POST - POLIO NETWORK (NSW) INC.

# NEWSLETTER

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## Editor's Corner

Welcome to the last Newsletter for 1994. This issue contains details of our upcoming seminar entitled "Medical Acupuncture" which will be held on **Saturday 26 November** at the NSW Society for Children and Young Adults with Physical Disabilities, Parramatta. This is the venue where the August seminar (see report below) was held. Full details are on page three. We look forward to seeing you there, and hope you will stay on afterwards to join us for our traditional "bring a plate" pre-Christmas celebration.

On page two you will find brief reports on the Post Polio Support Society NZ (Inc.) National Conference held in Auckland on 23-25 September, and our own Networks' recent Fifth Anniversary Luncheon. Major articles this time focus on the polio scene in Denmark (pages 4-8) and a recent Post-Polio Conference in Bethesda, USA (pages 8-16).

**IMPORTANT NOTICE - NOTE YOUR DIARY NOW!** The first Seminar for 1995 will be held on Saturday 18 February. The topic and venue will be advised early next year.

## Seminar Report - August 1994

The "double bunger" Seminar held on 6 August was extremely well attended. First Elizabeth Hastings gave a lively and thought-provoking talk as she described her role as the Disability Discrimination Commissioner, and explained who is protected by the Disability Discrimination Act, what areas of life are covered, how a complaint is made, and what happens after a complaint is lodged. She concluded her talk with a couple of recent success stories which won significant gains for people with disabilities. Elizabeth left us a copy of her talk and I am sorry that space did not allow its inclusion this issue. It will appear in an upcoming issue.

Our second speaker was Associate Professor Simon Gandevia, who spoke of the research into the post-polio syndrome that he is doing at the Prince of Wales Medical Research Institute. He spoke about the aims of his research, why research needs to be stepped up, why the assessment of breathing muscles is an important priority, the establishment of a dedicated post-polio muscle testing laboratory and the development of new therapies. A brochure detailing the work was distributed with Issue 5 (Spring 1994) of the Information Bulletin. The Institute has now written to thank the twenty-four members of the Network who have donated a total of $950 in response to this brochure. Simon Gandevia says "We are most appreciative of this support from members of the Network. The money will go towards the purchase of specialised equipment which we need in order to establish a dedicated post-polio research laboratory". Further donations are naturally welcome. The Institute may be contacted on (02) 399 2680.

A home-made knee rug donated by Shirley Roach was raffled at the conclusion of the day's events. The raffle brought in $40 for Network funds. The rug was won by member Dr Mary Westbrook who will be known to many of you. An open invitation was then issued to those present to join the Management Committee as we gave Shirley a good send off over dinner. We've heard she has settled in quickly and is already offering her talents to a polio support group nearby. Our loss is certainly Queensland's gain.

## New Zealand Post-Polio Conference - September 1994

As foreshadowed in the last issue, President Nola Buck and I attended this important Conference. The Post-Polio Support Society (NZ) certainly did a magnificent job of organising a varied and interesting program and were rewarded with an attendance of over 200 people from both New Zealand and overseas. Nearly all the Australian State Networks were represented. As well as catching up with the latest overseas research, the Conference provided an invaluable opportunity to exchange information and ideas with Network delegates and I'm sure we all took back something. We are looking forward to improved communication between the individual Networks. More news on the Conference will follow next issue. We also brought back a set of audio tapes from the Conference for the benefit of members. A complete listing of audio and video tapes now held by the Network and available for loan will be included in the next issue of the Newsletter.

## 5th Anniversary Luncheon - October 1994

After months of planning the luncheon went ahead on 22 October. It was attended by 55 members and others from as far away as Goulburn and Tumut, and was considered by all to be a resounding success. So much so that we may not wait five years to do it again. Our guest speaker, Jack Keavney, lived up to expectations as he provided us with humorous insights into his life and tips on how to be a good public speaker. The Huntley kindly donated a dinner for two as a lucky door prize (won by Zena Graham from Tumut) and Robyn Robinson's donation of a flower arrangement and champagne also went down well with the lucky winners. A fifth anniversary cake looked (and tasted) magnificent, and table photographs together with a completed Guest Book donated by Morrie Foster made the day one to remember. Sincere thanks to all those who made the day so successful.

## Are you financial?

It's that time of year again when I go through the membership files to determine who has not yet renewed their membership. If you have a large **RED DOT** on your address label, you are **UNFINANCIAL** for the year 1 April 1994 to 31 March 1995. We hate having to delete people from the mailing list, but financially we have no choice. If you still want to receive the Network's Newsletters and Information Bulletins (eight issues in total per year), please forward your payment of $10 (employed) or $5 (not employed) to the Secretary, Post-Polio Network (NSW) Inc., PO Box 888, Kensington NSW 2033 **without delay**.

## DPI World Assembly, 3-9 December 1994, Darling Harbour

At this Assembly, people with disabilities world wide will be gathering to hear speakers on topics such as human rights violations, refugees with disabilities and aid distribution, and social, economic and cultural rights. Well-known Nobel Peace prize winner, Archbishop Desmond Tutu, will give a keynote address on Monday 5 December in the afternoon session on human rights. The Network has purchased two tickets to enable ten non-waged members to each attend one day of the Assembly. **You must contact Nola (636 6515) upon receipt of this Newsletter if you would like to participate**. It would be appreciated if each delegate would assist at the Network's display stand during breaks and also forward a report on sessions attended for the benefit of other members.

# Seminar - Saturday 26 November 1994
# Medical Acupuncture

| | | |
|---|---|---|
| **Time** | : | 1:30 p.m. - 2:30 p.m. |
| **Place** | : | The NSW Society for Children and Young Adults with Physical Disabilities<br>2 Grose Street, Parramatta<br><br>Ample parking is available in a car park at the end of the street (the venue is then a 100 metre walk away). Limited parking is available on the premises. It would be appreciated if those who are more mobile would leave this closer parking for members who are only able to walk or wheel short distances. |
| **Lunch** | : | 12:30 p.m. - 1:30 p.m.<br>Please bring your own lunch and a plate for a festive afternoon tea - tea and coffee provided. |
| **Afternoon Tea** | : | 3:00 p.m. |
| **RSVP** | : | Please phone Nola on (02) 636 6515 by 23 November. |

We are pleased to welcome renowned acupuncturist Dr Kit Sun Lau as the guest speaker at this Seminar. Dr Lau is the past President of the Australian Medical Acupuncture Society, and is currently the chief examiner for the Fellowship examination of the Society as well as the editor of the Society's Journal. Dr Lau has been lecturing and training doctors in acupuncture for the last eighteen years. At present, he is practising medical acupuncture and Chinese herbal medicine in combination with Western medicine in Macquarie Street, Sydney.

