Amyotrophic Lateral Sclerosis

A PERSPECTIVE WRITTEN WITH THE INTENT OF HELPING PATIENTS AND THEIR CLOSE ONES UNDERSTAND THEIR DISEASE

Experience has taught me over many years, that patients diagnosed with ALS are bewildered and shocked as to why they should develop such a rare and nasty disease, especially when many of them have been fit and well prior to developing ALS symptoms.

Despite considerable world-wide efforts, ALS, in common with Alzheimer’s disease (AD), Parkinson’s disease (PD) and other neurodegenerations, have thus far failed to respond meaningfully to therapies in many clinical trials. This adds further to frustration, and patients rightly question why after so many years of research there has been a failure to develop fruitful therapy. In the past investment into ALS has been limited because it was being felt by public institutions, funding bodies, and private industry, that research on rare diseases is not worthwhile, being too difficult to do and unrewarding in terms of return of profit. However, within the last couple of decades this attitude has dramatically changed, with the realization that research on rare diseases also helps finding solutions for common disorders.

The simple answer to the present failure of therapy thus for all neurodegenerations, not just ALS, is that they are very complex disorders.

Three factors stand out:

First, ALS (and all neurodegenerations), has a long protracted pre-clinical course spanning years or decades in the absence of clinical manifestations. It may even be a developmental disorder of embryonic origin. So, by the time clinical manifestations
are apparent, the disease is already in an advanced stage. This has spurred exploration to identify markers of early (preclinical) disease with the hope of interventions that might slow or prevent further disease progression.

Secondly, ALS (and other neurodegenerations), is characterized by a multistep complex cascade of events leading to cell dysfunction and death. Many components of the cascade have now been identified, but their sequence, which ones are a consequence of rather than a cause of disease, and how they interact with each other remains elusive.

Thirdly, ALS is, as discussed later, is related to the “aging nervous system”. There is much we do not understand about aging. But, the fact that many individuals maintain a well functioning nervous system and continue productive lives through their seventies, eighties and even nineties is encouraging. This implies that, if the cellular and molecular mechanisms that determine whether the nervous system adapts positively or develops disease during aging can be identified, and the disease processes can be averted.

My aim is to highlight the complexity of ALS. Below I will outline just some of the events leading to cell death in ALS, understanding of which will unquestionably open the way to a host of potential new therapies within the coming years. This is not an exhaustive commentary and there are other important bimolecular aspects that space does not allow me to cover.

Mis-folded proteins:
Genetically controlled specific proteins are essential for normal cell function. However, over time (years), protein mis-folding occurs, a process whereby proteins become structurally abnormal and lose their specific 3-dimensional spatial configuration. As a result, protein aggregates accumulate in the cell. Up to a point, this can be prevented or regulated through an extensive protein homeostasis network. But, these defense systems decline with aging, accentuating protein aggregate deposition, which when too extensive overwhelms the cell, which in time becomes dysfunctional and dies.

About 95% of ALS cases are associated with aggregates of a protein called TDP-43. Furthermore, about 50% of patients with Frontotemporal Dementia (FTD) also have TDP-43 aggregates. A number of ALS and FTD patients, also share a mutation in a gene, the C9orf72 gene. In a small number of patient’s mutations in the gene encoding TDP-43 has been identified, but in the majority of ALS patients TDP-43 aggregates occur in the absence of a genetic mutation. Aggregation in ALS may be also be caused by other heritable mutations in disease proteins, but this too is rather rare. More about the inheritance in ALS is later.

Mis-folded protein aggregates target specific neuronal populations in ALS, (the neurons responsible for its symptomatology), whilst neighboring neuronal populations seem to remain unaffected. Maybe this is because the types of aggregate that form between brain regions may differ with some being more toxic compared to others. Alternatively, the physiological and functional differences between cells in different brain regions, may vary in their response to accumulation of mis-folded protein aggregates.

An important question is how protein aggregates spread? Since stopping their spread is a potential treatment. Spread might occur from cell-to-cell, or less directly by affecting the cell’s communication with the one(s) it is connected with. It has become clearer that accumulation of mis-folded protein alone does not define the vulnerability of specific neurons of neurodegeneration, which instead results only when misfolded protein accompanies a specific immune response related to inflammation (see next).

