



International Symposium
on
**Rheumatic Diseases in
Indigenous North American
Populations**
... from Molecules to Communities

Meeting Outcomes Report
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CENTRE for Aboriginal Health RESEARCH

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Executive Summary

Rheumatic diseases exhibit a high prevalence among indigenous North American (INA) populations, causing significant debility for individuals, their families and their communities. These conditions often appear earlier in life and with greater severity than in the general population.

Yet, despite the high burden of rheumatic diseases in these groups, very few studies have been done to uncover the molecular origins of these diseases, document their clinical progression, understand differences between populations, map associations between rheumatic diseases and comorbidities, or describe how these diseases affect individuals, families and communities. Furthermore, little is documented about how well health care systems serve indigenous persons affected by a rheumatic disease, or whether traditional medicine could potentially offer benefits. Guidance is needed for research funding organizations to help address these gaps.

Conference objectives

The *International Symposium on Rheumatic Diseases in Indigenous North American Populations ... from Molecules to Communities* brought together a diverse group of over 100 participants from the research and indigenous communities to present and discuss what is known about rheumatic diseases in INA populations. The output of the meeting was a list of recommendations for research themes and questions that will inform the priorities of funding organizations. Taken together, these will help to shape a well-balanced and cohesive research agenda aimed at improving the health outcomes of indigenous peoples.

Key themes and learnings

The meeting was organized in two parts. Presentations describing the current state of research, including discussions among speakers and participants, were followed by a prioritization exercise in which recommendations for research questions were developed.

Key themes and learnings from the presentations included:

- The burden of disease is usually greater, in terms of prevalence and disease severity, among INA populations than in the general population;
- There are important differences between indigenous and general populations in the molecular basis of disease, clinical characteristics and health services delivery;

- The impact of environmental factors on rheumatic diseases is important but poorly understood; unique genetic characteristics of specific INA populations interact with environmental factors to increase disease susceptibility in these populations;
- There are significant variations among different INA populations related to all of the above factors;
- There are different perspectives on health between the Western model, which focuses on treatment of the individual with a disease, and the indigenous approach which focuses on the full spectrum of well-being and takes into account the individual, the family and the community;
- Indigenous practices, such as traditional medicines and integrated models of health services delivery, need to be further explored and applied;
- Engaging indigenous peoples in research projects requires a new approach, building on established ethical guidelines and rights of indigenous people, and considering the health and social implications for individuals, families and communities.

Community-based participatory research recommendations

Throughout the meeting, discussions focused on two distinct but inter-related areas: defining research questions of scientific interest and creating the enabling tools to achieve community-based participatory research (CBPR). CBPR means that indigenous groups are fully involved and make the final decisions at every stage of the research process, from the development of questions, to the conduct of the study, to the analysis, interpretation and dissemination of results. To achieve this state in the context of rheumatic diseases research, the meeting participants identified the following gaps:

- Ethical guidelines need to be expanded to address specific situations;
- Practical models of CBPR must be developed; and
- Capacity must be built within the research and indigenous communities.

Scientific recommendations

Research questions of scientific interest were addressed within six disciplines: ethics; partnerships, traditional medicine and knowledge translation; epidemiology; basic research; health services delivery; and pediatrics.

Research questions relating to ethics covered a broad range of topics that built upon the existing guidelines from the Canadian Institutes for Health Research. Priorities were developed under three broad themes: 1.) Rights related to data protection, cultural property rights, and the use and preservation of biological materials;

2.) Rights of the individual, the family and the community; and 3.) Social and cultural implications of disease risk testing.

In the area of ‘partnerships, traditional medicine and knowledge translation’, it was concluded that a much greater understanding of traditional medicine and healing is needed, although it was identified that an inherent mistrust of Western scientific methodology and opportunism is a significant barrier to achieving this understanding.

Many of the scientific questions attempted to address the paucity of research by building solid foundations for future studies. Robust databases of information need to be designed and populated which take into account the unique features of rheumatic diseases in INA populations. Epidemiologic information is needed that describes, among many other items, the characteristics of rheumatic diseases and the influence of environmental factors on the development of disease. In the basic and clinical research area, recommendations focused on developing new models with which to more accurately classify rheumatic diseases in indigenous populations, particularly through identifying biomarkers. Similarly, new models are needed that define optimal care for rheumatic diseases in INA populations, and against which current health care services can be evaluated.

These research questions and themes apply equally to pediatric INA populations. In addition, some specific questions were outlined. A better understanding is needed of the epidemiology of childhood rheumatic diseases (distinct from its adult counterpart), and to probe the earliest determinants of disease in INA populations. New health care service models are needed to address adolescent transitions in care.

Implications for research beyond rheumatic diseases

Each of the research areas discussed at the symposium is interconnected and in some cases they are interdependent. Also importantly, the study of rheumatic diseases offers a portal through which our understanding other chronic conditions affecting INA populations can be advanced. For example, because the etiology of rheumatic diseases is inflammatory, these conditions may offer clues about other chronic disorders with the same underlying processes, such as multiple sclerosis, diabetes and cancer. Many research disciplines offer learnings that can be broadly applied:

- Differences in genetic patterns seen in INA populations may offer new insights into disease classification;
- Environmental factors interacting with unique genetic predisposition affect the course and evolution of disease; understanding this interaction may point to new, integrated models of health care where intervention centred around

modulating key factors has a substantial impact on a wide spectrum of health outcomes;

- Associations of rheumatic diseases with comorbidities, such as depression and cardiovascular disease, may be applicable to other chronic progressive diseases.

At the societal level, studies of rheumatic diseases can offer insights into the impact of chronic disorders on the individual, the family and the community, since these conditions involve experiences of pain, disability, mental distress and stigmatization.

A key element is the research process itself, and the strong relationships between rheumatic diseases researchers and indigenous communities in Manitoba and British Columbia offer models of community-based participatory research that can be applied to all areas of study with indigenous populations. Similarly, ethical questions surrounding the conduct of research in rheumatic diseases apply across many other fields. Advancing our understanding of the power of traditional medicine and how this can be integrated into health care systems may help to improve the well being of all indigenous populations by creating harmony rather than tension in the care of individuals with chronic diseases.

Table of Contents

Executive Summary.....	i
Table of Contents.....	v
Definition of Key Terms.....	vi
Introduction	1
Meeting Outcome: Research Priorities.....	7
1. Research Priorities for ‘Enabling Tools’	7
1.1 A vision for community-based participatory research	7
1.2 Enabling tools for CBPR.....	9
1.3 Research priorities for ‘Enabling Tools’	10
2. Scientific Research Priorities	13
2.1 Ethics.....	13
2.2 Partnership in Science, Traditional Medicine/Healing and Knowledge Translation.....	17
2.3 Clinical Epidemiology	19
2.4 Basic Research	21
2.5 Health Care Delivery and Public Health.....	23
2.6 Pediatric Rheumatic Diseases.....	25
Conclusion	28
Appendix A Program	29
Appendix B Presentation Summaries	33
Appendix C CIHR Guidelines For Health Research Involving Aboriginal People	70
Appendix D Attendees.....	75
Appendix E Selected Bibliography	82

