coherence in that the supposed cause appeared to be in decline while the supposed outcome, the disease itself, was on the increase.

61. For the Review Council the most important impediment to the inclusion of trauma was that the studies are usually retrospective and by recall. They are therefore open to serious bias in the results. There was also the paradox of cause and effect. It seems that it was not possible for Dr Horsley in his original submission to the Authority to convince them that the issue of temporal ambiguity had been adequately resolved nor was this Review Council persuaded.

62. The studies available relied on the gathering of histories of antecedent trauma which are not sufficiently sound scientifically. The problems of recall bias and matching of controls together with the weak association did not justify the Review Council displacing the findings of the Repatriation Medical Authority. The Review Council also found that there was little support from the perspective of "coherence". Some more definitive studies might emerge in the future but these would no doubt be considered by the Authority if brought to its attention. The Review Council found that there was no change that it would recommend to Statements of Principles Nos 245 and 246 of 1995.

The "solvent " theory

63. The material before the Authority was stronger in relation to solvents. Much of the literature referred to by Dr McCullagh was available to the Authority but his particular interpretation of the findings was not.

64. Dr McCullagh did not propose in his submission that the strength of association between organic solvents and motor neuron disease was particularly marked. He placed strong emphasis on the effect of methylphenyltetrahydropyridine (MPTP) and its relationship to the development of extrapyramidal disorders and forms of Parkinson's disease. There is no direct nexus between extrapyramidal disorders and motor neuron diseases and although Dr McCullagh drew heavily on an article by Seaton (Seaton, A (1992) "Organic Solvents and the nervous system: time for reappraisal?" *Quarterly Journal of Medicine*,, 84, 367) this article was not available either to the Authority or the Review Council. Although Dr McCullagh claimed that this article establishes aspects of consistency, temporality, exposure. biological plausibility, coherency and analogy supported by experimental data, the Review Council noted that it dealt not with the specifics of motor neuron disease but with neurological disease in general.

65. Dr Horsley provided a very useful summary of the postulated "causes" of motor neuron disease in his paper dated December 8 1995. It seemed that the Repatriation Commission, having originally argued a case for inclusion of solvents as a causal mechanism, had looked at further evidence and decided that it was:

> "still of the view that there is some evidence of a causal relationship, but would also note that the evidence is weak and accepts that the Authority may well have been correct in judging that the relationship was not truly causal."

66. Dr Horsley pointed out three biologically plausible mechanisms by which solvent exposure could result in motor neuron disease. The first of these was that organic solvents are known neurological toxins that destroy neurons leading to the clinical deficit postulated by Dr McCullagh in his written submission. The second was that organic solvents have been shown to induce inactive viruses and the third that they have been shown to have induced genetic damage (see

Hawkes CH, Cavanagh JB and Fox AJ (1989) Motorneurone Disease: a Disorder Secondary to Solvent Exposure, *Lancet,* January 14 pp73-75).

67. The Council looked for the article referred to in paragraph 66 within the materials available to it and discovered that only the first page was included. In the circumstances of this review the Review Council was of the view that the article would have been one that the Authority would have needed to consider so that reference to the whole of the article is within the meaning of "the evidence available". In this setting the suggestion of coherence suggested by Hawkes above and Gunnarsson et al. also added to the association between organic solvents and motor neuron disease (see Gunnarsson LG, Bodin L, Saderfelat B and Axelson AO (1992) A case-control study of motor neuron disease: its relations to heritability and occupational exposures, particularly solvents. *Brit J of Ind Med*, Vol 49, pp791-8).

68. The Gunnarsson study looked at the combined effect of a number of supposed factors including family history, male gender and occupational exposure. Thus the specificity of the association with solvents was not clear. Other obscure aspects related to the degree of exposure, the duration and actual substances which are collected under the term "organic solvents". Without such specifics there was great difficulty in determining whether an actual contention within a Statement of Principles could be reached.

69. Because of all of the above, this Council, was unable to say what such a contention, involving the level of exposure or the duration or the type of solvent, might be for the purposes of Instrument 245 or 246 of 1995. Without the particular evidence on the specific criteria of exposure to any solvent, a contention was not possible for either Statement of Principles.

Inability to obtain appropriate clinical management

70. The Repatriation Medical Authority included, as a factor that can contribute materially to the aggravation of motor neuron disease, the inability to obtain appropriate clinical management.