Neuro-inflammation:
Theories related to the role of neuro-inflammation in the progression of neurodegenerative diseases, including ALS, have gained considerable interest due to their therapeutic potential. It is known that a special (non-neuronal cell) called microglia can exert both neuroprotective but also a neurotoxic effects. Microglia, are the primary cellular component of the brain’s immune response. These complex and dynamic phagocytic cells secrete a host of factors, some of which are helpful and others are deleterious. These include several inflammatory substances that can initiate and perpetuate chronic inflammation. Strategies that aim in neutralizing toxic inflammatory release by microglia are being vigorously explored.

The extent of neurotoxic vs. neuroprotective behavior of microglia seems to vary from person to person and this may be one explanation for the variable progression of ALS seen in different people. There is a well orchestrated cross talk between motor neurons and microglia, and many studies indicate that microglial activation occurs before (or concomitantly with) the onset of clinical symptoms of ALS and increases during its disease course. There are many potential therapeutic avenues to counteract the effects of neuro-inflammation and some of these are presently under exploration.
Risk Factors:
A frequent question raised by patients is “have I been exposed to something in the environment?” An important unanswered question is; are there environmental or occupational triggers that start the cascade of events that lead to neuronal death in ALS.

Trauma, occupational or sports related physical activity, cigarette smoking, exposure to electromagnetic fields or electric shocks, military service and exposure to environmental lead or organic solvents have all been reported to increase the risk of acquiring ALS, and are possible triggers (not causes). However, many of these studies are based on small case numbers, or have been criticized on other methodological grounds. For now, only increasing age, certain genetic mutations (see below), and male gender are considered definite risk factors, although, smoking, pesticide exposure and dietary factors, especially premorbid fat intake are likely also relevant.

Over many years a search for an infective agent, especially a virus has failed to prove positive in relation to ALS. However, attention has recently highlighted the fact that the chronic inflammatory cascade associated with neurodegeneration, I have discussed above, has many similarities to the events that follow an acute infection. This has led to the hypothesis that any variety of a single or repeated (viral) infections may trigger ALS in susceptible persons.

Genetics:
Over the last decade, our knowledge about the heritability of ALS has greatly improved. The genetic architecture of ALS is complex consisting of a mixture of gene mutations that differ in noxiousness and in frequency. At the same time, it is clear that there is considerable missing heritability. More than 25 genes have been identified to be associated (this does not equate to cause) with ALS. Very few gene mutations have a high penetrance and these are causative in people with familial ALS. But, most genetic variants have a low penetrance and merely act as ALS risk factors. Nevertheless, they are important in the overall story.

Aging:
Aging is an undisputed risk factor for developing neurodegeneration. Cells in all regions of the nervous system are affected by aging, as indicated by the decline of sensory, motor and cognitive functions as we age. However, there is considerable variability among individuals in the apparent rate of aging, as well as the neural systems most affected, and if and how age-related deficits are compensated. There is a dramatic increase in the probability of developing a neurodegenerative disorder during the sixth, seventh and eighth decades of life. A person who lives to the age of 85 years is as likely as not to suffer from Alzheimer’s disease (AD) or Parkinson’s disease (PD), both most common in those above the age of 70. But, the probability of developing ALS rises sharply above the age of 40. The reason for the younger age related risk of developing ALS is unknown, but an important question to answer. Similarly, ALS is much less frequent than PD, which in turn is less frequent than AD. This variability in incidence rates of the different neurodegenerations also requires explanation.

“The future is certainly brighter than the past. Once we understand the mechanics of a machine the more readily we can repair it when it goes wrong. The same is true of biology. In depth knowledge of a disease and dissection of its components is the only way to develop meaningful therapy.”
IT’S NOT YET TOO LATE TO DOUBLE YOUR DONATION

Did you support our fundraising events this summer? Check if your workplace might be one of the companies that support their employees and retirees through a charity matching gift. Please visit your human resources or payroll department if your employer offers the following:

- Match your charitable donation, normally an employer matching form needs to be completed by the employee in order to initiate the matching gift.
- If you like volunteering, some employers provide grants for the volunteer time of their employees.
- If your company is tied up with the annual United Way or HealthPartners campaign, you can designate your gift to ALS Society of BC.