Definition of Key Terms

ACPA	Anti-citrullinated protein antibody (see also CCP). Anti-CCP is a blood test used during the diagnostic evaluation of a person who may have rheumatoid arthritis. If present in such a patient at a moderate to high level, it not only confirms the diagnosis but also may indicate that the patient is at increased risk for damage to the joints.
allele	One of a series of different forms of a gene.
ANA	Anti-nuclear antibody. A biomarker indicative of autoimmunity that is frequently found in patients with systemic lupus erythematosus (“lupus”. SLE), rheumatoid arthritis (RA), and other autoimmune diseases. Detected by a blood test.
ankylosing spondylitis	A type of arthritis that causes chronic inflammation of the spine and the sacroiliac joints. Chronic inflammation in these areas causes pain and stiffness in and around the spine. Over time, chronic spinal inflammation (spondylitis) can lead to a complete cementing together (fusion) of the vertebrae, a process called ankylosis. Ankylosis causes total loss of mobility of the spine.
CAN	Canadian Arthritis Network Centres of Excellence
CCP	Anti-cyclic citrullinated peptide antibody (see also ACPA). Biomarker for rheumatoid arthritis, detected by a blood test.
CIHR	Canadian Institutes for Health Research
DAS	Disease activity score. A combined measure of clinical and blood test results that summarizes the overall activity of rheumatoid arthritis in an individual.
epidemiology	Epidemiology is the study of factors affecting the health and illness of populations, and serves as the foundation and logic of interventions made in the interest of public health and preventive medicine.
epigenetic	Molecular factors that influence gene expression and phenotype and modulate the effects of the inherited genome.
genotype	The inherited genetic constitution (the genome) of individual cells, and, in turn, of the entire organism or individual.
HLA	Human leukocyte antigen. Cell surface proteins involved in regulating immune responses that can serve as biomarkers associated with specific rheumatic diseases, detected by a blood test.
IAPH	Institute for Aboriginal Peoples Health. One of CIHR’s 13 institutes. Located in Edmonton, Alberta.

INA	Indigenous North American
NEAHR	Network Environments for Aboriginal Health Research. A network of nine research centres located across Canada and funded by CIHR, each having a focus on different aspects of Aboriginal health research.
NIHB	Non-Insured Health Benefits. Program of the federal government of Canada to cover health services that are not insured under the <i>Canada Health Act</i> for registered First Nations and Inuit, such as prescription drugs, dentistry and medical travel.
OCAP	Ownership, control, access and possession. Principles developed by the Assembly of First Nations for the collection, use and stewardship of research data.
phenotype	A phenotype is any observable characteristic or trait of an organism such as its morphology, development, biochemical or physiological properties, or behaviour. Phenotypes result from the expression of an organism's genes, as well as the influence of environmental and epigenetic factors.
rheumatic disease	Any of several systemic diseases characterized by inflammation and pain in joints and muscles, but can also involve other organs and tissues Common rheumatic diseases include: <ul style="list-style-type: none"> • rheumatoid arthritis (RA) and juvenile rheumatoid arthritis (JRA) • systemic lupus erythematosus (SLE) • ankylosing spondylitis (AS) • Sjogren's syndrome • gout • rheumatic fever
RA	Rheumatoid arthritis. A chronic, inflammatory form of arthritis.
residential schools	In the past, Aboriginal children in Canada were forcibly removed from their families and sent to live in distant schools. Residential schools, run by churches, operated in Canada from the 1800s until 1996. Many students were physically and sexually abused at these institutions, received inadequate food and clothing, and many died from diseases (often without their families being notified). This experience is generally accepted to have had a detrimental intergenerational impact. Since these children did not learn parenting skills, this is thought to have contributed to their own

	abusive behaviours towards themselves and their families in later life. (See also 'sixties scoop'.)
RF	Rheumatoid factor. A biomarker indicative of autoimmunity that is detected in the blood of persons with a number of rheumatic diseases, particularly rheumatoid arthritis.
SE	Shared epitope. A sequence of amino acids that is part of an HLA molecule (see HLA) that has been associated with risk for rheumatoid arthritis.
Sixties scoop	During the 1960s, a large proportion of Aboriginal children in Canada were forcibly removed from their families, according to government policies of the time, and placed into foster homes or were adopted by non-indigenous families. (See also 'residential schools'.) Many families were permanently broken apart and it was later revealed that many of these children were abused in their new homes.
SLE	Systemic lupus erythematosus (sometimes called simply 'lupus'). An autoimmune disease that can take several forms. It can affect any part of the body, but most commonly attacks the skin, joints, heart, lungs, blood, kidneys and brain.
SNP	Single nucleotide polymorphism. Variation in a single nucleotide in the DNA strand that may or may not result in a change in an expressed gene. SNPs are now used widely to understand how genetic variation causes diseases.

Introduction

Rheumatic diseases begin with molecular changes in the body, based on genetic constitution and influenced by environmental factors. These changes may initially be subtle and not cause any symptoms, but over time can progress to produce devastating life-long chronic diseases. Ultimately, the impact of these events is profound, as they affect not only individuals but also their families and communities. The subtitle of this symposium “... *from Molecules to Communities*” speaks to the many levels at which rheumatic diseases were examined during this meeting. These explorations are the subject of this report.

Rheumatic disease symptoms are frequent in INA populations. Surveys conducted in several communities indicate that up to one in four persons reports suffering from some form of “arthritis” – over 40 per cent more than that reported in the general population. Rheumatoid arthritis (RA), the most common form of inflammatory rheumatic disease, has been shown to be prevalent in many INA populations with prevalence rates of up to two to three per cent – more than twice the rate of most populations worldwide. Because RA and other rheumatic diseases tend to be more severe in indigenous populations, the resulting disability affects not only the individual’s health status, social capacity and economic well-being, but also those of their families and communities.

What are rheumatic diseases?

Rheumatic diseases are a spectrum of systemic conditions characterized predominantly by inflammation and pain in joints and muscles. Although the musculoskeletal inflammation causes many of the symptoms of rheumatic diseases, and can result in progressive functional disability, these disorders can also involve other organs such as the kidneys and lungs. These latter complications can lead to considerable decline in general health and premature death. Common rheumatic diseases include: rheumatoid arthritis (RA), juvenile rheumatoid arthritis (JRA), systemic lupus erythematosus (SLE) and ankylosing spondylitis (AS). In these diseases, the person’s immune system becomes activated, for unknown reasons, and attacks the musculoskeletal structures and internal organs. For example, in rheumatoid arthritis the synovium (a thin layer of tissue lining the joints and tendon sheaths) is the target of the immune attack. Chronic inflammation in the synovium results in damage to the adjacent cartilage and bone. Over the years, this progressive damage to the joints and surrounding structures causes pain and stiffness, and often leads to permanent deformity and disability. In lupus, the immune attack can be focused on

the kidneys leading to permanent loss of kidney function and ultimately the need for dialysis and transplantation. Similar processes occur in other rheumatic diseases which can affect different body systems.

What is the impact of rheumatic diseases on INA populations?

Awareness of the devastating impact of rheumatic diseases on indigenous North American peoples has been growing over the last decade or more. The lack of published literature on this subject, however, has made firm conclusions difficult. The few studies that do exist describe much higher rates of prevalence and greatly increased severity of rheumatoid arthritis in many of the indigenous populations studied. Other rheumatic diseases, such as lupus and spondyloarthropathies, are also more common and more damaging in some indigenous groups.

How is the field evolving?

