poor prognosis and extended natural history of infantile spasms. (Blue Book, pp. 103-4.)

A control group was selected in such a way as to make their chances of exposure to the factor being investigated (pertussis immunization) as similar to that of the cases as possible. Difficulty was found with the idea of matching controls with cases, and it was decided that, under the circumstances, control children selected from the local community would be the most appropriate group for comparison. A specified community health officer for the area in which each case lived was requested to select two controls of the same sex, either by taking the names of the next two children of the same sex as the case from the current immunization register, whose dates of birth were within one calendar month on either side of the birth date of the case, or, if that child had moved away from the area or had died, the next identified child on the register. (Blue Book, Appendix V.C., p. 159.)

The study group then obtained the immunization history of each case and of each control, both from the appropriate community medicine officer and from the child's general practitioner, if any, so as to cover any source which might have been expected to administer immunization doses to these children. The requested information included the date of each immunization, the type of vaccine given, the name of the

manufacturer and the batch number.

Approximately 1,180 of the children reported were assessed as "cases" under the study criteria. As information on the eventual condition and other data for some of the children was not complete at the time of analysis, and government pressure for a report was strong, the report in the Blue Book is concerned with only the first 1,000 cases accepted for the study.

Results of the N.C.E.S.

The N.C.E.S., in the section headed "Summary and Conclusions", of the preliminary report, makes the following statements, among others:

> Thirty-five case children had been immunized with DTP vaccine within 7 days before onset of acute neurological illness. By comparison with controls, cases showed a statistically significant increased risk of having received DTP vaccine within 7 days before the onset of their illnesses. The risk was greatest within 72 hours and in those with convulsions or encephalopathy. Analysis of the clinical findings did not reveal any characteristic illness associated with DTP vaccine that was not frequently found in unimmunized children.
>
> Of the 35 DTP vaccine-associated cases, 32 were regarded as neurologically normal before their illnesses, and 21 of these recovered completely. There were only nine cases (3 with minor defects and 6 with major defects) in which no alternative explanation for their condition was found.
>
> The estimated attributable risk was one in 110,000 immunizations for previously normal children irrespective of eventual clinical outcome, and 1 in 310,000 for those with evidence of subsequent neurological damage. These figures must be interpreted with caution owing to the nature of the underlying assumptions and the breadth of the confidence limits attached to them. [p. 148, para. V(VIII) 7.]

In para. V(VIII) 11 on p. 149 is found the following:

It is concluded that --

(a) Most cases of acute and potentially damaging neurological illness in early childhood are attributable to causes other than immunization.

(b) Such illnesses occur more frequently within 7 days, and particularly within 72 hours, after DTP vaccine and within 7 to 14 days after measles vaccine than would be expected by chance. Most affected children made a complete recovery.

(c) Taking account of possible alternative explanations of the clinical findings in cases associated with DTP, and of the fact that similar cases occur after DT vaccine, it seems likely that permanent damage as a result of pertussis immunization is a very rare event and attribution of a cause in individual cases is precarious.

In considering the report contained in the Blue Book, it must be borne in mind that it is a preliminary report concerned only with the first one thousand cases studied. No final report has ever been produced, although two papers attributed to one or more of the authors of the N.C.E.S. have appeared and have modified in part the Blue Book report. In 1984, a paper was presented to the Fourth International Symposium on Pertussis at Geneva, Switzerland, and that paper is reproduced as published in ex. 69-3, "Pertussis Vaccine and Whooping Cough as Risk Factors in Acute Neurological Illness and Death in Young Children" by D. Miller and others. At p. 392 of that report is found Table IV, "Risks of Vaccination with DTP". Section (b) of that table indicates that in the entire study seven, or 2.9%, of all cases of previously normal children had died or were neurologically impaired after 12 months from onset. Of the controls, three children, or 0.6%, were deceased or impaired. The table indicates that this shows a relative risk of 4.7 within a 95% confidence interval of 1.1 to 28.0 and an attributable risk of 1:330,000 with a 95% confidence interval of 1/18 million -- 1/50,000.

Something more will be said about the confidence intervals

below.

Obviously, the figures and the results continued to be debated by interested members of the profession, and in January, 1986, the Archives of Disease in Childhood published a letter from Dr. Ross and Dr. Miller which indicates a number of useful things. It first states that, with reference to the 1,000 children analyzed in the preliminary report, the addition of the extra 182 subsequently included did not materially alter the findings. The letter goes on as follows:

> Our analysis included all children without regard to any alternative explanation apart from pertussis immunisation. This epidemiologically essential approach is not always understood and has led some to believe that the study shows the risks of pertussis vaccine to be greater than they are. It has also been suggested that our estimate of risk is too low due to bias in case reporting, but, as explained in our report, this is unlikely to have materially affected the results.
>
> We reported two types of risk estimate:
>
> (a) Relative risk. There was a small but significant excess risk of children having had DTP vaccine in the seven days before onset of a serious neurological disorder. Most of this excess was in the first 72 hours. Furtunately, most recovered quickly and were apparently normal when followed up at least a year later. No recognisable "post pertussis immunisation syndrome" was found.
>
> (b) Attributable risk. The attributable risk of these events was about one in 140,000, but the central estimate of risk of death or permanent damage comes to around one in a third of a million doses of DTP vaccine in children who were assumed (but not proved) to have been previously fit neurologically. We stress that this figure must be interpreted with caution because the 95% confidence limits are very wide and it assumes all relevant cases were notified. In fact it is based on only seven children found in a three year period. Of these seven, two died, one with

Reye's syndrome and one with an overwhelming viral infection. One child with major defects had Coxsackie B5 virus isolated from the CSF, which could have been the cause of illness. This leaves four children, only one of whom was severely handicapped when last seen, with no alternative explanation for their illness. The real cause of the handicap in these children remains in question -- was it a reaction to vaccine or did they have some other undiagnosed problem? It must be remembered that pertussis immunisation is given at the very age when children are most likely to manifest serious neurological disorders. In the circumstances it is clearly unwise to attribute a causal connection in individual cases.

Our view remains, therefore, that the risk of death or brain damage attributable to pertussis vaccine, if it occurs at all, is a very rare event and far less than the risk of death or damage due to whooping cough.

Commencing at Tr. vol. 20, p. 2591, line 30, Dr. Ross discussed the N.C.E.S. report with reference to his report, ex. 69-2, and the two papers mentioned above. He indicated that that exhibit and the two papers mentioned are on the basis of the full count of 1,182 children rather than the 1,000 contained in the preliminary report. At p. 2600, line 17, Dr. Ross agreed that the attributable risk figure of one in 330,000 given in Table IV (b) at p. 292 of the Geneva report, is the most up-to-date attributable risk figure that has been published.

Dr. Ross went on in his evidence to explain that the attributable risk of one in 140,000 refers to all cases, that is, all children admitted to hospital with the type of neurological disease or damage referred to in the notice sent to British consultants, and the figure of one in 330,000 refers to the small group who were dead or neurologically impaired after 12 months.

He went on to indicate that the seven children with lasting problems must remain in the analysis because that is how the study came out. But he stressed that follow-up work is still being done and "... it is important that it is understood that

among those seven children, at least half have good logical alternative explanations for their disorders". And, at p. 2605, line 6, Dr. Ross testified:

> So, out of this enormous study for three years, we find four children with serious problems and no virus or no other explanation.
>
> And of those four, only one is very seriously damaged. Only one is really grossly backward.