71. A Review Council, when considering the same aspect of prostate cancer, said, (SMRC Decision 95/1: "*Statements of Principles Nos 95 and 96 of 1995* (Malignant Neoplasm of the Prostate) 23 Jan 1996 p47, Commonwealth Gazette 31 January 1996;

> "As a matter of logic, if the Defence service authorities are under a duty to provide medical treatment for service personnel, and fail to do so, then if, as a result of that failure, the course of the disease progresses faster than it would have progressed had appropriate clinical management been provided, then, it must be said that the disease has been made worse by service, and the Commonwealth would be liable to pay pension."

72. It seemed to the Review Council that there was no dispute amongst those making submissions that this was an appropriate factor to be included "in accordance with generally accepted medical practice" and which "would serve as the basis for the diagnosis and management of a medical condition". The material quoted is contained within the legislation and to the review Council reflected a proper attempt to deal with the problem of diagnosis. In so doing it provides a prudent path for the consideration of what would have been "appropriate clinical management" and whether in fact a condition could have been diagnosed at the time and not simply argued for on the basis of hindsight and superior knowledge in the present day.

73. The Review Council considered that the current Statements reflect a determination that the Review Council would have made in respect of the "inability to obtain appropriate clinical

management". In reaching this view the Review Council assumed that both the Statements of Principles require that motor neuron disease must have been present during an eligible period of service, or prior to it, and that its presence should have, with normal medical prudence, been recognised and appropriate clinical management provided and that as a result of the failure to so provide, the condition was permanently worsened. This would be a rare occurrence indeed but if such circumstances existed they would certainly have contributed to the course of the disease and we would regard this as enough to be a relevant contention for both Instrument 245 and 246 of 1995.

Herbicides, insecticides, pesticides

74. Also contained within the material available to the Review Council were mentions of herbicides, insecticides and pesticides, either independently or in conjunction with each other or "solvents". Once again no submissions made to the Review Council for the purpose of this review advanced any further argument on the issue and that seemed a proper outcome. Any suggestion of a causal link was not supported by enough medical and scientific work to be sufficient to enable any reasonable person to accept the proposition. Such evidence as exists is weaker than that for solvents alone. Nor was there sufficient in the argument contained within the papers to establish that any combination of toxicides causes motor neuron disease.

75. Dr McCullagh in his written submission did not find much support for a connection to pesticides. In all he pointed to just three studies or reports and two of those involved simple Case Reports. Even the remaining article was more concerned with the solvents used in preparation of the particular insecticide that the insecticide itself.

76. The proposition was advanced in the material available to the Review Council from the RMA that paraquat ingestion causes motor neuron disease. The cases referred to all resulted in death very soon after the ingestion and the parallel with motor neuron disease has been made only because of some similar symptoms and post mortem findings. In the Review Council's view this was simply an association and not sufficient to indicate any causal link for either Instrument 245 or 246 of 1995.

Service in a particular area and slow viruses

77. A paper by Dr N. Bennett MBBS; FRACP; FRCP [Ed]; FRACMA, Specialist in Infectious diseases and dated 27/1/95 and which appeared at folio 2.7 was apparently submitted in support of a connection between service in New Guinea and motor neuron disease and possibly a slow virus infection as the agent of causation. With respect to the organisation submitting the material and to Dr Bennett it was not sufficient to argue from a previous position, in this case from Parkinson's Disease, that

> "the same evidence can be used to argue that another chronic neurological disorder, amyotrophic lateral sclerosis or motor neuron disease, can similarly, be caused by war service."

78. Dr McCullagh, in presenting material on the solvent issue, made reference to the documents available to the Authority and the Review Council in a 1994 report on a particular veteran's case. He sought to make a postulate, not on the scientific material available as to cause, but on the particular location and assumed consumption of dietary toxins from the cycad palm. Such references to individual cases did not assist the Review Council to make a judgement about

the scientific worth of the proposed cycad connection. Dr McCullagh did not make an oral submission on the matter of cycad palm as a cause for motor neuron disease.

79. Despite the fact that there was some limited information on these matters that would have been taken into account, there was no sound medical-scientific evidence, within the meaning of that term under the Act, to which the Repatriation Medical Authority or the Review Council could have responded to include any of these other proposed causes in either Statement of Principles.

Other factors

80. Contained within the material supplied to the Repatriation Medical Authority are some matters relating to other postulated causal factors. They appear to have been addressed in material supplied to the Authority by the Repatriation Commission. No discussion on the theories that **diet**, **electrical shock**, **heavy metals** such as lead and mercury, other **metals** such as aluminium and magnesium or **viral** infection occurred during these proceedings and the Review Council had no reason to view the evidence in a different manner to the Authority and therefore did not find any reason to include these as factors for either Statement of Principles.

Summary

81. After consideration of all the material the Review Council was of the view that apart from questions concerning exposure to solvents in the Statements of Principles No 245 and 246 of 1995, none of the submissions to the Review Council caused it to consider that further investigation was required in respect of any other possible or probable postulated "cause" of motor neuron disease.