Don’t miss the opportunity to double the impact of your support to the charity you are helping.

Legal Name of the Society: Amyotrophic Lateral Sclerosis Society of British Columbia
Charitable Tax Number: 10670 8985 RR0001
Phone: 1-800-708-3228   Fax: 604-278-4257   Email: info@alsbc.ca

ALS Compassionate Heart  $59.95
$20 from the sale of each necklace will be donated back to the ALS Society of BC

Contact:
Jeannine Barnett, Jewelry Stylist

(604) 808-5824
Email: jeannijewel@telus.net
www.fifthavenuecollection.com/jbarnett
Living with ALS Support Groups

The groups provide an open, friendly and safe environment for ALS patients, family members, friends and caregivers to discuss issues related to living with ALS. ALS BC trained volunteers facilitate the groups, and they are a major point of contact between the Society and the ALS community. We recognize support groups aren’t for everyone, but we also know that not too many people know exactly how fun support groups can be. We laugh and learn so much that it is hard to imagine why some people choose to “go it alone.” Just know we’re here when you need us.

<table>
<thead>
<tr>
<th>Location</th>
<th>MEETING</th>
<th>LOCATION</th>
<th>CONTACT</th>
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</thead>
<tbody>
<tr>
<td>Abbotsford</td>
<td>Last Saturday of each month</td>
<td>Ross Road Community Church</td>
<td>Dave Walman</td>
</tr>
<tr>
<td></td>
<td>(except July, August, and December)</td>
<td>3160 Ross Road, Abbotsford</td>
<td>604.837.5383</td>
</tr>
<tr>
<td></td>
<td>2–4pm</td>
<td></td>
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<tr>
<td>Kamloops</td>
<td>3rd Friday of each month</td>
<td>Brock Activity Centre</td>
<td>Pat Tomlinson</td>
</tr>
<tr>
<td></td>
<td>1–3pm</td>
<td>9A 1800 Tranquille Road, Kamloops</td>
<td>250.319.4516</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td><a href="mailto:pa1697@telus.net">pa1697@telus.net</a></td>
</tr>
<tr>
<td>Kelowna</td>
<td>Last Friday of each month</td>
<td>Trinity Baptist Church</td>
<td>Louise Adderley</td>
</tr>
<tr>
<td></td>
<td>(except July, August, and December)</td>
<td>1905 Springfield Road</td>
<td><a href="mailto:loumar4@shaw.ca">loumar4@shaw.ca</a></td>
</tr>
<tr>
<td></td>
<td>1–3pm</td>
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<tr>
<td>North Central Island</td>
<td>1st Wednesday of each month</td>
<td>Nanaimo Ecumenical Centre</td>
<td>Shirley Theriault</td>
</tr>
<tr>
<td></td>
<td>1:30–3:30pm</td>
<td>6234 Spartan Road, Nanaimo</td>
<td><a href="mailto:Shirley.Theriault@yahoo.ca">Shirley.Theriault@yahoo.ca</a></td>
</tr>
<tr>
<td>Surrey</td>
<td>Last Tuesday of each month</td>
<td>17567 57th Avenue, Surrey</td>
<td>Alexandra Guerrero</td>
</tr>
<tr>
<td></td>
<td>(except July, August, and December)</td>
<td></td>
<td><a href="mailto:patientservices2@alsbc.ca">patientservices2@alsbc.ca</a></td>
</tr>
<tr>
<td></td>
<td>2–4pm</td>
<td></td>
<td></td>
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<tr>
<td>Vancouver &amp; Area</td>
<td>Last Wednesday of each month</td>
<td>The Fair Haven United Church Homes</td>
<td>Alexandra Guerrero</td>
</tr>
<tr>
<td></td>
<td>(except July, August, and December)</td>
<td>2720 E 48th Avenue, Vancouver</td>
<td><a href="mailto:patientservices2@alsbc.ca">patientservices2@alsbc.ca</a></td>
</tr>
<tr>
<td></td>
<td>10:30am–12pm</td>
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<tr>
<td>Victoria</td>
<td>3rd Sunday of each month</td>
<td>Health Unit</td>
<td>Ellen Mahoney</td>
</tr>
<tr>
<td></td>
<td>(except June [the 2nd Sunday]; July and August)</td>
<td>1947 Cook Street, Victoria</td>
<td>250.920.9502</td>
</tr>
<tr>
<td></td>
<td>2–4pm</td>
<td>Use side door off parking lot.</td>
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</tbody>
</table>