Dr. Ross proceeded further to point out that there have been many improvements in diagnostic technique in the years since 1979, and if it were possible to examine these children today other causes might be assigned for their condition. He stated further, at p. 2606, line 25, that:

> We, at the time -- it is impossible, in the light of the encephalopathy study, to really make a confident statement that there is a brain-damaging problem that can be attributed to whooping cough vaccine.
>
> The fact that we found this small number of children with time-associated problems does not make convincing causal evidence; and as we've seen, the more these children were looked at, the fewer that had no alternative explanation.
>
> I base this both from this study -- but I think just as powerfully from my everyday work as a clinician as well.

Dr. Ross testified that he would like his final word on the subject to be considered as that with which he and Dr. Miller concluded the published letter of January, 1986, namely:

> Our view remains ... that the risk of death or brain damage attributable to pertussis vaccine, if it occurs at all, is a very rare event and far less than the risk of death or damage due to whooping cough.

As already indicated, virtually all the experts who testified on the subject were in agreement that the N.C.E.S. was regarded

as the most complete and accurate study with respect to attributable risk that has been done. Nevertheless, there was criticism from a number of sources. These criticisms must be examined.

Dr. Geier, at p. 3023 of Tr. vol. 24, stated that the study was "... done backwards". He describes this as the opposite way of looking at the problem to that in which many of the early studies had been done. However, contrary to what first appeared to be the case, this does not seem to be a criticism by Dr. Geier. He explained himself by saying:

> Of those who reported encephalopathy, the first one thousand that were reported in the British Registry, we were then going to go back and look and see how many of these had DTP shots. It's the opposite way of looking at it.
>
> Both studies are prospective, in the sense the data was begun before the studies were collected. You say, "let's see, of the first thousand children that have brain damage in England let's see what the odds were that they had a DTP in the close proximity to the report," rather than, "let's look at all the children who had DTP and see how many of them had encephalopathy".

It would appear that what Dr. Geier is really doing is comparing a prospective case-control study to a cohort study. No one questions that a cohort study is regarded as a better method, but, as several witnesses testified, the enormous numbers and the length of time required can make the method impractical.

Dr. Geier does claim support for the view that DTP can and does cause encephalopathies in the report, or at least in the condensed version of it published in the British Medical Journal in May of 1981, found as ex. 73(i). He accepts the relative risk figure given as 2.4 and he stresses the P value of 0.001, making it a probability of less than one in a thousand that the relative risk figure is wrong.

Dr. Geier believes that there is general agreement among

knowledgeable people that the N.C.E.S. shows that encephalopathies are related to DTP.

Dr. Ross, one of the authors of the study, acknowledged some potential sources of bias in it. One of these may be what Dr. MacRae would call inclusion bias or notification bias. It was likely that the doctors who were asked to notify the study of cases were fully aware of the purpose of the study if for no other reason than the fact that the notepaper on which they received notice of the study had on it, "A Study of Serious Neurological Disease and Immunization". The result might well be that doctors readily notified the study of children whose problems were time-associated with vaccine and may have been a little slower to notify children with the neurological conditions specified for the study but who had not recently been vaccinated.

Dr. Ross acknowledged severe criticism by one paediatric neurologist because she had become aware of a number of cases that were time-associated with the vaccine that should have been notified and were not.

Dr. Pollock also considered that there might well have been notification or selective bias in the study because of his experience in connection with his own study, referred to already as the Northwest Thames Study. He found that, when physicians were asked to report serious or unusual reactions which followed the administration of DTP or DT, reports of convulsions in temporal relation to DTP and to DT began to come in and there were many more reported in relation to DTP than to DT. Thus, it appeared that DTP was causing many more convulsions than was DT.

As time passed, however, Dr. Pollock and his associates discovered by other means that there was serious under-reporting of convulsions associated with DT, far fewer than would have been expected even by chance alone.

Dr. Pollock hypothesized that because there had been so much media reporting of DTP as causing problems, any cases in which trouble developed which were temporally associated with DTP

were reported even though a large number of them had conditions readily attributable to some other cause. The Pollock group therefore arranged to obtain the computer record of all children who had entered hospital with any condition that might ever have related in any way to DTP immunization. From a study of these records, Dr. Pollock testified (Tr. vol. 22, p. 2845) that:

> We found that, in contrast of what we had found earlier from doctors reporting, that using this objective way, we found that febrile convulsions were just as common after diphtheria-tetanus-pertussis as after diphtheria-tetanus. There was virtually no difference between them.
>
> And we also found that with the serious neurological disorders, we found just the same numbers turning up in DTP and the DT -- as in the DT group.

They found that every case of a serious neurological condition after DTP which had been found by the computer search had already been reported by the voluntary system, but in contrast none of the children found from the computer search to have brain disorders in temporal relation to DT vaccine had been reported.

Dr. Pollock concluded that physicians, like everyone else, tend to see only what they expect to see and that a voluntary reporting system will contain serious flaws if the reporters are aware of what is being looked for.

Bias

The report by Doctors Pollock and Morris of the Northwest Thames Study became ex. 69-8 before me. Much of what I have been saying about it is found in the summary at the commencement of that article, as follows:

> Voluntary reporting of vaccine reactions was intensified in a single large region for seven years. Anaphylaxis and collapse, convulsion, and neurological disorder were reported most frequently after diphtheria/tenatus/pertussis (DTP). The

> greater frequency of recorded reactions after DTP than after DT could have been due to bias caused by the adverse publicity accorded to pertussis vaccine, since no major difference was found when the immunization histories of children admitted to hospital with such conditions were compared. No convincing evidence that DTP caused major neurological damage emerged from this large and lengthy study.

I add in passing that the study ran from January, 1975 to December, 1981, during which time approximately 134,700 children completed three doses of DTP vaccine and 133,500 children completed courses of DT vaccine.

The purpose of mentioning the Northwest Thames report in some detail is simply in recognition of the fact that Dr. Pollock had considerable experience with case reporting before he undertook to give an opinion about the N.C.E.S. Dr. Pollock's criticism of the N.C.E.S. was mainly that it did not eliminate bias as a factor reducing the validity of the results. As with the Northwest Thames Study, it was a fact that the medical profession in Britain, because of media prominence given to the issue and the well-known conclusions reached by such studies as Byers and Moll and Kulenkampff, were conditioned to believe that DTP did, on occasion, cause serious neurological disorders. Hence they were quick to report cases where such disorders occurred in a temporal association with DTP but not when they followed DT. It was known at the time that many of the milder sorts of reaction did in fact follow DT with the same frequency as those that followed DTP.

Incidentally, the Hertfordshire Study (ex. 69-9) went to greater lengths to eliminate the possibility of bias, and in passing it is interesting that that study detected virtually no difference with respect to the rare, serious neurological disorders in the DTP group of children as compared to the DT group.

Dr. Pollock also indicated a possible bias by virtue of the need to assess the children in the N.C.E.S. The classification was carried out for each case in the N.C.E.S. by one

individual, Dr. Bellman, and Dr. Pollock was of the view that the tendency of Dr. Bellman, and others involved in conducting the study, was to err on the side of including doubtful cases if difficulty in classification existed.

The latter suspicion is supported by the evidence of Dr. Ross at Tr. vol. 21, p. 2714, where he stated:

> But we did, the whole time, try and make a "worst case" estimate, so that -- I mean, that it is highly likely that the [NCES] study will be biased towards children with problems time-associated with vaccine, knowing the ways of human nature.