Over the past two decades there have been profound innovations in the treatment of rheumatic diseases such as RA, lupus, and ankylosing spondylitis. In particular, the early identification of disease combined with timely use of highly effective therapies has dramatically affected the burden of these diseases and improved the outcomes. Yet, despite the clear need for greater knowledge about rheumatic diseases in INA populations, this field of investigation is still at a very early stage. We know little about the epidemiology of rheumatic diseases in these peoples and the impact of environmental forces on the manifestation and progression of rheumatic diseases remains at a very early stage of understanding. Intriguing differences in genetic and phenotypic patterns suggest that conventional medical assessments and interventions may be inappropriate, yet there are no validated tools to measure the impact of these diseases in North Americans of indigenous descent. Traditional medicine is an integral part of INA culture and plays a potentially beneficial role in the management of a spectrum of diseases, however this aspect of native cultures is not well understood.

Throughout the past two decades, a network of researchers with an interest in this area has evolved. Encouraged by the federal funding agencies of the American, Mexican and Canadian governments, specialized multidisciplinary teams have formed to address these wide-ranging research questions.

A relatively new phenomenon that will shape the future evolution of the field is the movement towards active participation in research by indigenous communities themselves. Community-based participatory research (CBPR) involves indigenous groups setting the research agenda and collaborating with university-based

researchers to do the work. This concept is quite advanced in some areas of the U.S., where federal research funding flows directly to some of the larger Native health organizations. In Canada, the approach to CBPR is becoming more organized. Historically, individual First Nations have engaged in formal or informal research partnerships with university-based researchers for specific projects. Canada is now at a turning point in this regard, as a broader vision of CBPR is being promoted by the Institute for Aboriginal Peoples Health – one of the Canadian Institutes for Health Research (CIHR) – and adherence to these guidelines will be a prerequisite for future funding.

Towards a research agenda

Recognizing the importance and urgency of these issues, the Canadian Arthritis Network (CAN) and the CIHR jointly requested that a symposium be held to develop a cohesive research agenda on rheumatic diseases in indigenous North American populations. Both of these organizations are prepared to commit funds for research in this area and are seeking guidance from stakeholders on the directions that these investigations should take.

The International Symposium on Rheumatic Diseases in Indigenous North American Populations...from Molecules to Communities was a response to this request. Organized by the Division of Rheumatology and the Centre for Aboriginal Health Research (CAHR) at the University of Manitoba, the symposium consisted of a two-day meeting involving a diverse array of stakeholders from Canada, the U.S. and Mexico. Participants included researchers, physicians and students from a number of disciplines (epidemiology, genetics, pediatrics, rheumatology, nursing, sociology, statistics) and representatives from INA communities (consumers, elders, political leaders, community health resources and health policy advisors).

Although preliminary, the research agenda developed at this conference addresses many aspects of rheumatic diseases which have broader implications for other health conditions. Because of the commonalities among chronic diseases (such as diabetes, heart disease and chronic inflammatory diseases), research strategies for rheumatic diseases may potentially become models for improving health outcomes in other disorders affecting indigenous peoples. For instance, techniques used to understand the interplay between genetic predisposition and environmental factors in the onset and progression of disease can be applied to other chronic diseases. Unravelling the interrelationships between rheumatic diseases and mental health may offer clues for interventions that could benefit other conditions. Models of community-based

participation in studies of rheumatic diseases will find application in all areas of health research.

Theme and objectives of the symposium

The theme of a dream-catcher, made especially for this symposium by a First Nations man with severe psoriatic arthritis, embodied the spirit of the meeting. By capturing the expertise, perspectives and hopes of many people from different backgrounds, the best ideas were debated and distilled as priorities for research.

There were five main objectives for the meeting:

1. To describe what we know;
2. To explore the scope of what we don't know;
3. To discuss what we need to know and why;
4. To find out how we can work together better; and
5. To establish research priorities.

Meeting organization

The symposium was organized in two parts. To create a common foundation of knowledge, information was shared through presentations and posters by researchers and by persons from indigenous communities who are affected by rheumatic diseases. Discussion and dialogue followed each section. The presentations were grouped into topic areas, beginning with the patient's perspective on the disease, then moving to a discussion about how rheumatic diseases are managed within health care systems in North America and to ethical considerations of researching rheumatic diseases in indigenous populations. Finally, a discussion on scientific topics such as genetics and epidemiology explored our understanding of the molecular basis for rheumatic diseases and the implications for people.

The second part of the meeting addressed the development of a research agenda. This consisted of a priority-setting exercise which built on the information presented. Beginning with a list of research priorities submitted by participants in advance of the meeting, the attendees were invited to add further suggestions, resulting in a 'long list' of priorities in each of six subject areas:

1. Ethics;
2. Partnerships/traditional medicine/knowledge exchange;
3. Epidemiology;
4. Basic research;
5. Health services delivery/public health; and
6. Pediatric rheumatic diseases.

Small group sessions in each topic area were tasked with narrowing down the long, unabridged list to a few research priorities, which were then presented back to the main group.

Meeting outcome

The symposium participants identified many fundamental areas of need for research. Because there are so few existing studies and little research infrastructure, many of the recommendations focused on building a foundational platform that will enable researchers to investigate important questions about rheumatic diseases in INA populations.

It is also important to note that, although the areas of focus are presented separately in this report, these disciplines operate synergistically in practice. For example, genetic research will inform how epidemiology studies are conducted, and vice-versa. In turn, these will inform research in health services delivery. Pediatric rheumatic diseases research cuts across all of the disciplines. Research into ethics, models of community partnerships and traditional knowledge will provide guidance to the conduct of all studies involving indigenous populations.

In the discussions throughout the meeting a clear distinction was made between questions of purely scientific interest and those related to advancing models for collaboration between researchers and INA communities. There was considerable overlap among the topic areas concerning the tools needed to work effectively with communities. For this reason, the research priorities advanced at the symposium are presented in this report in two parts: 'Enabling Tools' and 'Scientific Questions'.

The priorities are described in broad terms and are intended to give general direction. Under each priority, specific research questions are identified as examples that give the reader a sense of the variety and scope of projects that could be contained under this heading.

Feedback and knowledge gained

The participants' response to the symposium was very enthusiastic. Meeting evaluations reflected the importance of a multi-stakeholder approach to addressing the research agenda and appreciation for the diversity of viewpoints expressed at the meeting.

Feedback also indicated that there had been an important exchange of knowledge, not only among the scientific disciplines but also between the indigenous and non-indigenous participants.

This symposium was an important first step in building relationships that will help the scientific and indigenous communities take the research agenda forward. A critical component will be the continued inclusion and expanding role for indigenous peoples in determining the research agenda and in working collaboratively with researchers to improve the health and well-being of those affected by rheumatic diseases.

Meeting Outcome: Research Priorities

A key goal of the symposium was the development of a list of research priorities intended to guide funding organizations. These will be useful in directing research grants to areas of greatest need and in creating synergies between fields of research.

As noted in the Introduction, the research priorities identified by the meeting participants fell into two broad categories: ‘Enabling Tools’ and ‘Scientific Research Priorities’. Because the movement towards a community-based participatory research (CBPR) approach is still relatively new in many jurisdictions, there was much discussion about how this could be achieved in the field of rheumatic diseases research.

For this reason, the research priorities are presented here in two parts. Those concerning ‘Enabling Tools’ are presented first. These will provide context to how the scientific questions will be addressed. In addition, specific recommendations within the area of ‘Enabling Tools’ are intended to drive forward the development of CBPR, which will have application to the study of rheumatic diseases and other areas of research.

1. Priorities for ‘Enabling Tools’

Research priorities related to the development of community-based participatory research (CBPR) approach were defined by the meeting participants.