Dr Lau has first-hand knowledge treating people who are experiencing the post-polio syndrome. His talk will be illustrated with slides and the usual question and answer session will follow. This will be a Seminar you won't want to miss.

The Committee hopes you'll stay after the Seminar and chat to friends while you enjoy afternoon tea. Our pre-Christmas meeting is always a festive occasion. If this will the first Seminar you have attended, please introduce yourself to a Committee member. And remember, suggestions about Seminar topics or speakers are always welcome, as are suggestions or comments on Network activities and publications.

***Don't forget to collect your copy of the Summer edition (Issue 6) of the Information Bulletin when you arrive.***

## Support Group Report

I'm sorry I could only give Support Group Co-ordinator Suzanne Rangi a few lines this issue. Most importantly, Suzanne has moved. Her phone number is now (02) 533 1505. After 4 p.m. is a good time to contact Suzanne. We would like to welcome Vera White who begins a telephone support group for the Cowra District. Vera's number is (063) 42 2647, and her address is "Woodlands", PO Box 61, Cowra 2794. Why not get in touch?

# Danish Polio Society

Kay Johannsen, an Australian polio survivor now living in Denmark, spoke at a Network seminar in December 1993. After her return home, Kay wrote an account of her talk for the benefit of members who were unable to attend the Seminar.

## 1. INTRODUCTION

I am a 46 year old woman. I was born in Orbost, Victoria, where I grew up. I contracted polio at age 7 (in 1954, the last epidemic), and was paralysed in both legs and the lower back. I was in Sale Hospital for approximately 6 months, and later I had several short stays in Lady Duggan Home, Malvern, Melbourne. I had physiotherapy treatment, splints, calipers, hydrotherapy, exercises and plaster casts. After splints, I then had a long caliper on my left leg, then a short caliper. I was finished with calipers at age 12-13 and functioned almost normally. I came to Denmark at age 22. I studied Occupational Therapy in Denmark and worked as an OT. Post-Polio Syndrome (PPS) started about 4 years ago in the late 1980s. I stopped work in June 1992, and applied for a disability pension, which I now receive. I am very active on the polio scene in Denmark, doing committee and support group work. I wrote an article about PPS in the Occupational Therapy Journal.

Disabled peoples' organisations in the European Community have the following hierarchy:

- HNR (Nordic Council of Organisations of Disabled People) - was founded in 1979 and consists of 7 umbrella organisations. HNR co-operates with and within the European Community.

- DSI (Danish Council of Organisations of Disabled People) - was founded in 1934 and consists of 27 handicap organisations (of which PTU - see below - is one). The objectives of DSI are to take care of the common interests of the 27 member organisations.

- PTU (National Society of Polio and Accident Victims) - Chief Management Level.

- PTU (Divisional Level - 20 Local Branches).

- PTU (Support Groups).

Today I will be focusing on the work of the PTU in Denmark. I also wanted to talk to you in your Network for the following reasons:

- to inform you about what is happening with PPS in Denmark,
- to inform you about what treatment and help is available in Denmark,
- to find out what is happening with PPS in Australia,
- to exchange news/ideas/tips/treatment to support post-polios in Australia and Denmark, for our mutual benefit,
- to support international work for post polios, and
- to tell you my own personal story.

## 2. PTU

***Aims and Goals***

PTU's "target group" is persons with a motion/movement disability due to polio, persons with damaged spinal cords or persons who have become disabled due to an accident, including traffic accidents. PTU's main purpose is to relieve this "target-group's" disabilities, plus to support action against polio.

The above-mentioned is fulfilled by:

- giving treatment, training, rehabilitation, social advice and other types of support,
- spreading information by holding courses, seminars, plus publishing journal articles,

- working for integration and abolition of a society-created handicap,
- working with other handicap organisations in Denmark, and the rest of the world, and
- supporting handicap research.

PTU is a society of, and for, physically handicapped persons, but membership is open to anyone.

The former "Polio Society" was formed in 1945. Traffic and accident victims joined up in 1985.

***Assistance and Activities***

Physiotherapy, transport, instruction in use of wheelchairs, adaptions to homes and workplaces, obtaining of aids/appliances/wheelchairs, Ergonomic counselling, testing of cars and advice on adaptions, motoring school, canteen, workshop, holiday travel & country cottages, social guidance, legal assistance, pyschological assistance, exercise centre.

***Members/Financing***

| | |
|---|---|
| Membership fees ($36) annually | $ 0.35 million |
| Trust funds/grants | $ 0.35 million |
| Lotteries and gambling | $ 0.65 million |
| Public patient payment | $ 3.50 million |
| Other sources | $ 0.35 million |
| *Total funding* | *$ 5.20 million* |

*Members* - The number of registered members is 3,300, of which the majority are polios. (The population of Denmark is just over 5 million).

*Financing of Local Branches* - The 20 local branches receive contributions from PTU (Chief Management Level - see below) in relation to the number of members. For instance, in my local branch we have 260 members and we receive $3520, which means we get about $13.50 per member per year.

*Financing of Support Groups* - These groups can apply for individual contributions from the Chief Management Level.

***Structure of Network***

I PTU - Chief Management Level - governing body - 9 members
(PTU is 1 of 27 handicap organisations in Denmark)

II PTU - Divisional Level - 20 local branches = 20 executive committees each with 9 to 10 members

III PTU - Support Groups

***Employed PTU***

82 employees

1 Chief Physician
1 Medical Consultant
35 Physiotherapists
4 Swimming Instructors
1 Psychologist
1 Journalist
3 Social Workers
2 Lawyers
1 PR man
Motoring School Instructors
Canteen Staff
Workshop Staff
Bus Drivers
Secretaries & Bookkeepers
President (who has polio)
Managing Director

***Facilities***

- PTU has an Outpatient Clinic, for disabled persons in the provinces. Treatment is provided in the form of short-term (usually 2 weeks) intensive training. Two flats, adapted to the needs of wheelchair users are available free of charge to polio and accident victims whilst undergoing intensive training in Copenhagen.