In Dr. Pollock's view, the biases that in all likelihood operated in the N.C.E.S. were all in such a direction as to overstate the risk of vaccination.

It is interesting that Dr. Ross acknowledges that Dr. Pollock's criticisms were justified because Dr. Pollock had done an independent survey where he found, as we have discussed, that if one looks at notifications by doctors one obtains a figure, but if one goes directly to computerized hospital admission diagnoses quite different reasons for admission may be obtained.

As we have indicated, Dr. Mortimer is an eminent paediatrician who has held many important appointments, including that of director of the department of paediatrics at Cleveland Metropolitan Hospital, and he is presently vice-chairman of the department of epidemiology and bio-statistics at Case Western School of Medicine, Cleveland, with privileges at the University Hospitals of Cleveland and Cleveland Metropolitan General Hospital. Dr. Mortimer has done a good deal of work in the field of epidemiology, both as a professor and consultant to the United States Government, as well as to private organizations.

At Tr. vol. 31, p. 4035, he stated that, although he continues as professor of paediatrics and sees patients both in the out-patient and the in-patient divisions of two Cleveland

hospitals, his "... primary appointment is not paediatrics any more; it is epidemiology. I changed careers so to speak in 1975." He is president-elect of the American Epidemiological Society. He has been asked by the American Academy of Paediatrics, which is responsible for making recommendations to paediatricians regarding the control of infectious disease in children, to assist in the preparation of what is known as the Red Book. This is a publication containing systematic recommendations for the control of disease, including immunization, quarantine and treatment. He has reviewed and updated the most recent chapter on whooping cough (pertussis) and several other diseases. The Red Book is distributed throughout the western hemisphere to all members of the American Academy of Paediatrics and it is available for purchase by others.

That portion of the 1977 edition of the Red Book is found as tab 3 of ex. 101-A.

Dr. Mortimer expressed very concisely, on p. 8 of his report, ex. 100(A), his view that, "... pertussis vaccine does not cause acute encephalopathy with permanent brain damage or, if it does, such occurs sufficiently infrequently to be immeasurable". Perhaps the first three of the reasons he gives for this opinion are most valuable as illustrating his criticism of the results of the N.C.E.S.

> First, although British physicians have a far better understanding of the requirements of epidemiologic studies than do U.S. physicians, there is a strong possibility that children with acute encephalopathy were more apt to be referred to the study if there was a history of pertussis vaccine administration than if there was not. [Dr. MacRae's "admission bias".]
>
> Second, there is clear evidence in the NCES that some of the unfortunate illnesses in these children represented inevitable manifestations of pre-existing disorders and that pertussis vaccine, probably because of its well-known systemic effects, either attracted the parents' attention to these symptoms or brought them forward in time. Third, the

data indicate that there was an elevated risk of these symptoms following diphtheria and tetanus toxoids without pertussis vaccine.

We come next to Dr. MacRae's opinion, but before doing so it is useful to refer to p. 7 of Dr. Mortimer's report, as it ties in with the considerations that concern Dr. MacRae and because Dr. Mortimer's experience in epidemiology makes him one of the few witnesses qualified to comment on the statistical aspect of these studies.

On p. 7 of Dr. Mortimer's report is found the following:

> In the United Kingdom during the years 1978-1979, a complex nationwide study was undertaken to try to determine the frequency with which pertussis vaccine produced permanent brain damage. This is the only study of its kind, and in my view probably could only be done in the United Kingdom because of the organization of its health care system. It is this study that produced the now-familiar estimate that pertussis vaccine induces permanent brain damage in previously normal children once per 330,000 doses. However, because the number of possibly affected children was only seven, the so-called 95% confidence interval is one in 50,000 to one in 18,000,000, which simply means that it is 95% probable that, if the study were extended to include tens of millions of children, the true risk would be somewhere in that range.

With respect to his criticisms of the report generally, Dr. Mortimer expressed the same views in his evidence, as shown in Tr. vol. 31, commencing at p. 4145, as follows:

Q. Could you please explain to us your reasons, following the sequence set out in the report?

A. All right.

The first reason is that the people who conducted the study were dependent upon learning about every child in Britain, during the period of the study, who had an acute brain disorder

as defined in the study, of unknown explanation, or that was not immediately evident in terms of causation.

> The study was widely publicized in Britain, and I think it was known that it had to do with the question of brain damage from pertussis vaccine.

> Accordingly, as sophisticated as the British physicians are -- I think they're more sophisticated than those in the U.S., in the main -- I think it would be quite understandable if some physicians, when such a child came to their attention, were more likely to refer the child to the study personnel -- in other words, were more likely to notify the people involved with the study that, "I have a candidate child for the study" if that child had received whooping cough vaccine than if the child had not.

Dr. Mortimer went on to say that the N.C.E.S. also indicates that there appears to be an increased risk following diphtheria and tetanus toxoids without pertussis vaccine, even though the increase is not sufficient to be statistically significant. That fact alone might make one say that when there is an increase following DTP and also one following DT possibly some of the risk attributable to the pertussis vaccine might have been due to the diphtheria or the tetanus.

After reviewing other aspects of the study Dr. Mortimer concluded this part of the discussion on p. 4147 at line 24 as follows:

> For these reasons, I, and many of my colleagues, have developed increasing doubts as to whether the National Childhood Encephalopathy Study does indeed show that there truly is a risk of permanent brain damage from pertussis vaccine.

Dr. Kenneth MacRae has already been referred to with respect to some of the general principles of epidemiology. Dr. MacRae is critical of the N.C.E.S., in which he participated, not so much from the point of view of the study design, although he does emphasize biases which he finds inherent in the study, as

from the point of view of its statistical significance, given not only the originally small number of unexplained cases but the reduction of that number to the even smaller total of four, as found by the subsequent investigations. To state his conclusion at the outset, Dr. MacRae was asked for his opinion, as a statistician, with respect to the association, if any, between DTP vaccine and serious permanent brain damage or death, as drawn from his examination of the study. In Tr. vol. 38, p. 5040, line 28, he gave it quite unequivocally in these terms:

> I think the study shows no statistical association between DTP immunization and brain damage or death.

He was subsequently examined and cross-examined in detail respecting his reasons.

In dealing with the study, Dr. MacRae dealt first with the selection of cases. And at p. 5066 he indicated that there were 1,600 odd children notified by doctors to the study, but the study team decided that 1,182 actually met the guide-lines of the study. As we know, the initial report was confined to the first 1,000 of these children. As pointed out on p. 5067, with an annual birth rate of 600,000 and a duration of the study of almost three years, the target population from which those relatively few cases were drawn was approximately 5.4 million child years over the period.

Explaining the selection of controls, Dr. MacRae pointed out that what was done was to put together a notified case and two controls, selected from the general population in the way indicated in the study, and then determine whether any of those three had been vaccinated.

Dr. MacRae analyzed the selection process, pointing out that the mere requirement of admission to hospital under the classifications described in the study may not be an entirely reliable method of catching all the serious cases; a bias which he calls "Berkson's bias" may exist, meaning a possibility of differences between children admitted and children who were not admitted, stemming from such things as extraordinary parental

anxiety, or the lack of such, or a previous relationship with the local health care facilities, or the lack of such. Thus, the children admitted to hospital may not be a totally typical random sample of the population. However, he did not consider Berkson's bias to be a major consideration in the N.C.E.S.