1.1 A vision for community-based participatory research

Much discussion occurred throughout the meeting about how research should be conducted in indigenous North American (INA) communities in ways that are inclusive of indigenous governments and consistent with a shared philosophy of community-based participatory research (CBPR).

Community-based participatory research is conducted as an equal partnership between researchers and members of a community. In CBPR projects, the community participates fully in all aspects of the research process. Equitable partnerships require developing research capacity in addition to sharing power, resources, recognition, results and knowledge, as well as a reciprocal appreciation of each

partner's knowledge and skills – at each stage of the project, including problem definition, research design, conducting research and interpreting the results. Throughout this process, clear role definitions are needed so that the objectives of each party are met without creating conflicts of interest.

1.1.1 Vision for CBPR in rheumatic diseases

At the symposium, a vision was articulated in which – perhaps within the next ten years – INA communities, rather than university-based researchers, will drive the research agenda as they gain capacity. Ultimately, well-trained researchers from the INA communities would serve as the local and national leaders for the research projects. Participants expressed a desire that, going forward, they would work toward achieving this goal.

In this future state (which exists in some areas today), communities and patients are well positioned to define the priorities for research, as they will likely have novel insights and will become more engaged in the research process if the study questions are perceived as relevant. The research will be promptly translatable to action as the indigenous populations will be involved in the process from inception to completion.

This approach will help to:

- Coordinate and support research in INA communities and develop research capacity, particularly the education and training of highly qualified research personnel;
- Empower patients and community groups in research development;
- Provide more effective knowledge translation, education and support to the communities;
- Help facilitate health care delivery, including transition from pediatric to adult care; and
- Establish mechanisms and infrastructure to ensure sustainable and productive communications between INA populations and researchers.

Although this vision applies across many areas of health, rheumatic diseases could provide a leading model. Because rheumatic diseases are so prevalent in many indigenous communities, and because their study comprises social, clinical and genetic research components, these diseases provide an ideal lens through which to engage communities and researchers to re-examine the elements of existing guidelines and promote the development of future guidelines, and to help provide education and support to researchers and community members. In addition, rheumatic diseases are chronic conditions that manifest progressively over time. They

affect a full spectrum of physiological and sociological processes, and thus provide excellent opportunities for modelling the effects and outcomes of a wide range of interventions, truly ranging from ‘molecules to communities’.

1.1.2 From vision to reality

To become reality, the vision for CBPR must be acted upon in two specific ways. First, established ethical principles must be followed and expanded. Second, practical steps must be taken within a model or framework that has been proven effective in establishing productive, reliable and mutually beneficial relationships which lead to a positive outcome for the affected individuals and their communities.

It was noted that operationalizing CBPR is a progressive process that requires capacity building on both sides. Researchers must develop a deeper understanding of the cultures and communities with whom they work; communities must build up their capacity and confidence for research governance and participation. To enable these developments, funding agencies must allow for additional costs and accept timelines for consultation, capacity-building and knowledge translation and exchange.

1.2 Enabling tools for CBPR

The development of meaningful community participation in research requires a framework built on two basic elements:

1. Ethical guidelines for research in indigenous communities; and
2. Practical models of partnerships that have been proven effective.

1.2.1 Ethical guidelines

Ethical guidelines for the conduct of research studies in indigenous communities exist in various forms throughout North America.

In Canada, the Canadian Institutes of Health Research (CIHR) Guidelines for Health Research Involving Aboriginal People (see Appendix C for details) apply to research funded by this organization. These articles provide general guidance for collaborative partnerships involving researchers and communities. (Although comprehensive, gaps were identified in these guidelines needing further study and these are being evolved into a new Tri-council document (CIHR, SSRC, NSERC). These are presented as research priorities under the Ethics discipline in section 2.1.)

In the U.S., the Indian Health Service’s area offices and some individual tribes have established Institutional Review Boards which oversee research conducted in their

facilities. In addition to national ethics guidelines, some bands have developed their own, such as the Navajo Nation Human Research Code. Beyond these, an advisory panel to the U.S. Department of Health and Human Services, the American Indian and Alaska Native Health Research Advisory Council, is developing similar guidelines for federally-funded research in the U.S.

1.2.2 *Practical models*

Practical models of partnerships between researchers and communities are needed to achieve effective CBPR; ideally these should be ones that have been proven to work. The following essential elements of such a model were identified by the meeting participants:

- Capacity for all aspects of research governance (from agenda-setting to research ethics board review) must be present at the levels of the community, tribal council and provincial assembly;
- Researchers and communities must engage early and continuously, according to protocols specified by the various levels of indigenous governance;
- Appropriate representatives of the patients, families and indigenous governments need to be identified; patients are to have an equitable voice;
- Researchers need to understand and respect the cultures and values of the populations, including rules governing research (such as the First Nations' principles of ownership, control, access and possession);
- Researchers need to ensure that communities and their governments have adequate information, and communities and their governments need to build sufficient empathy to be able to understand and to develop the research questions and anticipate the impacts on the individuals, families and community;
- To achieve lasting benefits for the populations studied, individuals within the indigenous communities need to undertake integral roles as assistants, scientists, health care providers, research directors and members of ethics review boards. This will require considerable capacity-building efforts.

1.3 **Research priorities for 'Enabling Tools'**

Gaps between the tools that are available today and those needed for full community-based participatory research (CBPR) were identified as follows.

1.3.1 Models of CBPR are needed for meaningful community participation in research that respect indigenous ways of thinking, cultural traditions and the health priorities of indigenous communities

More specifically, methodologies are needed to answer the following questions:

- How to apply CBPR to etiological, clinical and basic science studies;
- How to set up systems of two-way knowledge translation and exchange that explain advances in research to communities (at all levels) and provide insight into indigenous world views for researchers and health care providers;
- How to comprehend the differences and similarities between Western and indigenous reasoning, perspectives and learning processes and to incorporate this understanding into effective tools for knowledge translation and feedback.

One potential approach is for granting agencies to issue a dedicated request for applications (RFA) relating to rheumatic diseases in INA populations to which only indigenous groups who are partnered with investigators can apply. The applications to this competition would be driven by INA groups in collaboration with an appropriate group of researchers.

The process of development and dissemination of CBPR models would involve the following groups: local, regional, provincial/state and national existing indigenous administrative structures; patient groups; and facilitators experienced in bridging linkages among researchers and indigenous groups.

1.3.2 Building capacity for CBPR at the local level

Capacity building is needed within the research and indigenous communities. Researchers need to develop an understanding of and respect for indigenous cultures, protocols, customs and beliefs. Research tools, clinical interventions and communications must be culturally appropriate.

As communities prepare to assume responsibility for tasks such as agenda-setting, research ethics board review, research facilitation and data and sample management, this will provide benefits in terms of research decision-making capability, employment and knowledge translation within the community. It will also help to provide more safeguards, thus enabling and encouraging research in indigenous communities.

A key approach to fulfilling this need is to train researchers with an indigenous background and perspective. Training could be provided in any of the areas of scientific interest, including pediatric rheumatology, basic research, epidemiology

and clinical care. Reciprocally, researchers without an indigenous background could be exposed to indigenous cultures and trained in traditional healing.

Specific research projects to address capacity-building are the following:

- Identify students with potential interest in pursuing a future research career in rheumatic diseases (this could take the form of summer or weekend workshops or retreats, which are actively happening in some areas of Canada, or could be a longer commitment);
- Identify indigenous students early in their post-secondary education and, in a retreat or summer school setting, introduce them to an aspect of rheumatology research; and
- Identify health sciences students (medicine, nursing, physiotherapy, etc.) and specialist residents with indigenous backgrounds who might be encouraged to pursue a rheumatology research career and offer summer studentships.

