Polio Biology XII
Genetics of the Post-Polio Syndrome

Eddie Bollenbach

A Lincolnshire Post-Polio Library Publication
24th January 2006

It has been a while since the last Polio Biology column and much has happened in the field of neurodegeneration since the last installment. It's too bad we don't have as much focused medical research that specifically targets the Post-Polio Syndrome, nevertheless we can learn much about ourselves from work occurring in the general field of neurodegeneration. Actually, in a very real sense, Post-Polio Syndrome is the result of neurodegeneration, or the loss of vitality, synaptic connections, and resilience of our motor neurons.

One of the facts about PPS that has always bothered me is the generally accepted cause of the syndrome as deriving from overuse. Two mental roadblocks for me in accepting this idea are:

1. Only 40% (the most frequently seen number) to 20% of people who have had polio develop the syndrome with its new weakness, fatigue, pain, and variety of complications. It is logical to infer that if one had paralytic polio which resulted in residual weakness, one should develop PPS because we all overuse weak muscles innervated by too few neurons. In a survey by Marcia Falconer and me, soon to be published here at Lincolnshire, we found no difference in incidence of PPS, or severity of PPS, between polio survivor couch potatoes, or those who have worked hard physical jobs throughout their lives or participated in regular vigorous physical activity*[1]*. There have been other survey reports that have since supported this since our finding two years ago*[2]*.
2. Sometimes, it seems, people with severe initial damage escape PPS while others with less severe damage, even some who have had what was thought of as non-paralytic polio, succumb to PPS*[3]*. Since those with severe damage are weaker throughout life, overuse would be greater for their severely damaged neuromusculature.

In any event, late neurodegeneration must involve several steps. It is obvious that a prerequisite is a susceptibility to late spinal neurodegeneration. There is a very interesting study about late neurodegeneration, after physical damage to the spinal cord, published in 2003 entitled: "Discrete Gene Loci Regulate Neurodegeneration, Lymphocyte Infiltration, and Major Histocompatibility Complex Class II Expression in the CNS". The title is a mouthful. The rest of this installment will explain the significance of this article to our problems with PPS and to it's possible treatment.

The above study involved the experimental destruction of motor neuron axons (referred to as avulsion of the ventral roots of the spinal cord) in two genetically different strains of rats. The authors also crossed the

two mating strains of rats and avulsed the offspring of these two mating types. Some rats developed a late neurodegeneration (as we with PPS) and some did not. The ones that did not had different genes in several areas of their chromosomal makeup which controlled immune responses in the spinal cord. The ones who did experience late degeneration had different genes in these locations.

RESULTS:

Four points (genes) on rat chromosomes labeled VRA1, VRA2, VRA3, and VRA4 acted to determine susceptibility to late neurodegeneration. Three of these loci determined whether or not immune cells (white blood cells or MHC II cells would present in the damaged areas after the original lesions healed). The corresponding (Synectic) locations on human chromosomes controlling a late immune reaction in the spinal cord after recovery are 8q12, 8q22.1, and 1p35.2-36.11, and 16p13. To explain the chromosomal notation there are 22 pairs of chromosomes along with a pair of sex chromosomes in the human. The first number, e.g., 8 above, indicates the gene is on chromosome number 8. The q designates that the location is on the long arm of the chromosome. Each chromosome has a narrow area called a centromere which separates a long arm from a short arm. The chromosomes are observed after they are stained and the second number, 12, designates the staining band when counted out from the centromere. The location 1p means the first chromosome's short arm (p) and the numbers following indicates that the gene is within the bands 35.2-36.11.