Dr. MacRae pointed out at pp. 5075-6 that what has already been described as admission bias may have existed, stemming from the fact that the study was undertaken at a time when there was widespread concern about the allegedly harmful effect of pertussis vaccine and that even the heading on the study's notepaper could well lead doctors to be more ready to notify inoculated children rather than those who had not been inoculated. He lists also the "exposure suspicion bias" and the "diagnostic suspicion bias", both of which cause problems of objectivity when one is attempting to collect cases in a scientific way.

Dr. MacRae pointed out in his report, commencing at p. 32, that although the guide-lines stated that all possible cases fulfilling an entry criterion should be notified to the study, Table V.3 (p. 110) of the report shows a substantial variation in numbers of cases and in the notification rate per year across the various health regions of Great Britain. He pointed out that there is considerable variation in the notification rate and in the sorts of cases actually notified from the various regions, and he suggested that this implies selectivity and incompleteness of notification in at least some of the health centres. It is thus likely that clinicians were selecting cases for notification in different ways and this may reflect a bias based on the knowledge or suspicion that the respective cases had been recently vaccinated.

Dr. MacRae also pointed out that there are reasons why the controls selected, remembering that this was done by local doctors throughout the country, may not have been fully representative and the proportion of immunized in the controls might be a little bit low.

Dr. MacRae, at p. 5082, discussed something he calls "retrospective recall bias". Though the name may not be

familiar, the concept is one with which all judges are familiar because of the length of time that may elapse between the happening of an event being described by a witness and the date of trial or description.

Dr. MacRae pointed to the Blue Book itself, at p. 102, as recognizing this problem, in the following terms:

> Even when the onset of illness was apparently acute, the significance of possibly minor prodromal events was sometimes in doubt, and in these circumstances assignment of a clear date of onset could be difficult. It was apparent that clinicians were not consistent in their interpretation of the histories in such cases, and this presented the NCES with a serious problem.

For purposes of the study, it was necessary to assign a date when a child was vaccinated and also to recall when the child started to become ill. Either or both of these events could be months or years before the study which asked for the assignment of date. He pointed out that, even though the study recognized this problem and tried to solve it by having an epidemiologist and a paediatrician member of the team assign for each case a date of onset, those experts were nevertheless dependent on the history that was given them by the doctors and the parents of the child cases.

Summarizing the opinions of the experts who testified with respect to the N.C.E.S. report, therefore, leaving aside for the moment the question of the confidence factor, all are agreed that, although the study was designed with great care and was by a long way the most exhaustive and systematic study that has been done, it is impossible to be confident that bias has been removed and the operation of chance eliminated. In Chapter 3 of the report, Blue Book p. 99, the authors acknowledge that any estimates of attributable risk "... should be interpreted with considerable caution". In their summary at p. 149, the authors state that:

> These figures must be interpreted with caution owing to the nature of the underlying assumptions and the breadth of the

confidence limits attached to them.

The final statement in the preliminary report at p. 149, is that:

> Taking account of possible alternative explanations of the clinical findings in cases associated with DTP and of the fact that similar cases occur after DT vaccine, it seems likely that permanent damage as a result of pertussis immunization is a very rare event and attribution of a cause in individual cases is precarious.

In making his analysis, Dr. MacRae made considerable reference to the two subsequent documents already mentioned, the article by Miller et al., at the Fourth International Symposium on Pertussis meeting in Geneva in 1984, and the letter from Doctors Ross and Miller, published in the Archives of Disease in Childhood in January 1986, exs. 69-3 and 69-4 respectively. As both articles make clear, the calculations of attributable risk and the conclusions of the study were based on a total of seven cases found in a three-year period. Looking, for convenience, at Table IV(b), on p. 392 of the symposium paper, ex. 69-3, the relative risk is given as 4.7 and the attributable risk as one in 330,000, with 95% confidence intervals of one to 18,000,000 to one to 50,000; meaning, as Dr. Mortimer pointed out, that if the study were extended to include tens of millions of children the true risk would lie somewhere in that range.

However, Dr. MacRae went on to consider what happens when the cases and controls are altered, as they were in fact and as reported on by Doctors Ross and Miller in ex. 69-4. Three of the seven children died of other causes, namely, Reye's syndrome, an overwhelming viral infection, and Coxsackie B-5 virus. In the words of the letter, "[t]his leaves four children, only one of whom was severely handicapped when last seen, with no alternative explanation for their illness".

Commencing at p. 5102, line 16, Dr. MacRae examined the statistical effect of losing one or more of the original seven cases.

He indicated, first, with reference to the table given at p. 47 of his report, ex. 124-2, that the effect of losing one case brings the attributable risk to one in 330,000 with 95% confidence interval of one to 2 billion, 800 million to one to 62,000 "... just totally unmeasurable", in Dr. MacRae's words.

With the loss of two cases the relative risk is reduced to 3.33 with the 95% confidence interval being 0.8 to 18.42 -- the lower limit is less than one and therefore is of no statistical significance.

Following p. 48, Dr. MacRae set out a series of figures indicating the relative risk and the 95% confidence interval with different combinations of cases and controls.

On p. 1 of the pages of tables, it is indicated that four cases and three controls, as reported in the Ross-Miller letter, gives a relative risk of 2.67 with 95% confidence interval of 0.60 to 14.90.

Dr. MacRae also performed calculations when testifying and this sheet became ex. 126. I quote from his evidence at Tr. vol. 39, p. 5105, commencing at line 24:

> Yes, what I've taken is four cases and three controls, where the relative risk is 2.67 -- that is 8, 4 times 2, divided by 3. That gives an attributable risk of one in 446,676.
>
> And the 95% confidence limits are from minus 2.9 million, if I can put it that way, to 93,995.
>
> And the minus means that it is possible that the vaccine reduces the risk of brain damage by this amount, by one in about 2.9 million vaccinations.
>
> Now, clearly these numbers are extremely low rates of anything, but it is possible that the data could have arisen from a vaccine which is actually protective.

Referring then to ex. 125, and to the N.C.E.S., he went on as

follows:

Yes, section A. The absolute risk is that one in a million children will develop brain damage in any one week.

Q. All right.

A. So -- regardless of exposure to anything, but the background rate is one in a million per week.

So it would be about 50 per million per year is the background rate, as estimated from the NCES's figures.

Q. And then how would that relate to those confidence limits that you have just calculated on 126?

A. Well what it does is, it shows that such a tiny rate as this, that to estimate rates of one in 446,000 or one in 2.9 million --

Q. Negative.

A. -- a negative rate -- from just four cases and three controls, is an extremely precarious exercise.

That to say a vaccine has made a risk increase by a number of one in 446,000, when you just have four cases, seems to me really using numbers in a rather far fetched way.

These are extremely fragile estimates of anything.

Q. And would you, in the background calculation that you made, would you end up with something less than or in excess of one in a million, in relationship to vaccination within one week?

A. Well, actually it's just under one in a million.

Remember, I said that we had 5.4 million children, child years, in the NCES. And we have got four cases out of 5.4 million child years, which is just less than one in a

million.

Q. As opposed to three controls?

A. As opposed to three controls, yes.

So this is -- well I mean I don't want to overinterpret these figures, but this is the sort of magnitude that is entirely consistent with a background rate of approximately one in a million per week.

Q. And then if you move to one serious case --?

A. If you move to one serious case, the whole thing becomes an exercise in astronomy. But I can give you the figures if you'd like to see them.

Dr. MacRae then calculated on ex. 127 that with one case and three controls the relative risk became 0.67 and the attributable risk one in minus 3,557,667. Ninety-five per cent confidence limits became one in minus 1,255,039 to plus one in 384,889.