1.3.3 Financial commitment for partnerships and training

In addition to the specific projects mentioned above, financial support is needed to implement a CBPR-style approach within all research projects involving INA communities.

Additional funds and extended timelines must be built into the grant architecture that allow for:

- Consultation with researchers by indigenous communities and allowing for discussions among the various levels of indigenous government;
- Training, knowledge translation and exchange, and dissemination of results to the communities and their government structures.

2. Scientific Research Priorities

The following scientific priorities were identified from the symposium and are presented for each of the six research disciplines addressed.

2.1 Ethics

The field of ethics provides guidance for the conduct of research in INA communities, ensuring awareness of and protection against the vulnerabilities that these groups may experience.

The scope of ethics in this context encompasses the role of the researcher with respect to the individual, the family and the community. It involves an understanding of and respect for different world views and systems of values and customs, and attempts to redress power imbalances that may exist (or be perceived to exist) between a researcher and the subject of his or her research. Ethical principles also urge that the benefits of research are maximized and flow to all persons involved, and that harms are anticipated and safeguards put in place. Ethics also covers recognition, ownership and authority over research conducted in INA communities.

Research Priorities

The CIHR Ethical Guidelines for Research in Aboriginal Communities provided the framework for the small-group discussion of the ethical relationships that should be observed by researchers and by leaders of First Nation communities.

Participants in the workshop included: individuals who played a major role in the development of these guidelines, leaders of First Nation communities, researchers, community members, health care providers, people with rheumatic diseases, and research participants.

Some of the research questions contained in the ‘long list’ of priorities discussed by the group have been covered in the preceding section on *Enabling Tools*. Many of the remaining list of questions were determined by the group to have been adequately addressed by the CIHR guidelines (see summary of guidelines in Appendix C), in the Canadian context. (It should also be noted that these guidelines are subject to continuing review and development by the government of Canada.)

There are a number of additional issues that need further exploration and development. These are grouped under the following themes.

2.1.1 The development of a mutual agreement on such issues as data protection, cultural property rights, and the use and preservation of biological materials

The CIHR guidelines embed many concepts related to indigenous communities' and nations' jurisdiction over the conduct of research. These include societal and national rights to knowledge and traditions, inclusive of intellectual property rights. The guidelines also address individuals' and communities' rights with respect to data and biological samples taken for research purposes, including the sensitive topic of secondary use of these samples.

One of the areas identified by the group as needing further examination was the handling physical and cultural remains in the context of historical and anthropological research and in the use of archeological evidence from which, for example, an incidental find could point to very early examples of changes in joint morphology.

Discussion with the indigenous communities and nations could lead to clarification of guidance in the case of:

- No consent from individual;
- No consent from community on this particular usage prior to making the find;
- Difficulty tracing family members for posthumous consent;
- Respect for grave, remains and related protocols; and
- Requirement for research ethics board approval. (Is it a 'human subject' in the same sense, as perceived by tradition or other?)

2.1.2 Consensus on the rights of the individual, the rights of the family, the rights of the community, and the circumstances under which one might prevail over the other

Several research questions were raised in the small group discussion under this theme.

“Who represents the community?”

In most, but not all, communities the leaders of the political structures are men. In this capacity, men can make decisions about whether and how research will be conducted in their communities. They also stand to benefit from the rewards of research. Yet most, but not all, rheumatic diseases predominantly affect females.

This situation poses ethical questions about who should represent the community in decision making regarding research into diseases affecting those who do not have the authority to decide. The rewards of research include goods such as employment,

training and financial compensation – which flow in greater part to the community. Research participants may benefit directly by receiving better care and indirectly by contributing to improving the treatment of their disease. The potential harms of research are borne in the greatest proportion by the research participant. There is a risk that an imbalance of these goods and harms may lead to inequities, which the patient is relatively powerless to resist.

Ethical guidance is needed regarding recognition of who is to represent the community and how the needs of the individual patient should be balanced against the power of the community representative.

What is the potential for multiple vulnerabilities of indigenous people with arthritis or other rheumatic disease?

There are clinically significant problems that are often found in those with arthritis that are generally under-recognized by the researchers and health care practitioners. These include psychological trauma and suicidality (particularly in men), and depression (particularly in women). Research to help further identify and address these multiple vulnerabilities could lead to better health care.

Research could help to unpack the meaning and nature of vulnerability among indigenous people with rheumatic diseases. Instead of assuming vulnerability on the basis of belonging to a certain subpopulation, research could help identify a more detailed taxonomy of vulnerability and assist in determining the appropriate response (i.e., better clinical guidelines for cultural competence and safety).

What are the ethics of conducting studies of disease risk in INA populations?

Studies of disease risk that involve testing of genetic susceptibility, and the identification of biomarkers such as autoantibodies that may predict future disease onset, have the potential benefit of identifying individuals in whom to target preventative therapies, when these become available. This approach is particularly relevant to rheumatic diseases in INA populations where strong gene-environment interactions are suspected to be at play. In the face of an incomplete understanding of how to build models of disease risk that appropriately weigh each risk factor, providing individuals, families, and communities with this information may do more harm than good. How should this ethical dilemma be addressed?

2.1.3 An understanding of the social and cultural implications of disease risk testing from the perspective of the individual, their family and their community

Two central questions were raised within this research theme.

How should the results of risk testing be disclosed?

While knowledge of risk profiles can provide benefits by informing and targeting therapies, there are potential pitfalls that may harm patients, families and communities. This situation can create ethical dilemmas for researchers and clinicians. Disclosure of test results could benefit the patient by targeting therapy early, or even by providing access to preventative therapies when these are available. Conversely, a person may be stigmatized if the person interprets the results of the tests to mean they are ‘destined’ to develop a particular disease such as rheumatoid arthritis.

This dilemma is further compounded by the fact that the exact implications of the risk testing are unknown or uncertain to the researcher or clinician, and that the longitudinal follow up of such ‘at risk’ individuals will be the only way to get a better understanding of the true implications of the risk profile.

These issues are pertinent to INA communities because the risk profiles for rheumatic diseases in these populations appear to be different from those observed in the non-indigenous population. Our understanding of the implications of these differences is incomplete. For example, we do know that rheumatoid arthritis is generally more prevalent in INA groups and its manifestations are more severe. Because early diagnosis and treatment generally leads to better outcomes, it is therefore important that individuals are informed of their risk as soon as possible.

Ethical principles surrounding disclosure of risk biomarker test results to individuals, families and communities need to be investigated further. As part of this, research is needed to understand the values of INA populations so that the associated ethical principles can guide researchers and clinicians. Which values should prevail in ethical decision-making regarding disclosure of test results? Are these the same or similar between indigenous groups? To what extent do these differ from Western ethical principles? What protocol should a researcher follow when making disclosure decisions based on indigenous values?

How should incidental findings be divulged?

Another example of the application of this research is guidance on the handling of incidental findings in the indigenous context. There is a fairly substantial body of

literature in bioethics on the topic of disclosing incidental findings, but little or none that relates specifically to the indigenous and isolated community context. This could be particularly salient for rheumatic diseases research, where it has been shown that key genes (with the potential influence of environmental influences such as infectious disease or tobacco use) could also be implicated in other diseases. How should such incidental findings be handled in the Aboriginal context? What are the unanticipated consequences and ethical dilemmas?