- Physiotherapy is provided free of charge, subject to recommendation by the patient's GP, and approval by the clinic's Chief Physician. Treatment available includes training in the heated swimming pool (34 degrees), stretching of tight muscles, relaxation of joint capsules and tendons, walking exercises, hot packs and remedial gymnastics. An exercise centre has training cycles, toners, strength training equipment, and equipment for muscle training and stretching. Physiotherapy is provided in an Outpatient Clinic.

- There are 10 mini-buses for treatment and medical examination. Some are equipped with a lift, and are designed for wheelchairs. 18,000 trips a year are made in Greater Copenhagen.

- Wheelchair schooling - instruction by physiotherapists, indoor and outdoor use of electrically and manually operated wheelchairs, and in road safety.

- Helping aids, home and workplace adjustments - physiotherapists visit homes and workplaces all over the country to offer advice and guidance. An application is sent to the local government authority for loan of aids and appliances, or for financial support of adaptions.

- Ergonomic counselling - workplaces of all kinds. Re-design, purchase of equipment, correct working postures and lifting techniques, PTU offers instructions.

- Motoring School - PTU has its own, with instructors giving both driving lessons and coaching. Physiotherapists design the interior of the cars, for instance, of how to get in and out, size and design of the car.

- Canteen - for staff and patients.

- Workshop - for tailor-made solutions, plus the undertaking of repairs. For instance, a transport chair has been designed and made for passages through narrow aisles (aircraft & buses).

- Travel and recreation - "to travel is to live", Hans Christian Anderson said. PTU owns cottages, adapted to the needs of wheelchair users.

- Social Guidance - nationwide counselling on social security questions, personal, financial, housing, occupational and educational problems. Help for social security benefits, grants, filing of complaints and petitions for appeal, pensions, allowances and benefits. Financial help for invalid cars is also included in this category.

- Legal Assistance - questions of compensation, accident insurance and free legal aid.

- Psychologist - mental relaxation, pain treatment, crisis therapy and guidance for couples.

- Journalist - 6 polio journals annually, with approximately 7000 numbers printed.

- Summer Holiday - a "Peoples' High School" stay for 1 or 2 weeks, for approximately 60 persons. This is not held every year. Physical challenges (parachute jumping, air-gliding, water-skiing, go-carts), plus more creative and cultural activities, and not to forget partying.

***Support Groups***
These groups stem from the local branches' need for more contact. At PTU, patients have always talked together. There is a need for this talking in smaller groups, outside the centrally placed PTU in Copenhagen. Therefore support groups were started.

Two groups were formed from the central group, but certain things cropped up, which were difficult to tackle. The local branches contacted the M.S. Society's psychologist, who had expertise in starting support groups, and she trained several voluntary PTU members to function as "starters" of the new support groups.

Money was found so that the M.S. psychologist and the polio members could hold two one-day courses. Here they worked with psychological group therapy, the mind's pitfalls and possibilities, solution models for the conflicts, plus the most important rules for group interaction. These meetings were advertised in the PTU journal.

Many thought that the groups were purely psychological and didn't want to be a part of these support groups. The name was changed to "Experiment Groups", which seemed to help. There have been two evaluations since the courses commenced, but at this stage it is difficult to say just how much of a success these "Experiment Groups" are.

***Committee Work***
The Local Executive Committees' main tasks are to:
- fulfill the governing body's aims/goals locally,
- represent the governing body in local issues, and to take care of the governing body's interests locally, and to establish the best possible collaboration between local authorities and institutions,
- establish contact with other handicap organisations and other interested committees locally,
- recruit new members and spread knowledge of PTU, and
- manage/administer the capital that has been given to the local branch.

Every October/November the Annual General Meeting is held. There are approximately 6 to 8 ordinary committee meetings per year. We arrange meetings, activities, courses and outings for members, and at times their families. Activities can be of relevance to polio or accident victims, but at times they can be purely just for pleasure. The Annual General Meeting for the Governing Body is held in May each year. Five members from each Local Branch attend, and vote for the members of the Governing Body. This meeting lasts two days.

***Knowledge of PPS and What is Being Done***
Two physiotherapists from PTU have a 2-year project going at the moment, where they are to go to all six physiotherapist schools in Denmark, and teach students about PPS. They are also teaching physiotherapists who have clinics throughout Denmark. They have made two video films, one of which is about my life with polio and now PPS. This way they hope that post-polios can obtain the relevant treatment outside of PTU. PTU is now unable to meet the demands of polios' physiotherapy needs, due to the increase in post-polio cases. The Chief Physician at PTU completed a survey on PPS, which he presented at an international Post Polio Conference held in Copenhagen in September, 1993. Denmark relies on news from abroad, and at the moment there is no research done on PPS in Denmark.

## 3. DANISH SURVEY

In a nationwide survey in 1990, a questionnaire was sent to 4800 polio survivors, entailing 92 questions. These questions were to do with - Items of Polio, Socio-Medical Conditions, Rehabilitation, and New Health Problems. 3607 polio survivors responded to the questionnaire, which meant that there was a response rate of 77%. Initially, this wasn't meant as a scientific study. PTU only wanted an accurate picture of the PPS situation in Denmark.

The survey is divided into the following sections:
I Presentation of results
II Risk indicators
III Socio-medical adaption

Results, very briefly, show that with PPS there is an increase in muscle fatigue and pain, and an increase in joint pain. There is a decrease in endurance and strength, and an increase in activities-of-daily-living problems. There appears to be a higher frequency of PPS amongst females and older age groups.

# The Post-Polio Syndrome - Advances in the Pathogenesis and Treatment

Dr Ian Neering wrote the following very comprehensive report for the Network after he attended a conference in the USA earlier this year. Dr Neering is Associate Professor in Physiology and Pharmacology at the University of New South Wales, where he teaches science and medical students and also undertakes research into nerve and muscle function. He has been associated with Associate Professor Simon Gandevia for some time and they have collaborated on a number of projects over the years. He and Simon Gandevia have both promised further articles in the future - watch this space!