Would you like to participate or start a support group in your area? We provide training!

To find out more details about dates and locations of upcoming events, please contact:

P 604.278.2257 ext. 226   E patientservices2@alsbc.ca

Thank you to the Province of British Columbia for sponsoring the Support Group Program of the ALS Society of BC through the BC Gaming Community Grant.
Donation of Stocks and Mutual Funds

Donating appreciated stocks or mutual funds is the most tax-effective way to make an outright gift during your lifetime or as part of a legacy gift.

Current legislation in Canada has eliminated the capital gain tax on gifts of publicly traded securities, mutual funds, and bonds to registered charities. A charitable tax receipt will be issued for the fair market value of the securities. No capital gains tax owing if gifted to a public charity.

If you want to learn more or plan to make a stock donation at year-end, please download the stock donation form available on our website at www.alsbc.ca. Alternatively, you can contact the office at 1.800.708.2257 ext. 225 or email info@alsbc.ca.

Legal Name: Amyotrophic Lateral Sclerosis Society of British Columbia
Charitable Registration #: 10670 8985 RR0001
Mailing address: ALS Society of BC
1233 – 13351 Commerce Parkway
Richmond, BC V6V 2X7

GOLFATHON FOR ALS

During the month of June, Golf Professionals lent their muscles and golfed from sunrise to sunset to support those living with ALS.

They raised over $188,000!

Thank you!

www.golfathonforals.com
This is a special day designed for those providing care to People with ALS. This invitation is for primary caregivers, family members, friends and also caregivers who have recently lost someone with ALS.

🌞 Burnaby: Wednesday, October 10th 2018
   The Element Vancouver Metrotown

🌞 Surrey: Thursday, October 11th 2018
   Northwiew Golf & Country Club

🌞 Kelowna: Thursday, October 18th 2018
   Kelowna Golf and Country Club

🌞 Nanaimo: Thursday, October 25th 2018
   Fairwinds Golf Club

🌞 Victoria: Friday, October 24th 2018
   Highland Pacific Golf

Registration fee of $25 includes continental breakfast & lunch
RSVP is mandatory. For more information contact:

Alexandra Guerrero
Patient Services Coordinator
Toll Free: 1-800-708-3228 / 604-278-2257 ext. 226
patientservices2@alsbc.ca

Funding provided by the George “Sonny” Williams Endowment Fund
Events Around the Province

Cam Fleming and Robert Boscacci owners of HME Mobility and Accessibility, presenting sponsors of the WALKs for ALS in BC and the Yukon.

Margaret Storey, President Prince George Legion Branch #43 presents donation to ALS BC volunteer Sheldon Clare.

Diana Wolensky, president and Wayne Saboe past president of the Kamloops Elks Lodge #44 present $500 donation to ALS BC Kamloops WALK for ALS Coordinator and Kamloops ALS BC Support Group facilitator, Pat Tomlinson.

Sandra Kumbier wins the trip for 2 anywhere West Jet Flies raffle.

ALS BC volunteer Karin Penner receives donation from Richard Poelman, president UCT Council 1024 Cranbrook.
Grade 7 student from Vancouver Talmud Torah, Ishay Levin raised $1,128.93 for ALS as part of the Mitzvah of Valuing Philanthropy initiative. He presents cheque to Wendy Toyer.