Going on, on p. 5108, Dr. MacRae stated:

So, it's now a protective, relative risk, and the attributable risk that this suggests is a reduction of one in about three and a half million shots of the vaccine.

And the confidence limits go from quite a strong protective effect -- well, when I say "strong" it's only one in 1.2 million, it mustn't be overstated -- to -- it's consistent also with a modest harmful effect of one in 384,889.

On pp. 5109-10 in his dialogue with counsel, Dr. MacRae stated that the calculations resulting from one case only meant that while the unvaccinated risk is one in 1.2 million the vaccinated risk would be one in 1.8 million, or a protective effect -- a slightly smaller likelihood of brain damage in the vaccinated than in the unvaccinated.

Dr. MacRae concluded his examination-in-chief, starting at p. 5120, line 27, as follows:

> It would seem to be that although one hesitates to state his positive conclusion too strongly, this study seems to show that this danger which had been suspected from case reports, when you actually look for it in a controlled objective way, inasmuch as that is possible, you don't find the problem.
>
> Q. Could you express the likelihood in percentage?
>
> A. Well I -- I would think that I would be 99% confident that this suspicion that pertussis vaccine is dangerous is -- is just a logical fallacy: post hoc ergo propter hoc.
>
> It's -- and there's no cause-effect link underlying this.

Dr. J.B.P. Stephenson was particularly emphatic in his view that the N.C.E.S. did not establish a causal relationship between DPTP and serious permanent brain damage. Indeed, he went to the extent of expressing the view that the study in fact found the opposite. He had the advantage of having access to the M.D. thesis of Dr. Bellman, a junior participant in the study who subsequently did much work with the data. The Bellman report is referred to not only in Dr. Stephenson's report, but also in some of his evidence and in that of Dr. MacRae.

Dr. Stephenson is a consultant in paediatric neurology at the Royal Hospital for Sick Children, York Hill, Glasgow, with many appointments and many publications to his credit. He readily admitted in cross-examination that he has the reputation in some quarters of being an extremist, and indeed his statement that the N.C.E.S. showed that there was no causal relationship goes well beyond what is required in the circumstances, and indeed goes beyond logical possibility. Nevertheless, Dr. Stephenson's evidence must be treated with respect and with considerable weight attached to it.

Having reviewed what I consider to be the most significant evidence relating to the N.C.E.S. and to the other studies and reports that preceded it, as well as some that followed, and

considering the very small number of cases yielded by the N.C.E.S. in relation to the large number of infant births during the relevant period, I am unable to conclude that the N.C.E.S. or any other epidemiological study to which I have been directed makes it more likely than not that the pertussis component of DTP or DPTP causes serious, permanent brain damage in infants.

The witnesses who felt that the relationship had been established had in no case participated in the study or made a thorough examination or analysis of it. The North American witnesses, on the whole, were prepared to accept the figure of one in 330,000 as a reliable estimate of risk to those who were vaccinated. Dr. Mortimer, however, freely admits that he once thought DTP caused brain damage, though rarely. He now feels "... it probably does not". (Tr. vol. 31, p. 4134.)

The figure of one in 330,000 was misunderstood by most of such witnesses as being an absolute risk. As demonstrated by Dr. MacRae, the figure was in fact one that demonstrated the excess risk to a vaccinated child and, even taking it at its face value, it represents a figure to be added to the absolute risk run by the population, regardless of vaccination status.

It is noteworthy that the witnesses from the United Kingdom who had participated in the study or who had been concerned with an analysis of the results were at one in the opinion that the published results, at least so far as attributable risk was concerned, must be treated with great reserve and do not establish a causal relationship.

Fragile as the original findings were, their significance is so diluted by the subsequent follow-up investigations that one cannot accept them as convincing evidence of causal relationship and I accept the opinions of the experts who so concluded.

The biological mechanism

Another area with respect to the causal relationship about which much evidence was led is that of the likelihood or

otherwise of a plausible biological mechanism being demonstrated. If the pertussis element in the DPTP vaccine is to cause brain damage, some mechanism must exist by which this can occur. Does the evidence demonstrate as a matter of probability such a mechanism?

In examining the plaintiffs' position I shall draw freely upon counsels' submissions and upon portions of the testimony of witnesses called by the plaintiffs in order that the case may be stated as accurately as possible.

The plaintiffs' position on this aspect was very briefly summarized at the commencement of argument at Tr. vol. 68, p. 8535 at line 14, as follows:

> And the theory of the mechanism of injury, my lord, is that endotoxin, which is contained in the whole-cell pertussis vaccine and situated in the outer wall, cell wall, of the vaccine, is released into the human body following inoculation and finds its way systematically into the human body, and more likely than not crosses the blood-brain barrier, and in consequence of that, damages brain tissue and creates an injury in the child that has been demonstrated and manifested in the infant plaintiff, Patrick Rothwell.

Much of the biological background was given by Dr. Arthur Clifford Zahalsky, a professor of immunology in the department of biological sciences, Southern Illinois University, Edwardsville, Illinois. Dr. Zahalsky received his Bachelor of Science degree in genetics from McGill University in 1952, and in 1967 he received a Ph.D. degree in microbiology from the New York University and Medical Centre, New York, N.Y. His major field of study was in the area of microbiology, particularly in protozoology.

He was, from 1971 to 1974, chairman of the faculty of biological sciences at his university, but in the latter year he was asked by other members of the faculty to resign the position and he did so. He has not taught at the university level since 1986. His principal research interest for some time was a parasite called trypanosoma. His acquaintance with DTP

vaccine and pertussis vaccine generally has been largely by literature review. In addition, he has testified in connection with a number of actions and, in the course of preparation and giving testimony, has examined documents and protocols produced by several manufacturers of pertussis vaccine.

Strictly speaking, Dr. Zahalsky is not qualified to testify as to the mechanism of encephalopathy and freely agreed with his own counsel in examination-in-chief that this was so. He did claim, in my view correctly, that he was in a position to testify as to the biologic activities of the principal pertussis toxins that would be present in the human body following immunization with pertussis.

Dr. Zahalsky's manner of testifying made him an extremely difficult witness to understand. Nevertheless, it was apparent that he spoke to a very large extent in general terms and was concerned to describe the properties and activities of these various components.

In fairness to Dr. Zahalsky, he was slow to claim that specific mechanisms did produce specific damage in the brains of children inoculated with pertussis vaccine. Instead, relying mainly on the literature in the field rather than on his own particular experience, he postulated a number of ways in which it might be possible for damage to result.

It is important to remember that the plaintiffs must prove their case and in medical and scientific matters it is not sufficient to show that a cause and effect sequence is theoretically possible. For the plaintiffs to discharge their onus they must show, on the balance of probability, that a cause and effect relationship does exist.

At p. 144 of his written submission, para. 196, counsel for the plaintiffs summarizes well the general description of the Bordetella pertussis organism given by Dr. Zahalsky in the following terms:

> The genus species name, Bordetella pertussis, identifies a gram-negative organism which is grown in a certain manner and

> which, when harvested, comprises a collection of organisms that are introduced into a vial, with the diptheria, tetanus and polio vaccine components to make up the combined product DPTP. During growth, the organism elaborates a number of substances within the cell wall, as a result of their synthesis within the organism itself. There remains some doubt as to whether a cell membrane exists under the cell wall. However, the synthesis of the components comprising the cell wall illustrates an organism that achieves densities of many billions of growth in an appropriate nutrient medium. Within the organism there is the synthetic capacity to make a host of antigens, some desirable, some undesirable, that the organism itself is capable of generating.