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During the polio epidemics of the mid twentieth century, huge funding programs were central to the development of vaccines and the eventual control of the disease. Because these vaccines were so effective, it became unnecessary for scientific policy makers to emphasize continued basic research on polio. As a result there are still significant gaps in our understanding of the mechanisms by which the poliovirus causes paralysis and the consequences of such paralysis, partly because of loss of interest in the problem after generation of the vaccine. The appearance and general acceptance of the Post Polio Syndrome (PPS) as a clinical entity has rekindled interest and research into the poliovirus. The effective lobbying of the PPS afflicted, particularly in the US, has provided funding to enable this research to take place.

The following report describes what I found to be the most interesting communications at a meeting entitled "The Post-Polio Syndrome: Advances in the Pathogenesis and Treatment" that was organised by the New York Academy of Sciences and was held on April 27-30, 1994 in Bethesda, Maryland. Included in the one hundred or so participants at the meeting, were most of the well known workers who have published on PPS over the last 10 years. It was, pretty much, a "state of the art" meeting. I found it particularly interesting to observe that a significant proportion of the participants and those actively involved in the research, showed evidence themselves of having been afflicted with either old polio or some other neuromuscular disorder.

For convenience, I've grouped the material into a number of categories.

## 1. ACUTE POLIO

In the light of new changes in patients with a history of polio some 30 to 40 years previously, there has been a re-examination of the acute condition both from the point of view of archival records and clinical material and to a lesser extent from examination of new cases which are relatively rare.

**Mulder** reported the acute findings and symptoms of 201 patients with paralytic poliomyelitis in the population of Rochester MN (home of the Mayo Clinic) from 1935-1955. In view of the fact that in most clinicians minds, Polio is associated with an invasion of spinal cord motoneurones by the poliovirus, it was of interest that mention was made of

signs related to motor and sensory changes in the brain during the acute phase of the disease. i.e. positive Babinski Sign and sensory abnormalities. The involvement of spinal cord and brainstem (respiratory paralysis) made it difficult to document other central nervous system (CNS) abnormalities. Mention was also made of the work of the feisty Australian, Sister Kenny who advocated the use of warm, moist heat and limb movement rather than splinting. She was a powerful advocate of her technique who "continued to fight long after you had agreed with her."

**Weichers** identified 5 phases in the progression of polio affliction. Acute myelitis, early recovery (1 year), late recovery (6-8 yrs max), functional stability, late changes. Initially, there is a loss of voluntary motor unit action potentials (MUAPs) (a lack of electrical activity in nerves and muscles) in affected muscles and normally or mildly reduced nerve conduction velocity. Larger motor units appear to be preferentially involved. Within three weeks, the presence of positive sharp waves and fibrillation potentials predominate. In the following weeks as terminal axon sprouting characterises the process of reinnervation, long duration polyphasic MUAPs with an increase in fibre density, jitter and blocking are seen. Increases in jitter and blocking indicate that transmission of the nerve impulse to the muscle (the signal that causes the muscle to contract) is not taking place normally. Over time the number of MUAPs may increase while the MUAPs themselves become larger, 30-40 times normal.

**Isaacson**, a member of Dalakas' group, reported the use of *in situ* reverse transcription and PCR on archival spinal cord tissue sections to determine which cells in the spinal cord were infected during acute polio. Staining was restricted to anterior horn cells, axons and dendrites indicating that motoneurones were directly infected by poliovirus during acute infection.

Another interesting finding was that of **Monzon and Dalakas** who reported poliovirus in the lymphocytes of patients with acute polio, measured with PCR ( a very sensitive technique for measuring genetic material of viruses and other organisms).

## 2. CLINICAL ASPECTS OF POST POLIO PATHOLOGY

**Dalakas** made the point that PPS is a diagnosis by exclusion. It refers to new symptoms and signs that occur at least 15 years after stability in patients with prior acute paralytic poliomyelitis. It includes a) new muscle weakness and atrophy b) muscle fatigue c) a variable set of symptoms which may include joint or muscle pain, sensitivity to cold etc. All other medical, neurological, orthopaedic or psychiatric diseases that can explain the cause of these symptoms need to be excluded. PPS is a clinical diagnosis and lacks unique laboratory criteria. Routine electromyography is useful to confirm chronic and ongoing denervation and exclude neuropathies but it can't distinguish between old, stable polio and patients suffering new weakness with PPS (**Lange**). The same can be said for muscle biopsy. Both asymptomatic old polio and post-polio patients show scattered angular fibres indicating ongoing denervation. This pattern of denervation is different from that of Amyotrophic Lateral Sclerosis (ALS) where all muscle fibres of a single motor unit become angulated as the motor nerve dies. In old polio, muscle cell atrophy and death is likely to be associated with degeneration of terminal motor axonal sprouts (the small nerve branches supplying individual muscle fibres), hence the scattered appearance of the angulated fibres.

An interesting new insight on this process was reported by **Cashman** who made use of neural cell adhesion molecular staining (NCAM) as a more sensitive indicator of muscle denervation. He reported that some old polio patients had up to 10% of NCAM positive fibres. This indicates that active remodelling (ongoing denervation and reinnervation of muscle fibres) of motor units in all old polio patients is much more significant than previously realised. Serum chemistry is necessary to exclude other diseases. Elevation of Mild Creatine kinase (a protein released from damaged muscle and believed to be a useful index of muscle destruction) up to 4 times normal may be seen in PPS but is in no way discriminative. Serum antibody titres to polio virus are not helpful for clinical diagnosis.

A small amount of data was shown indicating the slow **average** rate of PPS progression about 1% over a period of 9 years. Of course for individuals, year to year changes might be much greater than this. While estimates as to the incidence of PPS among the old polio population remain uncertain, **Dalakas** suggested that 30-40% of polio patients would be affected. Also earlier onset of PPS would be associated with acute bulbar involvement (i.e. if patients suffered from respiratory paralysis during the acute phase of the disease). PPS subjects may show increased susceptibility to competitive neuromuscular blockers, syringomyelia and inclusion body myositis.

Interestingly, **Bartfelt** and others reported that while it is slightly more likely for males than females to contract poliomyelitis, females predominate in terms of incidence of PPS.