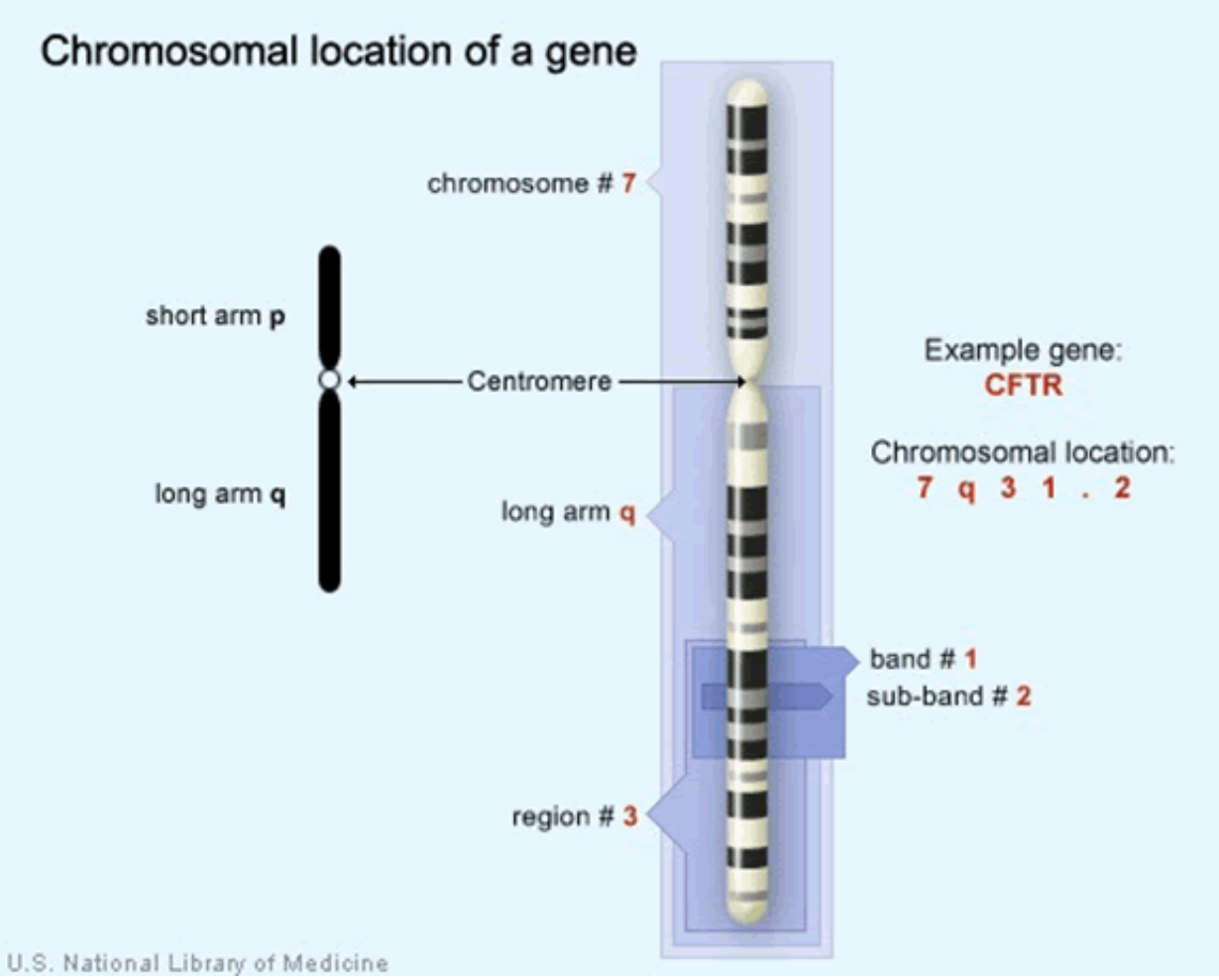

Figure 1 Diagram of one human gene with its loci and designation criteria
(US Library of Medicine)

SIGNIFICANCE:

In the past three years researchers at the Karolinska Institute in Sweden have demonstrated the presence of immune activity in the spinal cords of people suffering the Post-Polio Syndrome but not in patients who had polio with no late neurodegeneration. This immune activity was detected by the presence of immune chemicals derived from the same immune cells discussed earlier. Physicians at Karolinska have treated patients with intravenous immunoglobulin, which cleared the intrathecal space and spinal fluid of these immune chemokines and cytokines which directly attack motor neurons. Several patients treated with IVIg reported an increased vitality and quality of life, less pain and fatigue, and a general decrease in symptoms. *[4, 5, 6, 7]*. The work, which indicated a genetic basis for late neurodegeneration, strongly implies that late neurodegeneration is the result of T lymphocyte infiltration and macrophage type II instigation controlled by specific genes (which control the production of cytokines and chemokines, immune chemicals resulting from immune activation within the spine). I believe these two lines of inquiry outlined above fit nicely together to give us a picture of what may be happening inside the spinal cord ventral roots in Post-Polio Syndrome. If so, some unresolved questions about PPS are closer to resolution:

1. Why does PPS only happen to some of us? *(Because we are genetically different from one another.)*
2. Why does it occur with different degrees of severity? *(There are several genes at work that may differ.)*
3. And finally, can it ever be treated? It seems we can improve our lot by decreasing the immune activity in the spinal cord. Possibly through the use of drugs to diminish the cytokines found in PPS, or possibly by infusion of IvIg or a smaller defined antibody immunoglobulin as yet uncovered. Plainly, we can interrupt PPS by finding ways to turn off the effects of immune chemicals inside our spinal cords. If these ideas pan out PPS should be manageable in the near future.

References.

1. Falconer, M. and Bollenbach, E. Survey results in process. Lincolnshire, 2006.
2. Rekand T; Kõrv J; Farbu E.; Roose M.; Gilhus N.E.; Langeland N.; Aarli J.A, "Lifestyle and late effects after poliomyelitis. A risk factor study of two populations" Acta Neurologica Scandinavica, Volume 109, Number 2, February 2004, pp. 120-125(6).[PubMed Abstract]
3. Falconer, M. and Bollenbach, E. "Late Functional Loss in Non-Paralytic Polio", Am J Phys Med Rehabil. 2000 Jan-Feb; 79(1):19-23.[PubMed Abstract]
4. Gonzalez, H. et al "Prior poliomyelitis - evidence of cytokine production in the central nervous system" J. Neurol Sci. 2002 Dec 15; 205(1); 9-13.[PubMed Abstract]
5. Gonzalez, H. et al "Prior Poliomyelitis - IvIg treatment reduces proinflammatory cytokine production" J. Neuroimmunol. 2004 May; 150(1-2): 139-44.[PubMed Abstract]
6. Kaponides, G. et al "The effect of intravenous immunoglobulin in patients with post-polio syndrome - an uncontrolled pilot study. Submitted at the Karolinska Institute 2005.
7. Gonzalez, H. et al. "Intravenous immunoglobulin for the post-polio syndrome'; a randomized controlled trial. Submitted as PhD Thesis at the Karolinska Institute 2005

The Lincolnshire Post-Polio Network
Registered Charity No. 1064177
An Information Service for Polio Survivors and Medical Professionals

All enquiries, book requests, medical article requests, membership fees, items for newsletters and donations to
The Secretary, Lincolnshire Post-Polio Network
PO Box 954, Lincoln, Lincolnshire, LN5 5ER United Kingdom
Telephone: +44 (0)1522 888601
Facsimile: +44 (0)870 1600840
Email: info@lincolnshirepostpolio.org.uk
Web Site: www.lincolnshirepostpolio.org.uk

The Lincolnshire Post-Polio Network takes great care in the transcription of all information that appears at this site. However, we do not accept liability for any damage resulting directly or otherwise from any errors introduced in the transcription. Neither do we accept liability for any damage resulting directly or otherwise from the information available at this site. The opinions expressed in the documents available at this site are those of the individual authors and do not necessarily constitute endorsement or approval by the Lincolnshire Post-Polio Network.

Document preparation: Chris Salter, Original Think-tank, Cornwall, United Kingdom.
Created: 25th January 2006.
Last modification: 21st January 2010.
Last information content change: 26th January 2006.