At para. 197, counsel goes on:

> The outer boundary of the organism contains a number of substances including: (a) hemagglutinin; (b) Endotoxin (Lipopolysaccharide); (c) Agglutinins.
>
> These molecules are produced within the organism, and form part of the matrix or structural component of the wall of the organism itself.

The last-noted quotation will be of some importance when consideration is given to the steps taken or neglected by the defendant, Connaught Laboratories, with reference to its treatment of the whole-cell pertussis bacterium it grows and the elimination or the toxoiding of those parts of the bacterium cell known to be or thought to be harmful in the live state.

To toxoid a toxic substance such as endotoxin or exotoxin is to treat it so as to remove as completely as possible its toxicity while retaining the properties of stimulating the formation of antitoxin. Such a toxoided product is known as a toxoid.

In my opinion, it is unnecessary to review in detail the specific ways in which, in Dr. Zahalsky's view, damage to the brain might result. The significance of the word "might" is not

to be overlooked as Dr. Zahalsky was unable to point specifically or categorically to any such process as having been shown to produce permanent devastating brain damage, nor was he able to point to an authority in the literature that has accepted his views.

The various theories advanced by Dr. Zahalsky were put to those of the defendants' witnesses who were qualified to comment upon them and they were able, in my opinion, to point in each case to the modifications and reservations expressed by the authors named by Dr. Zahalsky in support of his positions, and in some cases they pointed to conclusions reached by the authors opposite to those which Dr. Zahalsky professed to find.

Of the several mechanisms suggested by Dr. Zahalsky, the only one, in my opinion, that remains to any degree plausible as an agent of causation is the theory that an endotoxin is thought by some to weaken the blood-brain barrier that exists in the circulatory system within the brain; it is somehow able to attack the brain directly and cause damage, whether by itself or in a synergistic combination with exotoxin.

While the possibility that shock or a shock-like condition may be produced in such a fashion is conceded by at least some of the defendants' experts, they assert that shock that would produce disastrous permanent brain damage would be a dramatic event, calling for immediate intervention by a parent or by medical personnel.

Conclusion

While one dislikes in a case of such serious import to rely excessively upon the principle of onus, it cannot be forgotten that the onus does lie upon the plaintiffs to establish, if only by the slimmest balance of probability, that a named cause is likely. To demonstrate a possibility is not enough; probability must be established.

While there are certainly major differences in fact and not all of the evidence was the same, Lord Justice Stuart-Smith, in Loveday v. Wellcome, supra, had to decide the precise question

of causation that is before me. In dealing with the question of proof and with reference to Wilsher v. Essex Area Health Authority, [1988] 1 All E.R. 871 (H.L.), he had this to say, at p. 16 of the unreported judgment:

> In my judgment the decision [Wilsher] made it clear beyond doubt that the Court must decide as a question of fact whether the vaccine can cause permanent brain damage in young children and that the onus of doing so rests on the Plaintiff and the standard of proof is the balance of probability.

That statement accords precisely with our law, as I view it: see, for example, Buchan v. Ortho Pharmaceutical (Canada) Ltd. (1986), 54 O.R. (2d) 92, 25 D.L.R. (4th) 658, 32 B.L.R. 285 (C.A.), and Rogin v. Shannon (1986), 37 C.C.L.T. 181 (Ont. H.C.J.).

In my view, the plaintiffs have not discharged the onus of showing that it is more likely than not that the pertussis component of the DPTP vaccine can cause serious permanent brain damage. The evidence persuades me that it cannot do so.

Having, with profound regret, reached the conclusion that I have, it inevitably follows that each of the actions must be dismissed. However, while that finding is sufficient to dispose of the cases, out of respect to the thorough and voluminous evidence advanced pertaining to liability on the assumption that a causal connection could be made, and the excellence of the submissions of counsel, I shall endeavour to indicate the findings I would have made had I come to the contrary conclusion, and the reasons for such findings. Should the matter go further it is possible that such findings would lighten the task of the parties and of the court.

. . . . .

[His Lordship reviewed the evidence concerning administration of the vaccine and concluded that it was administered on the advice of Dr. Raes, who injected the first dose. The other two were given by his locum tenens Dr. Hall. Neither was negligent

but even if Dr. Hall had been, Dr. Raes would not have been vicariously liable as Dr. Hall had been exercising her own judgment in dealing with patients coming to the office. The limitations defence raised by Dr. Hall was unsuccessful since s. 47 of the Limitations Act, R.S.O. 1980, c. 240, provided that the time did not begin to run until the minor plaintiff was of full age. The Health Disciplines Act, R.S.O. 1980, c. 196, did not restrict the application of s. 47. The manufacturer's leading researchers were familiar with the literature postulating encephalopathy and grave brain damage as possible consequences of administering the vaccine and the manufacturer would have been liable in negligence for failing to warn the physician. It could not be presumed that he would have failed to discuss the possibilities with the child's mother, or at least mention them. It was not negligent in failing to manufacture the Japanese version of the vaccine since no tests had been done which would have led to its acceptance by the scientific community as superior to the product then in use.

The province reasonably relied on the federal government to license and monitor vaccines. The province's decision not to exercise the authority it had, and had at one time used, to regulate and monitor did not subject it to liability. No other province issued warnings at the time. Only one monitored drugs used. Hence no negligence could be found on the part of the ministry.

His Lordship continued:]

Damages

I come now to the assessment of damages which must be made regardless of my decisions on liability.

In addition to the evidence that has been reviewed in the course of these reasons, I have had the advantage of seeing in court and reviewing subsequently in private the video tape, ex. 8, illustrating some of the normal activities that occur in Patrick's daily life. I have also heard the testimony of Dr. Peter L. Rosenbaum and examined his two reports, dated June

10th and September 22, 1987, respectively, filed together as ex. 36. Dr. Rosenbaum is a McGill-trained physician whose internship was at the Royal Victoria Hospital in Montreal and who subsequently took two years of paediatric training at the Hospital for Sick Children, Toronto, and three years of fellowship training at the Institute of Child Health, University of London, England. He is presently a professor with the department of paediatrics at McMaster University and medical director of the cerebral palsy centre in Hamilton, director of paediatrics at the Chedoke Child and Family Centre in Hamilton, and a member of the active staff of the Chedoke Division of the Chedoke-McMaster Hospitals.

He teaches students and trainees at all levels of paediatrics and he has concentrated on developmental medicine which he describes as concern with the problems faced by children and their families when those children have development disorders, usually related to the nervous system. He further describes that activity as concern with children who have various types of brain damage or impairments in neurological function which do or may put their long-term development at risk.

Dr. Rosenbaum saw Patrick on June 10, 1987, for the purpose of assessing his current status, with special regard to the question of independence and dependency and long-term needs.

As a result of such evidence, it is apparent that Patrick is almost entirely dependent on others with respect to all activities of daily living. He cannot actually feed himself. He can to a degree bring a spoon to his mouth if it has been filled by others, although this activity involves a good many failures as well as successes.

He requires daily suppositories for bowel action and occasional enemas. He must be bathed, dressed and undressed by his mother, or perhaps another care-giver, and he requires diapers for bowel control, day and night. He is carried upstairs and downstairs, is moved from place to place in his special wheelchair, and spends his day when not resting or napping in the wheelchair or in a standing frame, one of which he possesses at home and one at school.