**Windebank** reported a well conducted prospective study of polio survivors in Olmstead County (where the Mayo Clinic is) who had polio 1935-1960. Fifty representative subjects were chosen for detailed clinical studies on two occasions 5 years apart. 60% of subjects demonstrated PPS symptoms; 20% had lifestyle changes, but, as a group, neuromuscular function was well maintained although **Daube** reported a non statistically significant decline in motor unit numbers.

In terms of psychological effects, **Grafman** and colleagues found no differences between PPS and normals on psychological (MMPI) or depression scores. Though **Bruno** (1993) (and see below) has reported impaired ability to maintain attention and rapidly process complex information as being characteristic in post-polio survivors reporting severe fatigue.

## 3. VIROLOGY

The role of the poliovirus in the disease process has been examined not only from the point of the virus itself but also from the point of the poliovirus receptor. The poliovirus receptor for the picornavirus has a molecular weight of approximately 85,000 Daltons.

**Wimmer**'s group developed a modified version of the polio virus. This was infectious but the animal recovers thus enabling the study of the long term recovery. What was particularly clear was that the polio virus does not have a high affinity for neurons.

Although the polio virus receptor (PVR) (the specific protein molecule to which the virus must attach before it can gain free access to the cell) has been cloned, lack of knowledge of its precise tissue distribution makes assessment of its role in mediating poliomyelitis difficult. PVR is expressed at many sites.

**Freistadt** pointed out that PVR is present in both susceptible and non-susceptible tissues. It appears in motor cortex, on axons and cell bodies and also in the cerebellum. PVR is even present in non susceptible regions of the brain such as the olfactory bulb. Freistadt had recently demonstrated that poliovirus receptor is expressed in human monocytes. Further CD-14-positive cells (monocytes) support polio virus replication but only about 10% of the cells become infected. Thus it may be that the initial round of virus replication in the gut and transport of the virus into the central nervous system or brain and spinal cord (CNS) might be mediated by the monocytes. Preliminary studies indicated that there was no difference in PVR expression between PPS and asymptomatic old polio patients.

Using the monoclonal antibody D-171, **Monzon, Illa and Dalakas** conducted single or double immunocytochemical studies for the location of PVR. Interestingly they found that there is no PVR in normal muscle but it is present in cultured muscle, in human myotubes (early developing muscle) for example.

During acute polio however there is PVR generally expressed in muscle. **Monzon and Dalakas** have shown that in acute polio, muscle supports replication of polio virus and cell death can occur with visible viral particles in the muscle. PVR is weekly expressed in motor neurons but is upregulated (there is more of it) in infection. PVR is also present in regenerating fibres. Monzon and Dalakas examined frozen muscle biopsies from patients

with acute polio 15 days to 12 months after paralysis. These samples came from Pakistan where the incidence of Polio is higher than for many countries. There was no evidence of virus in the muscle but this might be because by 15 days polio virus is no longer present in muscle. The generalised presence of PVR in the muscle of acute polio, but its absence or weak presence in the muscle of post-polio patients suggests that its expression may be upregulated by lymphokines or cytokines (naturally occurring substances released by the body's immune system) released during the acute viral infection. The presence of PVR in regenerating muscle may support the role of muscle injuries as risk factors in the acute infection. Monzon and Dalakas found a self-limiting T-cell inflammatory response localised at the motor endplates and most interestingly, there was significant PVR staining at the motor endplates (where a motor nerve meets the muscle fibre it controls) of both normal and infected muscle biopsies. These investigators put forward the suggestion that the motor endplates serve as gateways providing access for the polio virus to the CNS via retrograde transport up motor nerves. It must be said however on the basis of what was presented at the meeting that exactly which region of the motor endplate presynaptic, transynaptic or postsynaptic expresses the PVR is unresolved.

The question of viral persistence in PPS is a controversial one since the publication in the New England Journal of Medicine in 1991 by **Sharief** et al of a report detailing serological evidence that this might be the case. A number of papers dealt with this issue, though not all agreed with the proposition.

**Jubelt** and co-workers who analyzed serum and cerebrospinal fluid (CSF) from 19 PPS patients for antibody to poliovirus types 1 and 2 using ELISA (an analytical technique) found that few subjects showed evidence of intrathecal (within the region bathed by the CSF i.e. brain and spinal cord) production of anti-poliovirus antibody. It was suggested that in those few positive testing individuals, other inflammatory neurological diseases might have caused a non-specific elevation in CSF poliovirus antibodies.

**Muir** and colleagues, from Sharief's group examined CSF for enterovirus RNA also using PCR. Enteroviral RNA was detected in 3/24 PPS patients but in 0/36 subjects with stable old polio and 0/36 patients with other neurological conditions of non-infective origin. All three patients in whom viral RNA was detected had high intrathecal levels of poliovirus-specific oligoclonal IgM bands. Muir also examined post-mortem neural tissue from 7 patients with a history of paralytic poliomyelitis. He reported that enterovirus RNA was detected in spinal cord tissue from three patients but was not detected in cerebral cortex. Preliminary nucleotide sequence analysis indicates that the enteroviruses detected, are not polioviruses although this requires further confirmation by examination of additional sequences from other regions of the viral genes. In a blinded study (the investigators had no previous knowledge of patients condition so that the chance of biased observation was minimised) of 30 old polio patients, there appeared to be no correlation between the titre of antibodies and functional studies. The finding of non-polio enteroviruses may indicate that patients with previous poliomyelitis are susceptible to persistent enterovirus infection of the CNS.

Reports by **Monzon and Dalakas** and by **Kopecka** and colleagues were in approximate agreement with regard to the presence of viral RNA using PCR methodology. Thus Monzon concluded that some PPS patients have high titres of IgM anti-poliovirus antibodies implying an ongoing antibody response to a viral antigen. Evidence of viral RNA in the CSF of some PPS patients was suggestive of viral persistence. While Kopecka found no culturable viruses in any of the material she studied, PCR amplification of polio sequences in the 5'UTR and in VP1 genomic region was successful in several specimens from PPS patients. Restriction analysis of amplified fragments showed heterogeneity of viral sequences. Direct sequencing of the amplified material revealed polio-like sequences with a large number of point mutations and rearrangements compared to reference PV1, PV2 and PV3 strains of the poliovirus. It should be pointed out that while both of these studies inferred a long term persistence of poliovirus in at least some PPS patients, no asymptomatic, old polio patients were studied as controls. It is therefore unclear as to whether such investigations of viral RNA yield results unique to PPS. Accordingly, the usefulness of these measurements for the diagnosis or indeed as an explanation for the

underlying etiology of PPS remain unknown. Further, the inability to find live polio virus in any neuronal material from PPS patients is also problematic if persistent polio infection is to be supported.