The iconic sails sculpture located in downtown Kelowna lit up in the colour purple on June 1st, which was the launch of June ALS Awareness month, to show support of people living with ALS.

Employees of RBC received thanks for their volunteerism at the ALS Society of BC office preparing for the June WALKs for ALS.
ANNUAL MEETING
Sunday, September 9, 2018
Health Unit located at 1947 Cook Street. Enter side door off parking lot.

Agenda
- Meeting called to order
- Terms of Reference (distributed)
- 2017 Audited Financial Statements and Annual Report (distributed)
- President’s Report – President John Hamilton
- Election of Officers

Only members in good standing of the ALS Society of BC are eligible to vote and hold office. (Members in good standing have paid their annual/lifetime membership fees or are living with ALS).

CALL FOR NOMINATIONS
Any member in good standing is eligible to be nominated as a Director at Large. Elected Directors serve a term of one year, from September 2018 to September 2019.

The election of directors representing all elements of the ALS community in BC is critically important for the Chapter to fulfill its stated purpose. For the same reason, it is very important that elected directors commit the time needed to be effective during the year.

If you are able to commit the time needed and believe that you could play an invaluable role on the Chapter’s executive, please contact:

Wendy Toyer, Executive Director ALS Society of BC
Phone: 1-800-708-3228 ext. 222 or Email W.toyer@alsbc.ca
Bill Erving and Sandra Ayer cut cake

Victoria Support Group
Victoria WALK for ALS

Sunday, September 16, 2018
University of Victoria, Parking Lot 10
3800 Finnerty Rd, Victoria, BC V8P 5C2
Registration: 11:30 am | Walk Starts: 1:00 pm

FOR MORE INFORMATION
Walk Coordinator - Sean Houlihan
victoriawalk@alsbc.ca

REGISTER TODAY!
www.walkforals.ca

www.walkforals.ca
presented in BC and the Yukon by

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The ALS Society of BC & Yukon Believes

• Volunteers are a vital human resource.
• Volunteers have a unique and essential contribution to make to all aspects of ALS work.
• That the profile of our volunteer force should reflect the profile of the community in order that the ALS Society of BC & Yukon can benefit from a wide range of skills, experience, perspective, and have the greatest impact upon the community.
• Volunteers should be able to participate in the work of the ALS Society of BC & Yukon solely on the basis of their ability to contribute. There should be no discrimination on any other basis.
• That in particular those currently affected by ALS should be enabled to contribute their knowledge and skills through volunteering.
• That volunteers and staff will flourish in an environment of:
  - Respect, listening, and openness to new ideas
  - Willingness to give and take criticism
  - Responsiveness to the changing environment

Volunteer Positions Available

• Office Support Volunteer
• Support Group Facilitators (including Grievance Support Groups)
• Support Group Assistants
• Special Event Volunteers
• Fundraising Volunteers
• Public Awareness Volunteers (including ALS Display Booth & Speakers Bureau)
• Special Event Committee Member (help with the planning and execution of one of our many different fundraising/awareness events)

For more information contact: volunteer@alsbc.ca
North Central Island Chapter Contacts

Sheldon Cleaves  
President

Shirley Theriault  
Secretary

Betty Edwards  
Director at Large

NCIC President Sheldon Cleaves and Murray Chandler were recognized. Sheldon was named the ALS Society of BC Volunteer of the Year and Murray received the ALS Society of BC Outstanding Public Awareness Award.

↑ Ladysmith Eagles, Sheila Williams presents $1,000 donation to Shirley Theriault, North Central Island Chapter Secretary

↓ Cam Fleming and Robert Bosacci Presenting sponsors of the WALK for ALS in BC & Yukon attended the WALK 9 for ALS Golf Tournament held at Cowichian Golf Course in support of the Mid Island WALK.

↑ Mid Island WALK for ALS
Nanaimo Support Group. In memory of Bev Trickey, support group facilitator who passed away on July 30th (seated with flowers). She will be missed by many.