Ethics research in each of these areas will add considerable knowledge and lead to culturally competent protocols for individuals, families and communities. The benefits of this research will accrue not only to rheumatic diseases research but, since these disorders touch on diverse aspects of ethics, to other areas of research as well.

2.2 Partnership in Science, Traditional Medicine/Healing and Knowledge Translation

Although most of the priorities on this subject have been addressed under Section 1 on *Enabling Tools*, a further research priority was identified and elaborated by the small group discussing this topic.

Research priority

2.2.1 *Understanding traditional medicine and healing*

Traditional medicine is a gift from the Creator and is a reality for many indigenous North Americans. Healing encompasses a wide array of practices and knowledge. Traditional medicines from plants and minerals, methods for maintaining well-being and restoring health, such as ceremonies and specific interventions by healers, are examples of traditional medicine.

We know that there are similarities and differences in beliefs and in the practice of traditional medicine across INA populations. Participants reflected that the four traditional medicines in Canada, for example, are the same as those used in Mexico and parts of the U.S. One of these – weekay, in the Ojibwe language – is an aspirin-like plant extract which has long been used to treat joint pain.

The effectiveness of traditional medicine is bound up with the belief system of the individual and the support of family and community. These are inseparable, unlike

Western medical approaches which consider primarily the physical and individual contexts. The power of traditional medicine rests with its holistic approach to well-being and the maintenance of balance among the four dimensions of life.

Little is understood by Westerners about indigenous traditional medicine. In large part this is due to distrust generated by a history of repression and destruction of traditional knowledge. Fear of the misuse of traditional wisdom by Westerners continues today, and for good reason, as some have sought personal gain at the expense of indigenous North Americans.

Despite these barriers, the potential for improvement in the understanding and care of INA patients with rheumatic diseases by incorporating traditional knowledge is significant. Traditional healers who better understand Western medicine, and Western practitioners who better understand traditional medicine, will be able to recommend and deliver treatments that are optimal for their INA patients, and to avoid treatments having potentially harmful interactions.

Specific areas for research identified by the group include:

- Understanding the scope of traditional healers and their contributions;
- Understanding the beliefs of indigenous groups about rheumatic diseases and how these have changed over time;
- Best-practice models for the long-term collaboration of Western and indigenous treatment modalities. (Can Western and indigenous approaches be integrated into a new concept that respects both equally?);
- Determining which drug treatments and combinations work best for indigenous populations and then transferring this knowledge to health care practitioners; and
- Safety of traditional medicines.

The benefits of this research include practical guidance for all research projects involving INA populations. Also, an outcome could be the expansion of potential treatments for indigenous (and non-indigenous) persons with rheumatic and other diseases.

2.3 Clinical Epidemiology

The published literature describing the epidemiology (incidence, prevalence and clinical characteristics) of rheumatic diseases in indigenous North American (INA) populations is scant. What the few available studies tell us is that the incidence and prevalence rates of rheumatic diseases among indigenous adults and children are the highest in the world.

There are marked variations in the prevalence and phenotypes of rheumatic diseases across INA populations. Pockets of specific rheumatic diseases such as systemic lupus erythematosus (SLE), scleroderma, the spondyloarthropathies and undifferentiated arthritis (UA) have been noted that correspond to specific regions or language groups. Some researchers have suggested that these patterns may correspond to a common genetic ancestry in which there is a predisposition to certain types of chronic inflammatory diseases.

Rheumatoid arthritis (RA) is generally more severe in indigenous populations, for unknown reasons, and is present at an earlier age among adults (and show up later among children). There are several differences in clinical characteristics, including the number and size of affected joints.

Underlying genetic patterns suggest a predisposition to disease among some indigenous individuals and their families. These populations may also lack protective genes seen in Europeans. Certain lines of research suggest that some rheumatic diseases existed in North America before European contact and may even have originated on this continent. These patterns point to a unique set of characteristics that differentiate rheumatic diseases among indigenous populations compared with those seen in people of European ancestry.

The formulation of research strategies to better understand rheumatic diseases in INA populations must go beyond biology. The factors that influence the occurrence and outcomes of rheumatic diseases include not only those that are biologically based such as genetics, but also lifestyle choices including nutrition and physical activity. Environmental influences need to be better understood and need to encompass both the physical environment e.g. exposure to environmental toxins, and the psychosocial environment e.g. socioeconomic status and psychosocial stress.

More data are needed to complete this picture. A framework for the collection of key statistics will help to understand which rheumatic diseases are experienced by specific indigenous populations, identify their unique clinical characteristics, and

elucidate risk factors for the development of rheumatic diseases. In turn, this information will help in planning for health care resources and contribute to basic research that may lead to more efficacious treatments for indigenous populations.

Such a framework may also serve as a template for other chronic diseases, such as diabetes or cancer, where genetic characteristics and environmental factors play a central role in the manifestations of disease.

Research priorities

The following specific research priorities were recommended.

2.3.1 Develop a tailored system of classification and measurement of rheumatic diseases

This should take into account key differences between Western and indigenous populations, with respect to the course of disease and how it is experienced by indigenous peoples. The following elements should be included:

- Prevalence;
- Disease characterization (including genetics, assessment criteria, clinical outcomes, etiology, prognosis and/or response to therapy);
- Disease burden (types of disabilities; impact of disability on the individual, family and community; impact on educational achievement, development of children, social and economic roles);
- Co-morbidities (including psychological factors such as depression, anxiety and suicidality) and their impact on outcomes;
- Environmental factors (socioeconomic status, family and community support structures, lifestyle factors, urban/rural/reserve);
- Documentation of non-visible disability; evaluation of impairment in the context of the community and the individual's experience;
- Response to therapy;
- Qualitative factors (subjective experiences, beliefs, etc.); and
- Pediatric and adult populations.

The measurement system would be developed in collaboration with indigenous communities and would capture key qualitative, as well as quantitative, parameters.

This system would be used as a data collection tool and as a teaching and diagnostic tool for primary care practitioners.

2.3.2 *Develop methodologies to achieve priority #1*

With the appropriate involvement of indigenous communities, develop and populate a North American database containing basic information on rheumatic diseases in indigenous populations (using parameters from #1).

- Seek broad regional presentation of indigenous North American populations;
- Include testing of children and consideration of prenatal and early life events to determine the earliest signs of disease;
- Link to existing databases (e.g., health care utilization records).

The database would be developed in accordance with OCAP (ownership, control, access and possession) principles. Indigenous leadership will be involved in all phases and make the final decisions concerning the design, implementation, data extraction and utilization processes.

This will enable quantification of rheumatic diseases (prevalence, severity, linkages between rheumatic diseases, comparative population studies) and will assist in policy development and health care services planning.

2.3.3 *Historical examination of the effects of colonization, urbanization and intergenerational environmental stresses on the prevalence and characteristics of rheumatic diseases over time*

This research would elucidate the impacts of socioenvironmental stresses on the development of rheumatic diseases. The resulting knowledge would contribute to a more accurate forecasting of disease prevalence and burden in various communities, and would inform health care and social / economic development policy by governments at all levels. (The scope of this work could be expanded to include other chronic diseases.)

2.4 Basic Research

Basic research focuses on the molecular components of health and disease and attempts to understand the links between these variables and clinical outcomes. The scope of basic research in the context of rheumatic diseases includes genomics, biomarkers, proteomics and the rapidly developing field of metabolomics. Advances in basic research can help in the early detection of disease, to identify new targets for therapies, to personalize therapies, and to predict the course of disease and potential responses to treatment.