## 4. INFLAMMATION

**Dalakas**' group studied representative sections of spinal cords from patients who died 9 months to 44 years after acute paralytic polio. Apart from loss of motor neurones, severe reactive gliosis was noted and surprisingly, a mild to moderate perivascular and interparenchymal inflammation.

Similar findings were presented in a poster by **Tresser** et al. In an examination of spinal cord material in 9 patients from pathological archives with a history of previous polio (39-62 years) they reported white matter gliosis and a chronic inflammatory infiltrate in all sections. A chronic inflammatory infiltrate of the meninges (the membrane system surrounding brain and spinal cord) was seen in all specimens showing neuronal loss. This inflammation was present even in old polios and was unrelated to the presence of new symptoms (PPS). Axonal spheroids and occasional chromatolytic neurons were also noted.

Dalakas also reported signs of inflammation in muscle biopsies. In particular perivascular or interstitial inflammatory cells consisting of $CD_8$ cells > $CD_4$ cells > macrophages were noted along with MHC expression. These findings collectively suggest that there is a slow but continuing inflammatory process in both spinal cord and muscle as well as ongoing disfunction in the spinal cord motor neurons. Dalakas also confirmed the presence of high titres of GM1 antibodies and high levels of $IL_2$ and $IL_{2R}$ and oligoclonal bands in CSF indicating an on going immune response. Several pathogenetic mechanisms might underlie the inflammation; persistent, active poliovirus infection, autoimmune attack on central and peripheral nervous system elements or increased vulnerability of polio-virus damaged tissue to new infections.

On the basis of his study in which he reported almost pure B lymphocytes in inflammatory spinal cord infiltrates, **Miller** and colleagues suggested that PPS might be an autoimmune disorder mediated by antibodies produced *in situ*, and not by a cell mediated process. He too reported axonal spheroids in the anterior horns and moderate degeneration in the lateral columns. It should be noted however that Miller's study was performed on just one subject. The point was made by Miller and others that perhaps we should look at polio as an encephalitis rather than a myelitis.

## 5. NEUROMUSCULAR PHYSIOLOGY IN PPS

In an impressive study, **Maselli** and co-workers performed detailed morphological and electrophysiological analysis of the neuromuscular junction in muscle biopsies from 10 PPS patients to examine the basis of observed transmission defects. Intracellular microelectrode recordings showing histological evidence of prominent denervation, demonstrated reduced amplitudes and frequencies of miniature end plate potentials (MEPPs) corresponding to a reduced output of the chemical transmitter carrying the stimulus from nerve to muscle. EPP quantal contents were quite variable: diminished in biopsies showing predominant signs of recent denervation and normal or markedly increased in biopsies showing primary signs of chronic denervation. Electron microscopy revealed some nerve terminals of reduced diameter apposed to normal postsynaptic folds however whether these terminals are aging or are new sprouts remains unresolved. It seems that impairment of neuromuscular transmission in PPS may have multiple causes and is related at least partially to underlying denervation. The reduced quantal content at some neuromuscular junctions may provide the basis for the improvement seen in a very few patients trialled on anticholinesterases.

While an increased jitter on single fibre emg is common in both symptomatic and asymptomatic old polio patients, **Cashman**, using stimulation single fibre EMG demonstrated increasing failure of neuromuscular transmission at high rates of activation in about one third of post polio patients examined. He suggested that in this group,

neuromuscular junction defects are acquired with time after polio and that these patients may benefit from treatment with anticholinesterases, drugs which facilitate the communication between muscle and the nerve which controls its activation. A clinical trial of pyridostigmine is discussed below.

**Pachter** has tried to develop an animal model for post polio. He examined type I and type II muscle fibre areas, the incidence of axonal and collateral sprouting, force of contraction and motor endplate morphology over a 15 month period following partial denervation of the rat plantaris muscle. At 1 month there was group atrophy of muscle fibres with a decreased area of both type I and type II fibre groups. Full recovery of muscle function was attained at 6 months followed by a significant reduction in muscle force and fibre areas from 9-15 months. Scattered angulated fibres were present and fibre type grouping was noted. There were signs of degeneration at motor endplates and swollen terminal branches. While these observations have much in common with those described above for old polio and indeed with changes observed in aging whether they accurately model the peripheral changes in post polio requires further investigation. It should also be mentioned that while it is clear that there is a significant peripheral component of post polio, discussion below will also deal with the possible involvement of higher, cortical regions in the aetiology of the syndrome. Clearly, Pachter's model does not encompass this possibility.

Considering the importance of muscle weakness in PPS, there have been surprisingly few metabolic studies of muscle in old and post polio subjects. A poster by **Sivakumar**, a member of the Dalakas group reports a significantly greater depletion of phosphocreatine (a potential energy source for muscle) as determined by $^{31}P$ Magnetic Resonance Spectroscopy for every given workload in a group of PPS subjects compared with healthy controls. Unfortunately, there were no controls for asymptomatic old polio subjects or sedentary controls with similar muscle weakness unrelated to polio.

## 6. EVIDENCE FOR A POSSIBLE CORTICAL ROLE IN PPS

**Bruno** and colleagues presented evidence associating Post-Polio fatigue with findings of clinically significant deficits on neuropsychological tests of attention. In addition he reported the presence of white, hyperintensities on MRI in paraventricular nucleus, arcuate nucleus, periaqueductal grey, associated white matter tracts and the dorsal striatum in 55% of old polio patients suffering from fatigue. While the significance of such hyperintensities remains controversial amongst the imaging fraternity, the fact that no such white intensities were detected in the asymptomatic old polio subjects is interesting. Bruno suggested that this was good evidence for the involvement of the reticular activating system in the etiology of PPS. In support of this contention Bruno reported a decreased secretion of adrenocorticotrophic hormone (ACTH, released from a site within the brain) in response to a stressor. The levels of ACTH appeared to correlate with fatigue scores. On the basis of these findings, and their resemblance to other viral encephalidities in which fatigue is a major symptom, Bruno put forward a model for a putative brain fatigue generator in which the neurotransmitter dopamine figures importantly. Much of the Bruno discussion was of a speculative nature, however stronger evidence of the involvement of higher motor cortical centres in PPS came from a study by **Gandevia** et al.