Murray Chandler and Christina Brown share a pint with Jennifer Dwyer at the launch of the Brenna A Saison beer at Mount Arrowsmith Brewery, Parksville. $3,732, proceeds from the launch, were donated to the Mid Island WALK for ALS. Partial proceeds from the sale of Brenna A Saison will be donated to ALS BC.
ALS PATIENT SERVICES PROGRAMS

Equipment Loan Program
With 3,030 pieces of medical equipment our Equipment Loan Program is designed to help people cope with the daily challenges of decreasing mobility and independence, through obtaining basic and essential assistive equipment. This includes mobility equipment, lift equipment, beds & accessories, communication devices, and bathroom aids, if needed. All equipment loaned is available at no charge to registered ALS patient members.

Transportation Support Program
The Transportation Assistance Support Program provides transportation assistance for people living with ALS who are unable to fund transportation themselves to attend appointments at the ALS Centre and ALS BC sponsored events such as support groups. Determination of financial needs will be on the honour system.

Support Groups
Support groups provide an open, friendly and safe environment for ALS patients, family members, caregivers and friends to discuss issues related to living with ALS. Groups are facilitated by experienced volunteers.

Psychological Treatment Services
Psychological treatment services are available free of charge at locations across BC. Registered Psychologists and Clinical Counselors provide much needed therapy and counseling to ALS Patients, their families and caregivers at any stage of the illness. Services will be provided throughout the disease and up to one year following.

Day of Caring
Held every Fall in communities around BC, Day of Caring is a chance for the full-time primary caregivers of ALS Patients to have a day of respite. This event allows for people who devote themselves to the care of their loved ones to come together and share experiences. It also provides the opportunity to learn how to take better care of themselves and how to cope with grief.

Camp Alohi Lani
In August ALS BC hosts a camp for youth who have a Parent (or Grandparent in a significant role) Living with ALS. ALS BC is extremely pleased to be able to offer this weekend retreat at no cost to families. Camp Alohi Lani, which means ‘Bright Sky’ in Hawaiian, is a safe setting in which youth aged 8–17 years can come together and receive support for their own journey. Most importantly Camp Alohi Lani offers campers an opportunity to meet other youth from across BC and make connections with peers.

Care Connections
The primary purpose of forming a Care Connection is to reduce caregiver responsibilities and reduce the worry the person with ALS has about their caregiver. By caring for the caregiver, the person with ALS is helped as well. The ALS Society of BC’s Care Connection is a program to aid your own group of caring family and friends to help their loved ones with ALS and their caregivers.

Mobile Clinics
In partnership with Vancouver Coastal Health and the ALS Centre @ GF Strong Rehab Centre, the ALS Society of BC provides Mobile Clinics to outlying communities. ALS Centre healthcare professionals and an ALS Society of BC representative travel to clinic locations to provide follow-up appointments for people challenged to travel.

All that is required to access these programs is the patient’s registration with ALS Society of BC. No fees are charged.

PARTNERS WHO CAN HELP

ALS Centre at GF Strong Rehab
604-737-6320

Respiratory Equipment and Support:
Provincial Respiratory Outreach Program
1-866-326-1245

Communication Equipment and Support:
Communication Assistance for Youth and Adults
604-326-3500

SUPPORT NETWORKS:
ALS BC Support Groups
www.alsbc.ca/Services

Patients Like Me
www.patientslikeme.com

BC Caregivers 24 Hour Support Line
1-877-520-3267

THANK YOU TO OUR PROVINCIAL PARTNER

British Columbia
The Best Place on Earth

Amyotrophic Lateral Sclerosis Society of British Columbia

1233 – 13351 Commerce Parkway
Richmond BC V6V 2X7

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F 604.278.4257
TF 1.800.708.3228
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E receipt@alsbc.ca

Danielle Capa
Support Coordinator
E support@alsbc.ca

Angela Schibild
Administration & Support Coordinator
E admin@alsbc.ca

The ALS Society of BC is dedicated to providing direct support to ALS patients, along with their families and caregivers, to ensure the best quality of life possible while living with ALS.

Through assisting research, we are committed to find the cause of, and cure for Amyotrophic Lateral Sclerosis (ALS).