The field of genomics is advancing rapidly. Until very recently, few biomarkers were available to assist clinicians to classify rheumatic diseases and to predict the course of disease. The human genome project has resulted in an explosion of new information including the identification, during the past two years, of 25 new genes that are associated with susceptibility to rheumatoid arthritis.

This flood of information has yet to be interpreted on the clinical stage. Much more work is needed in the fields of proteomics and metabolomics to understand how these genetic changes translate into clinical manifestations. Interrelationships between molecular factors need to be better understood, as well as the influence of environmental stresses such as prior infection.

The application of this work potentially goes beyond rheumatic diseases. Clues to commonalities among chronic inflammatory diseases may be contained in this molecular-level information. Models developed for linking genetic markers to clinical outcomes and drug response in rheumatic diseases could be applied more broadly across other disease areas.

Research priorities

2.4.1 *Good clinical observation*

We know that the phenotypes of INA populations are different from the general population, therefore we cannot rely on the accuracy of our current system of disease definition and classification. We need to explore changes to the current American College of Rheumatology guidelines and to use these revised criteria to also measure desired outcomes. Comorbidities and risk factors need special attention in this context.

In addition, we need to take advantage of advances in imaging technologies such as magnetic resonance imaging (MRI) and ultrasound to detect disease at the earliest possible stage.

2.4.2 *Biomarkers*

Genomics, proteomics and metabolomics can be used to understand the impacts of environmental stresses and pathogens at the molecular level. These stresses include bacterial and viral infections, small molecule toxins and other phenomena such as prions and misfolded proteins. More information is needed in the area of proteomics, with greater detail on autoantibody profiles and on cytokines and lymphokines.

Metabolomics has shown remarkable specificity in other disorders and rheumatic diseases could be tested using these methods.

Interpretation of molecular-level information in the context of INA populations is important. Cross-cutting themes include understanding the synergistic effects of using various molecular techniques in a systems biology approach. Also, these methods will help to understand the interrelations of rheumatic disease with other chronic inflammatory diseases, such as lupus and diabetes, and with comorbidities.

Strong capabilities in bioinformatics (array technologies and genome scans, for example) are an essential enabler for this research.

2.5 Health Care Delivery and Public Health

Because rheumatic diseases among many INA populations are more prevalent and more severe, the health care needs of these groups are necessarily different. There is great heterogeneity in the clinical needs of indigenous populations across North America. Many INA communities are isolated, for example, which presents logistical challenges to the delivery of health care services. Jurisdictional differences may also complicate the picture.

Health care delivery can refer to a broad continuum of care including education, prevention, diagnosis, treatment and follow up. Systems thinking is required when considering models for optimal care. From an indigenous perspective, the definition of health care is based on an integrated model which encompasses all aspects of health and well-being – physical, mental, emotional and spiritual – and may include traditional and Western medical approaches. The scope of health care should also encompass surveillance and linkage of data, measurement of outcomes, and knowledge translation. A patient-centred approach, including families, is a basic principle of an integrated system.

The comprehensive set of factors described above suggests that health care delivery needs to be redesigned for indigenous populations in order to optimize its effectiveness. For example, the high prevalence and genetic predisposition to rheumatic diseases in many INA populations indicates a need for widespread access to specialist care, starting at an early age. Access to medical specialists (in many cases, several specialties are required), regular follow-up and good communication among specialists and primary care practitioners are essential. Access to disease-modifying treatments such as biological drugs must be facilitated. Educational efforts should

incorporate the family and community – to support the patient and to dispel myths about the disease that may lead to stigmatization. Western and traditional approaches should be respected equally, and health care delivered in a culturally competent manner.

There are at present no models for optimal care of indigenous populations with rheumatic diseases and no studies have been done to evaluate the current level of care with respect to these standards. Best practices were described at this meeting, including delivery of specialist care in Alaskan communities, legislated requirements for the timeliness of government decisions on health services, and integrated holistic health care models run by indigenous groups. New technologies were also described that could address gaps and improve care in the future, such as diagnostic imaging techniques and communications technologies.

While the research questions elaborated below focus on rheumatic diseases, addressing gaps in health care will provide benefits across the entire spectrum of health care needs. By following the principles outlined above, new models of care can be tried and evaluated, building up a foundation of knowledge that can be exchanged across jurisdictions.

Research priorities

The following areas were identified as needing further study to understand and advance health care delivery for indigenous peoples with rheumatic diseases.

2.5.1 Define optimal care for rheumatic diseases among INA populations and evaluate current care

Define quality standards, including the following considerations:

- Incorporating indigenous definitions of health and well-being;
- Scope includes continuity of care between health care centres and community, determinants of health and prevention;
- Identify differences between recommendations/standards of care for Western populations and indigenous populations (controlling for distance to health facilities);
- Quantify gaps in care; assess barriers to and facilitators of care; and
- Assess the priority status of rheumatic diseases compared with other needs that compete for the same resources.

2.5.2 Develop a model of care that improves health outcomes for rheumatic diseases (as defined by indigenous groups) within existing resource levels

The following parameters should be incorporated into this model:

- Operates at the levels of the individual, family, community, tribe and at the systems / policy level;
- Includes pharmaceutical, traditional and complementary interventions;
- Flexibility to adapt to different communities;
- Describes and compares best practices from across North America (e.g., diabetes programs in Canada; Alaskan model for RA; Mexican model of involvement of industry as a partner);
- Includes community-based assessment tools to measure outcomes and evaluate the basis of disease severity (i.e., how much variation is attributable to poor access to health care).

These priorities will improve health outcomes by optimizing care and will inform health policy decisions by all levels of government.

2.6 Pediatric Rheumatic Diseases

What studies have been performed indicate that the prevalence rate of polyarticular juvenile arthritis is three to five times higher than in the broader population. Yet, we know little else about how this disease affects indigenous children, their families and communities, or about what the disease in pediatric populations may tell us about its effects in adult populations. These gaps can be viewed on several levels.

The first level focuses on individual children and their families. From an epidemiologic viewpoint, the impact of pediatric diseases on scholastic achievement or general physical and social well-being is not well understood. Also, there are unique considerations regarding health care services. Many indigenous children with rheumatic diseases who are treated and followed regularly throughout their childhood and into their teenage years experience a disruption in care when they reach adulthood – at age 18 or 19. As adults, they do not receive the same level of support (for flights from remote communities, for example), holistic care or access to specialists.

The second perspective relates to how interventions in childhood may benefit the general population. Almost all rheumatic diseases have their origins before the disease becomes manifest and those origins almost certainly occur during childhood,

adolescence or even prenatally. Consequently, any strategies to improve the health and well-being of INA populations, including those afflicted with rheumatic diseases, must include aggressive investment in research pertaining to children, youth and the fetus. Discovering the earliest origins of rheumatic diseases will help to improve outcomes and make disease prevention realistically achievable.

The third level relates to the impact of environmental factors on biology. The interaction of an individual's biology with lifestyle risk factors and external environmental factors was discussed in the section on *Clinical Epidemiology*. This pertains to children also, and it is noted that the scope of the research priorities for clinical epidemiology would include pediatric as well as adult rheumatic diseases.

As a principle, children should be included in all research priorities, rather than being considered in a separate silo. It is essential that existing birth cohorts in Canada and the U.S. are approached as opportunities for research.