**Gandevia**'s group investigated maximal voluntary drive in a group of old polio patients. Using a modified twitch interpolation technique, they were able to distinguish between central and peripheral fatigue in a group of 90 patients affected by poliomyelitis at least 20 years previously. Subjects are required to perform maximal voluntary contractions (MVC's). The degree of muscle activation can be assessed by applying an electrical stimulus over the motor point of the contracting muscle. Any additional force indicates that the subject was not fully recruiting motor units. When the amplitude of this "superimposed contraction" is related to the amplitude of a single evoked muscle twitch, an index of activation can be computed. This activation index can be interpreted as a measure of central drive. Evoked twitch amplitude is a measure of muscle competence and hence depends on peripheral factors. In unfatigued muscles, 24 of the 90 subjects had levels of maximal voluntary activation below the lower limit for normal subjects. Subjects were then submitted to a fatiguing protocol. The results indicated both peripheral and central

components are involved in the new weakness reported by some old polio patients. This finding supports the histological observation by Bodian in 1947 of damage in motor paths rostral to motoneurones. Not only is this of interest in terms of the etiology of PPS but it may provide the basis for a diagnostic tool in the detection of PPS. Dr Gandevia will be presenting a more complete description of this work in this Newsletter at a later time.

## 7. DRUG TRIALS

The problems of conducting clinical trials were discussed in a talk by **Dalakas**. He pointed out the difficulty of such studies related to a number of factors. 1) The innervation of muscles in old polio patients may differ from limb to limb or even within the same limb because of the segmental nature of the initial involvement and the varying degree of subsequent recovery. Thus the compensatory effort of the neighbouring muscles varies even in the same limb. In PPS and old polio subjects the various muscle groups differ according to whether they were affected during the acute phase of the disease and have recovered (partially or completely) or whether they were clinically spared. Because the impact of the late effects of polio is also variable in these muscle groups, the effect of therapies may be different, not only from patient to patient and from limb to limb but also from muscle to muscle within the same limb. 2) Defining the endpoint of potential therapies. The two most disabling symptoms associated with PPS are excessive fatigue and new muscle weakness. Experimental therapeutic designs should focus separately on the fatigue, using validated fatigue scales and on muscle weakness using quantitative muscle testing (maximum voluntary isometric contractions). 3) Patient selection is crucial and should include asymptomatic old polio patients as well as those suffering new symptoms. 4) Also of importance is the placebo-controlled design. 5) The length of the trial remains unresolved because of the slow and unpredictable progression of PPS that varies from patient to patient. Dalakas observes "that until the natural history of PPS is defined, therapies aimed at arresting disease progression are not reliable.

***Insulin Like Growth Factor I***

In this study **Shetty** and co-workers have confirmed earlier findings that the concentration of IGF-I in old polio subjects was significantly lower than in control subjects. Plasma concentrations of IGF-I lower than 0.35 U/ml in adults indicate that there is little or no growth hormone secretion since growth hormone mediates many of its actions through IGF-I. In old polio subjects, 38% of plasma IGF-I values were below 0.35 U/ml compared to 19% in the healthy group. This finding is consistent with the suggestion enunciated by Bruno of neuroendocrine disorders consistent with hypothalamic lesions. Univariate analysis showed that low IGF-I in old polio subjects was significantly correlated with age, male gender, body mass index and also difficulty in the activities of daily living which was independent of other factors. There appeared to be no correlation between levels of IGF-I and subjective report of recent decline in functional status. Shetty suggested that the low IGF-I levels might have an adverse effect on neuromuscular function since it has been shown that IGF-I both enhances motoneurone survival and neuronal sprouting in muscle. Shetty confirmed that (at least in the 8 PPS subjects he studied) administration of human growth hormone (hGH) was able to normalise IGF-I levels. In a subsequent study, Shetty examined the effect of hGH treatment and normalisation of IGF-I levels on muscle function in PPS subjects. IGF-I levels were corrected to the target youthful range by relatively low doses (quarter to half the usual dosage) of hGH without significant adverse effects. After three months of hGh treatment, the majority of muscle tests showed little or no improvement although some subjects did demonstrate improvements of strength and endurance in individual muscles and one quadriplegic subject showed an improvement in blood gases which decreased to baseline level following discontinuation of therapy. Shetty suggests that perhaps the three months of the trial might not have been long enough for full beneficial effects to have been realised. One important sidelight to these studies which was not discussed at the meeting is worthy of mention here. Sleep disorders are a common feature of PPS. Since most growth hormone secretion occurs during sleep and particularly in the first four hours of sleep, fragmentation of sleep patterns may interfere with growth hormone release and IGF-I levels. Long-term elevation of IGF-I levels such as might have been achieved in Shetty's study might not have the same effect as those engendered from rhythmic pulses of growth hormone which occur physiologically.

***Prednisone***

The observation previously discussed of inflammatory signs in spinal cord and muscle biopsy specimens of PPS subjects led **Dinsmore** and his colleagues to a trial of an anti inflammatory steroid, prednisone in 17 PPS subjects. This was a well conducted, double blind placebo-controlled (neither the investigators nor the subjects knew if they were given prednisone or placebo until the end of the study, again, to avoid bias) trial taking place over a period of 6 months. Muscle strength was tested by manual and quantitative methods. There was a modest improvement in strength in the third month but this effect was short lived and did not translate into meaningful improvement. Both placebo and treated groups reported equal (about 50% of each group) levels of subjective improvement. This high level of placebo effect emphasises the importance of properly designed studies. Interestingly, a number of subjects who received only placebo, reported prednisone-like side effects.