He is conveyed to school daily but his activities there are entirely passive and he requires constant attention.

He appears to have some hearing and there is some indication that he enjoys listening to music and other sounds conveyed through a special FM transmitter which has been acquired for him.

He has some perception of light but he is not consistently visually attentive and it is agreed that he is functionally blind.

He requires Dilantin and Rivotril several times daily for the control of seizures, and during most of the year he is given Mogadon at bedtime as a sleep-inducer.

He has very little responsiveness to his environment, other than the general response to music and noise of certain kinds, referred to above. He displays spastic quadriplegia affecting the left side of his body more than the right, with a mixture of hypotonia, i.e., floppyness of head and trunk and spasticity in his limbs.

He has a quiet, systolic heart murmur of no clinical significance, his blood pressure when last taken was 92/58 in the right arm, and the heart, lungs, abdomen and genitalia appear to be normal. Patrick's skin is clear and clean and he gives obvious signs of being well cared for.

His cerebral palsy results in limitation of passive movement at the ankles and knees, contracture at the elbows, and over-all there is a severe limitation of active purposeful movement.

Dr. Rosenbaum is of the opinion, as were other physicians who examined Patrick, that the boy will remain totally dependent with no prospect of any significant functional change from his present habits and limitations.

Patrick is at risk of pneumonia by reason of his feeding

difficulties and aspiration and his general immobility and dependency. This dependence and his limited ability to communicate with others increases the risk of his being misunderstood or ignored at a time when some illness or acute discomfort requires attention.

No physician was comfortable with an exact prognosis regarding Patrick's life expectancy, but the consensus was that he would be unlikely to live beyond the age of 25 or 30 years.

To deal first with Patrick's non-pecuniary damages, one must make the assumption that by virtue of the policy declared by the Supreme Court of Canada in Andrews v. Grand & Toy Alberta Ltd. (1978), 83 D.L.R. (3d) 452, [1978] 2 S.C.R. 229, [1978] 1 W.W.R. 577 (S.C.C.), it must be considered that the upper limit for non-pecuniary damages is the present equivalent of the sum of $100,000 in 1978. The evidence before me was that as of November, 1987, that amount would have been $199,200. A further adjustment for inflation during the subsequent year would bring it to approximately $209,000.

Submissions were made to me that I should follow the majority decision of the British Columbia Court of Appeal in Wipfli v. Britten (1984), 13 D.L.R. (4th) 169, [1984] 5 W.W.R. 385, 56 B.C.L.R. 273, where an award of $75,000, representing at that time approximately one-half of the permitted maximum, was made, apparently on the ground that the plaintiff's appreciation of his environment was limited by reasons of mental handicap. I can appreciate that a severely damaged but totally and permanently unconscious plaintiff might properly be awarded no non-pecuniary damages because he would have no pain, no suffering and no appreciation of his loss of expectation of life.

Patrick, however, has some appreciation of his environment. As stated, he has some hearing and apparently enjoys music played in such a way that he can appreciate it. He is conscious of his mother's presence and there is communication between them on a primitive basis; he appears to enjoy the presence of his sister and he takes pleasure in his bath.

In Lindal v. Lindal (1981), 129 D.L.R. (3d) 263, [1981] 2 S.C.R. 629, [1982] 1 W.W.R. 433 (S.C.C.), Dickson J. discussed at some length the principles upon which non-pecuniary damages will be given in cases of disastrous injury, and at p. 274 D.L.R., p. 643 S.C.R., is found the following:

> We award non-pecuniary damages because the money can be used to make the victim's life more bearable. The limit of $100,000 was not selected because the plaintiff could only make use of $100,000 and no more. Quite the opposite. It was selected because without it, there would be no limit to the various uses to which a plaintiff could put a fund of money.

In the present case, after compensation is given for loss of earnings and provision is made for future care, as will be dealt with, there are still ways in which money can be used to make Patrick's life more bearable, and, as suggested in the evidence of several witnesses, the chance of some improvement in Patrick's ability to communicate cannot be ruled out, neither can the development of technology that will make it simpler for him to do so. As non-pecuniary damages, therefore, I would have awarded the sum of $209,000.

As to future earnings loss, as invited by counsel I find certain assumptions that should be made and leave it to counsel to obtain the actuarial figures required.

The assumptions on which the calculations should be made start with a life expectancy of 30 remaining years. In view of the great uncertainties that exist, I feel that this assumption is fair to all parties.

The average industrial wage figure of $23,200, assumed by Mr. Siegel, makes no allowance for the possible "apprenticeship factor" proposed by Mr. Winokur. However, I feel Mr. Winokur's proposed deduction of one-half that wage for the age bracket 18 to 25 is excessive and the assumption should be made that earnings from 18 to 25 will be 75% of the A.I.W., and the average from that age on.

As to possible retirement income, for the reasons advanced by

Mr. Winokur I am persuaded that because of Patrick's young age and the scheduled increases in the contribution rate, the net present value of pension income is nil.

As to the gross-up required for taxes, I accept Mr. Winokur's assumptions of a 5% figure, based only on the statement in his report that he had the advantage of reading the presentation of the Minister of Finance made in December, 1987, subsequent to the calculations being made by Mr. Siegel.

Turning to the cost of future care, I agree generally with Ms. Soini's approach. However, a number of deletions must be made. In the first place, Ms. Soini herself agreed that there was an error made in assigning an additional figure of $2,200 for the years after 1997 and thus $4,400 must be deducted from her "initial outlay".

Next, the evidence of Dr. Blake is that the Assistive Devices Program (ADP) of the Ministry of Health would provide for a number of the devices required by Patrick, on the recommendation of Ms. Soini, in a prescribed proportion. Deductions of $6,876 and $1,294.50 should therefore be made from the medical equipment total and the equiment replacement reserve respectively estimated by Ms. Soini.

Ms. Soini's recommendations and estimate of amounts required for personal support services took no account of the fact that various benefits are now available to the family and Donna Rothwell's evidence was that she had no reason to believe that the assistance she had been receiving would not continue in the future. There is no precise evidence of the dollar value of the deductions that should be made because of the existence of such services, but in my view it would be fair to deduct 10% from the claim for personal support services, sch. 6 of ex. 41.

At present, prescription drugs are covered by benefit programmes. As there is no evidence that this practice will be discontinued, a deduction of $1,000 annually should be made with respect to sch. 5 of Ms. Soini's estimates. At present there is no evidence that Patrick would be able to use a computer and its appliances for the purpose of communication.

The amounts included in sch. 3 for these purposes will therefore have to be deducted. The contingency that such appliances might enable Patrick to derive more appreciation and pleasure from his environment is amply provided for in the award for non-pecuniary damages.

It is plain that Donna Rothwell has received a varying monthly sum, at present $225, by way of a handicapped children's benefit. In my view, this is not a source which should be used to relieve tortfeasors of an obligation they might otherwise have and no deduction will be made on this account.

As to contingencies that it would be proper to apply, on balance, in my opinion, some slight deduction should be made from the calculation of future earnings because of negative contingencies. On the other hand, with the uncertainties arising from Patrick's condition, there is the very real possibility that Donna Rothwell, whose physical and emotional condition is already cause for concern, may become unable to continue the contribution she makes to Patrick's care, and additional help may be required. On balance, therefore, there should be no deductions made for contingencies.

As to the appropriate figure to be used in calculating the present cost of future earnings and future care costs, while there is evidence that in the short term the 21/2% rate now prescribed by the rules may be too low by a considerable margin, that prescription is there and the circumstances of this case are not sufficiently novel to justify a departure from that rate.