EVIDENCE BEFORE THE REVIEW COUNCIL

82. The evidence that was considered by the Review Council consisted of all of the material which was available to the Repatriation Medical Authority and the written and oral submissions made to the Review Council. These materials are listed below.

83. Material supplied to the Repatriation Medical Authority as contained in the documentation includes a paper written by Dr Keith Horsley for the Repatriation Commission entitled "**Motor Neuron Disease**" and dated 13 April 1995 accompanied by the articles mentioned in the paper.

84. A submission from Mr Geoff Trevor Hunt of the Vietnam Veterans' Association of Australia (NSW Branch Inc) entitled "**Motor Neuron Disease**" and dated 25 April 1995 and a further letter that was undated but received by the RMA on 10 May 1995, containing additional material.

85. The Council also had written submissions from the Repatriation Commission dated 8 December 1995 entitled "**Motor Neurone Disease: Submission to the Specialist Medical Review Council**" and an oral presentation from Dr Keith Horsley for the Repatriation Commission.

86. The Vietnam Veterans' Association of Australia (NSW Branch Inc) provided an undated covering letter received by the Review Council on 7 December 1995 to a further submission entitled **"Submission to the Specialists Medical Review Council: Motor Neuron Disease and**

Exposure to Solvents and Insecticides". The accompanying submission is entitled "**A Hypothesis which provides the basis for an association between service with the Armed Forces and Motor Neuron Disease**" by Peter McCullagh MD, D. Phil., MRCP and dated 15 September 1995.

87. In addition to this material the RMA gathered the following articles for its own consideration:-

Gresham, Louise S, Molgaard, Craig A, Golbeck, Amanda L, Smith, Richard (1986) "Amyotrophic lateral sclerosis and heavy metal exposure: A case-control study" *Neuroepidemiology*. 1986; vol.5: pp.29-38.

Garruto, Ralph M, Yanagihara, Richard, Gajdusek, D Carleton (1988) "Models of environmentally induced neurological disease: epidemiology and etiology of amyotrophic lateral sclerosis and parkinsonism-dementia in the Western Pacific" *Environmental Chemistry and Health*. 1988; vol.12: pp.137-151.

Fonseca, R G, Resende, L A L, Silva, M D, Camargo, A (1993) "Chronic motor neuron disease possibly related to intoxication with organochlorine insecticides" *Acta Neurologica Scandinavia*. 1993; vol.88: pp.56-58.

Scottish Motor Neuron Disease research Group (1991) "The Scottish motor neuron disease register: a prospective study of adult onset motor neuron disease in Scotland. Methodology, demography and clinical features of incident cases in 1989" *Journal of Neurology, Neurosurgery, and Psychiatry*. 1992; vol.55: pp536-541.

Kurland, Leonard T, Radhakrishnan, Kurupath, Smith, Glenn E, Armon, Carmel, Nemetz, Peter N "Mechanical trauma as a risk factor in classic amyotrophic lateral sclerosis: lack of epidemiologic evidence" *Journal of the Neurological Sciences*. 1992; vol.113: pp133-143.

Garruto, Ralph M, Yase, Yoshiro (1986) "Neurodegenerative disorders of the western Pacific: the search for mechanisms of pathogenesis" *Trends in Neurosciences*. Aug, 1986: pp.368-374.

Kurland, Leonard T (1988) "Amyotrophic lateral sclerosis and Parkinson's disease complex on Guam linked to an environmental neurotoxin" *Trends in Neurosciences.* 1988; vol.11, no.2: pp.51-54.

Deapen, Dennis M, Henderson, Brian E (1986)"A case-control study of amyotrophic lateral sclerosis" *American Journal of Epidemiology*. 1986; vol.123, no.5: pp790-799.

Gresham, Louise S, Molgaard, Craig A, Golbeck, Amanda L, Smith, Richard (1987) "Amyotrophic lateral sclerosis and history of skeletal fracture: a case-control study" *Neurology*. Apr 1987; vol.37: pp.717-719.

Granieri, E, Carreras, M, Tola, R, Paolino, E, Tralli, G, Eleopra, R, Serra, G (1988) "Motor neuron disease in the province of Ferrara, Italy, in 1964-1982" *Neurology*. Oct. 1988; vol. 38: pp.1604-1607.

Armon, C, Daube, J R, O'Brien, P C, Kurland, L T, Mulder, D W (1991) "When is an apparent excess of neurologic cases epidemiologically significant?" *Neurology*. Nov.1991; vol.41: pp.1713-1718.