***Pyridostigmine***

Reasoning that since jitter is a common finding on recordings of single fibre EMG in PPS patients, and that one possible explanation for jitter is variability of transmitter release, **Cashman** and colleagues suggested that anticholinesterases might improve the apparent defect in neuromuscular transmission underlying such jitter. Accordingly they examined the effect of edrophonium on jitter in response to stimulation single fibre electromyography on 17 PPS patients. Jitter was significantly reduced in 7 patients, unchanged in 8 and increased in 2. Patients were then treated with oral pyridostigmine and 9 patients noted improvement in fatigue as assessed on the subjective Hare fatigue scale. Edrophonium induced reduction of jitter was significantly associated with pyridostigmine induced subjective fatigue improvement. However, based on an examination of isokinetic contractions of the quadriceps muscle, pyridostigmine did not change the amount of work done on exercise by PPS patients reporting subjective improvement as a group. Given the high placebo effect of the previous study, the fact that neither subjects nor investigators were blinded and that neither normal nor asymptomatic old-polio subjects were used as controls, it is difficult to determine the value of the subjective data presented. While it is possible that in some individual PPS patients, anticholinesterases may objectively improve physical performance, overall, this study provides little evidence that these compounds will be of general benefit in the treatment of PPS.

***Amantadine***

Dopamine is a chemical transmitter in the brain. A 1991 open label study suggested that the dopamine like drug or agonist, amantadine decreased fatigue in PPS patients. **Stein** and colleagues established a double-blind, placebo-controlled study on 25 PPS patients over a period of 6 weeks to test this observation. Fatigue was measured with visual analog scales, numerical fatigue severity scales and global impression. No muscle testing was performed. Approximately half of all patients noted an improvement. However, on all measures there was no significant difference between treatment and placebo groups. Three patients in the treatment group but none in the placebo requested to continue amantadine therapy because the improvement had a major impact on their life styles. While overall, these studies suggest that amantadine is not significantly better than placebo in reducing fatigue associated with PPS it is interesting to note that Bruno, in his communication to the meeting, reported subjective improvement in two PPS subjects administered another dopamine agonist, bromocriptine. As Stein points out, although more patients improved with amantadine and their improvement was more pronounced, the fatigue scales were too insensitive to discriminate such a subjective response. Better designed studies need to be carried out. Further, it should not be assumed that dopamine is uniquely implicated should such studies indicate a beneficial outcome on PPS since the actions of both amantadine and bromocriptine are not confined to dopamine receptors.

Other drugs for which anecdotal information exists regarding their actions in PPS patients include interferon (no apparent effect in 1 patient); The MAO-B inhibitor, Deprenyl (possible improvement in 1 patient) and unspecified nerve growth factors (no information).

## 8. EFFECT OF EXERCISE IN PPS

The role of exercise in the PPS patient is controversial. Some argue that the problem itself arises from muscle overuse and therefore overactivity might lead to an exacerbation of the patients clinical situation. On the other hand inactivity can lead to a reduction in aerobic enzyme systems, a reduction in muscle capillary density and weight gain which increases work load. Certainly weight gain has been reported in up to 60% of PPS subjects studied. In his own study **Agre** found no changes in EMG parameters of PPS subjects who underwent a limited training program. There was also no improvement in objective muscle performance although a number of subjects reported subjective improvement. This subjective improvement may be another expression of the placebo effect. Interestingly there was no change in the levels of creatine kinase levels in subjects over the whole training program. Agre was of the view that a mild exercise program with appropriate rest breaks is unlikely to be harmful and while its beneficial effects on muscle strength are questionable, a positive effect in terms of cardiovascular fitness could be expected.

The concept of muscle overuse is not fanciful. In an impressive study, **Borg** et al demonstrated very high levels of tibialis anterior muscle use in 25 subjects with a history of prior polio. The old polio patients were driving the tibialis at 30-40 Hz compared with 10 Hz for normal subjects. This indicates that the weaker subjects were forced to use high threshold motor units. Another important finding was that muscle biopsies from the overused tibialis muscles showed a predominance of type I fibres (up to 96% compared with 76-88% in normals). This increase in the proportion of type I fibres was accompanied by an increase in the mean cross sectional area of these fibres and a significant decrease of capillary density. Despite these changes, the maximum voluntary force at fast relative to slow speeds of foot dorsiflection did not differ from control subjects indicating that the contractile properties of the overused muscle fibres do not change in parallel with histochemical fibre type. Possibly transitional fibre types are induced by the variations in usage pattern.

## 9. CONCLUSION

It would seem that directions for further fruitful research lie in three main areas. Firstly, the continuing role of the poliovirus in the etiology of PPS remains unclear. While it seems doubtful that there is ongoing poliovirus infection, the possibility of inflammatory and other responses to viral fragments or susceptibility to other viral infection needs to be examined. The availability of fresh post-mortem spinal cords and brains from PPS and asymptomatic old polio patients will presumably be increasingly available and will assist study significantly. Secondly, the possibility of viral damage to cortical and subcortical centres during the acute phase of the disease and resultant lesions which may contribute to the symptoms of PPS needs to be examined more fully. Why the effects of such lesions should only become apparent after 30 to 40 years following initial infection is a question yet to be considered. Is it possible that neuronal cell death is suddenly taking place around the sites of these lesions? Thirdly, the processes which underly the denervation-reinnervation of skeletal muscle which occurs in all old polio subjects is an area which has the potential to provide therapeutic measures which might reduce the effective rate of muscle denervation. In this context, growth factors which encourage neuronal sprouting or muscle development have the potential to provide support for the weakening PPS patient.

In a recent article in Nature dealing with the future directions for research in AIDS, Bernard Fields pointed out the importance of basic research in the development of the polio vaccine. The critical discovery came when Enders, Weller and Robbins (who received the Nobel Prize for their efforts) working at Harvard University found that poliovirus could be propagated in human embryo cells in culture. At the time their studies were not focussed primarily on polio but rather on cell culture and viruses in general. This work, however provided the stimulus and the knowledge for Salk to develop his "killed" polio vaccine. The message here for polio and indeed probably also for AIDS is that in addition to studying the viruses individually responsible for these diseases (applied research), we need to know more about viruses in general, about how nerve cells die, how the immune system works and the factors which control cell growth. We need to support basic research as well.