Mrs. Rothwell claims special damages by way of expenses for articles required and services provided to Patrick to the time of trial. These total $28,051.94. Included in the total is $4,600.46 for prescription drugs. As she has been totally reimbursed for these, that amount will be deducted from her claim, which should otherwise be allowed.

Additionally, Donna Rothwell claims for an injury to her back resulting from the excessive amount of lifting she has to do in

Patrick's care, and for lost earning capacity. There would seem to be no evidence of the cause of Mrs. Rothwell's injury, although there was evidence that it exists. Similarly, there is no evidence of a loss of earning capacity, although this might almost be assumed by virtue of the many hours required for Patrick's care. To quantify such an award would be a matter of great difficulty. It is, however, a pecuniary loss, however difficult to value, and in my view it would be proper to award her a nominal sum which might well be based upon the average industrial wage, of which evidence has been given. I would have awarded Mrs. Rothwell $25,000 on this account.

As to the derivative claims of Donna and Colin Rothwell for loss of care, guidance and companionship, I would have awarded Donna Rothwell the sum of $50,000. Mr. Rothwell gave little in the way of evidence. His attachment to the family may be of a different nature from that of Donna Rothwell and his award should be less. I would have made an award to Colin Rothwell of $25,000.

A claim is made for Whitney Rothwell, a sister born after Patrick's problems had developed. In MacIsaac v. Smith (1987), 58 O.R. (2d) 289, 35 D.L.R. (4th) 451, 39 C.C.L.T. 239 (Div.Ct.), the Divisional Court found that a person claiming under a derivative cause of action must have been in existence when the cause arose. For that reason, no claim of Whitney Rothwell is sustainable. Had I been entitled to do so, I would have made an award in her favour of $25,000.

I have indicated above certain claims that I would have allowed and what guide-lines are appropriate for the computing of others. With the assistance of their actuaries, counsel may now be able to agree upon the appropriate figures if they are required to do so. I shall be available to assist in this regard if requested to do so.

All counsel requested the right to reserve their submissions on the matter of costs until my decision should be known. I am prepared to hear such submissions at the request of counsel on a date to be fixed by the registrar or, if all counsel agree, written submissions may be made.

In the result, therefore, all actions must be dismissed. Costs may be spoken to.

Reflections

I cannot leave this tragic and extremely difficult case without expressing the view, perhaps unbecoming to a trial judge, that the normal process of litigation is an utterly inappropriate procedure for dealing with claims of this nature. As I hope is apparent from my judgment, the basic issue that had to be resolved was whether or not, as a matter of scientific fact, a biological substance, widely used for the purpose of protecting the health of infants from a virulent disease, was capable of causing catastrophic brain damage. Unless this could be established on a balance of probability the claim of the parents of a small, grievously handicapped child to be reimbursed for the extraordinary expenditures they have been compelled to make, and to obtain funds which might, to some degree, ameliorate the lot of their child, could not succeed.

Rightly or wrongly, I found that the actions failed and, to the already considerable burden borne by the adult plaintiffs, the strain of a long trial, the suspense of a long waiting period, and the disappointment of an unsuccessful outcome have been added. Had the actions succeeded, on the basis of my assessment and the guide-lines I indicated, judgment for something on the order of $2 million, or a little more, might have been obtained.

The expense involved in submitting to the litigation process has been inordinate. The cost of preparation, including motions, examinations for discovery and other preliminary proceedings, to say nothing of the need for counsel to educate and prepare themselves for trial, is almost impossible to estimate.

The trial itself occupied 74 days. Fifty witnesses were called, several from the United Kingdom and from the United States. Many of them testified for several days. Two hundred

and eighteen exhibits were filed, most of them documents of some substance and a good many of them consisted of several parts. A total of 9,493 pages of evidence were transcribed and the relatively new process of computer-assisted transcript was adopted. This system was of great assistance to the parties and to the court, but the bare cost of providing transcript was just under $110,000. While the names of thirteen counsel are shown in the transcript, on any given day eight or nine counsel were usually present. In addition, much use was made by counsel of support personnel, in and out of court. Assuming an average daily counsel fee of $800, no doubt a conservative figure, counsel fees alone would have amounted to $473,600. All in all, there can be no doubt that the cost of these three actions was well in excess of $1 million.

I suggest these figures, not in any way to be critical of counsel or their principals but simply as an indication of the staggering cost of trying to resolve the questions posed by this tragedy.

I have found, on the balance of probability, the test I was required to use, that there is no causal relationship between DPTP vaccine and severe permanent brain damage. It is too much to hope, however, that this decision and my judgment will set the matter to rest for all time. The slightest difference in the evidence, or a new scientific advance on any one of several fronts, or even the different intellectual make-up of a different trial judge, might easily ensure a different result. By the nature of the problem, there can be no certain or permanent answer.

In several jurisdictions, including the United Kingdom, statutory provision has been made for the recovery of compensation by persons who have suffered neurological damage in close temporal association with vaccine administration. Such a programme has been provided for in the United States, although no funding has as yet been arranged.

The administration of such schemes and the granting of awards must, of course, be in the hands of a board or some such entity. It will still be necessary to prove certain facts.

However, though I have found a causal relationship to be unlikely, there will continue to be cases in which it seems more than possible, if not likely, and there still appears to be a respectable body of medical opinion that considers a causal relationship likely, even if rare. Surely it would be worthwhile for our society to agree to a certain adequate, though not lavish, standard of compensation upon proof of prior good health, the administration of vaccine and catastrophic damage within a limited period of time. Proceedings before a tribunal established to administer such a scheme need be neither protracted nor expensive. My brother Krever in Ferguson v. Hamilton Civic Hospitals (1983), 40 O.R. (2d) 577 at pp. 618-19, 144 D.L.R. (3d) 214 at pp. 258-9, 23 C.C.L.T. 254, stated:

> I confess to a feeling of discomfort over a state of affairs, in an enlightened and compassionate society, in which a patient, who undergoes a necessary procedure and who cannot afford to bear the entire loss, through no fault of his and reposing full confidence in our system of medical care, suffers catastrophic disability but is not entitled to be compensated because of the absence of fault on the part of those involved in his care. While it may be that there is no remedy for this unfortunate and brave plaintiff and that this shortcoming should not be corrected judicially, there is, in my view, an urgent need for correction.

I end this protracted exercise by recording my whole-hearted agreement with that view.

Actions dismissed.

* * * * *

Supplementary Reasons for Judgment
Heard: May 29, 1989
Released: June 1, 1989

OSLER J.:-- Pursuant to the invitation indicated at page 513 of the reasons for judgment as reported in 66 O.R. (2d) 449, counsel attended upon me today with respect to certain

questions.

In my reasons I indicated that a life expectancy for Patrick should be the basis of certain of the calculations. To make the matter clear, with respect to the loss of future income, the standard or normal life expectancy should be used. So far as the expense of future cost of care is concerned, the assumption of a 30-year life expectancy should be employed.

With respect to the gross-up required for taxes, my reference to Mr. Winokur's assumptions of the 5% figure was to his preference for a 5% rate of inflation. It will therefore be necessary to calculate the increase required for gross-up on the basis of that finding.

I would have awarded pre-interest judgment against each defendant on the basis of the average rate of interest, to which counsel state they can agree, dating from the date of service or, with respect to the Crown, from the date notice was given.

The parties have agreed upon the disposition of costs that is appropriate.

OSLER J.