Research Priorities

With these basic principles in mind, the group identified three predominant pediatric rheumatology research priorities.

2.6.1 *Epidemiology of childhood rheumatic diseases in INA populations*

We need to have a better understanding of the prevalence, distributions, genetics and environmental factors related to pediatric rheumatic diseases in INA populations. Only with a clear appreciation of the epidemiology of pediatric rheumatic diseases can we begin to formulate rationally conceived research strategies.

It is worth noting that the Canadian pediatric rheumatology community has large, nationwide and regional databases of rheumatic diseases that can serve as an initial resource for epidemiological analyses in this population.

With comprehensive epidemiological information, we can more effectively engage and communicate with INA communities and help identify the health and health care challenges that will advance the research priorities and agendas.

2.6.2 *Earliest determinants of rheumatic diseases in INA populations*

We must commit to investing more aggressively in identifying the very earliest factors that influence both the outcomes and the occurrence of rheumatic diseases. This knowledge will inform future health care delivery and research, empower people and

communities, improve outcomes and enable the development of approaches for early diagnosis and disease prevention.

The consortium of Canadian pediatric rheumatologists is well positioned to lead such a research effort. These investigators are well coordinated and have access to a large array of databases that will facilitate such research. In addition there are opportunities to link with other research groups, including birth cohorts, to advance this research agenda. The approach, which will require a multidisciplinary / transdisciplinary team approach, will integrate genetic, lifestyle and environmental influences on disease occurrence and outcomes.

This strategy may be the only way to substantially improve outcomes by earlier diagnosis and by attending to the multiple factors that influence disease outcomes. In addition, this approach is required to promote disease prevention in a realistically achievable way.

2.6.3 Adolescent transitions in care

Health care delivery to children involves specialized teams that take a case management approach to meeting the child's health care needs in a holistic manner. Yet, when the child reaches adulthood, they transition to the adult system where health care is fragmented and barriers to access are higher.

What can we do to avoid these gaps in care?

This situation needs to be assessed and potential solutions developed. In Canada, all indigenous children with rheumatic diseases are treated by a pediatric rheumatologist who is part of a nationwide group, providing an ideal opportunity to conduct census studies of this population, to share best practices and to advocate for new models of health care.

Conclusion

As stated earlier, the research priorities identified in the preceding two sections address the need for enabling tools as well as specific scientific knowledge in each of six disciplines covered during this symposium. While each of these areas represents a single field of enquiry, the implications of the questions raised span all disciplines.

Each of these fields of research also offers broader potential benefits for other health areas, particularly for other chronic diseases. For example, genetic risk factors may offer clues about other chronic inflammatory diseases such as multiple sclerosis, psoriasis or inflammatory bowel disease that affect indigenous populations. The interrelations between biological factors and socioeconomic determinants of health in the onset and progression of rheumatic diseases also apply to diabetes, heart disease and cancer. Epidemiological models tracking variations in rheumatic diseases in different indigenous populations may elucidate patterns that can be applied to ethnic populations in general. The interplay between chronic diseases and mental states such as depression, anxiety and suicidality can be better understood through an examination of rheumatic diseases. Models of integrated care apply across the spectrum of health care and offer examples for Western health systems.

Studies in rheumatic diseases in indigenous North American populations are scarce. Although this situation is regrettable, it offers a unique opportunity to build from the ground up a cohesive and integrated system of research that addresses the full scope of factors implicated in these diseases. The fruition of this system will benefit not only patients suffering from these diseases but will have a ripple effect on other health areas, resulting in improved health status of indigenous individuals, families and communities across North America.

Appendix A - Program

International Symposium
on
**Rheumatic Diseases in
Indigenous North American Populations ...
from Molecules to Communities**

September 24 & 25, 2009
University of Manitoba Bannatyne Campus
Frederic Gaspard Theatre
Basic Medical Sciences Building
730 William Avenue
Winnipeg, Manitoba, Canada

Thursday - September 24, 2009

12:30 - 12:45 Welcome and Program Overview

Dr. Hani El-Gabalawy / Dr. Brenda Elias

12:45 - 1:00 Opening Prayer and Drum Ceremony

Elder Margaret Lavallee

1:00 - 2:00 **Living With Arthritis and Rheumatic Diseases**

Moderator, Dr Hani El-Gabalawy - University of Manitoba

A Life with Rheumatoid Arthritis

Ms. Joyce Greene

A Collective Account of the Impact of Arthritis on INA Populations

Dr. Brenda Elias - University of Manitoba

The Indigenous Person's Dilemma: Western vs. Traditional Medicine

Elder Margaret Lavallee

Plenary Discussion

2:00 - 3:00 **Gaps in Health Care Delivery for Indigenous Peoples**

Moderator, Dr. Bruce Martin - University of Manitoba

Provision of Care for the Alaska Native Population

Drs. David W. Templin and Elizabeth D. Ferucci

Clinical Care for INA Patients with Arthritis & Rheumatic Diseases

Dr. David Robinson - University of Manitoba

Integration of Health Services for INA Communities

Mr. Richard Jock, Executive Director - Norway House Cree Nation

3:00 - 3:15 Panel Discussion

3:15 - 3:30 Break & Poster Viewing - 2nd floor Concourse, Basic Medical Sciences Building

3:30 - 5:30 **Ethical Considerations for Research in INA Populations**

Moderator, Dr. Brenda Elias - University of Manitoba

Ethical Conduct for Studies in Vulnerable Populations

Dr. Danielle Bromwich - National Institutes of Health, Bethesda, MD

Canadian Guidelines: CIHR Guidelines for Research in INA Populations

Dr. Malcolm King, Scientific Director

Institute of Aboriginal People's Health - University of Alberta

Individual vs. Community Consent

Chief Marcel Balfour, Chief - Norway House Cree Nation

Genetic Studies in Indigenous Populations - Opportunities and Threats

Dr. James Jarvis - University of Oklahoma

Ethics of Informing Indigenous Individuals of Disease Risk

Drs. Joseph Kaufert, Patricia Kaufert and Dhiwya Attawar - University of Manitoba

5:15 - 5:30 Panel Discussion

Thursday evening -September 24, 2009

6:30 Reception and Dinner: Hotel Fort Garry - 222 Broadway Ave.

Keynote Speaker: Steve McNair, President and CEO, The Arthritis Society

Friday - September 25, 2009

7:30 - 8:00 Breakfast and Poster Viewing, 2nd floor Concourse, Basic Medical Sciences Building

8:10 - 10:15 **Clinical Phenotype of Rheumatic Diseases in INA Populations**

Moderator, Dr. David Robinson - University of Manitoba

Juvenile Idiopathic Arthritis in INA Children

Dr. James Jarvis - University of Oklahoma

SLE in INA Populations

Dr. Christine Peschken - University of Manitoba

Undifferentiated Arthritis in the Mexican Mestizo Population

Dr. Daniel Xibille-Friedman - Mexican College of Rheumatology

Spondyloarthropathies in British Columbia Indigenous Populations

Dr. Kevin J. Keen - University of Northern British Columbia

10:15 - 10:30 Break and Poster Viewing - 2nd floor Concourse, Basic Medical Sciences Building

10:30 - 12:30 **Why is RA So Common in Some INA Populations?**

Moderator, Dr. Carol Hitchon - University of Manitoba

Prevalence of Arthritis Based on Questionnaire Data

Dr. Brenda Elias - University of Manitoba

Prevalence & Phenotype of RA in INA Populations

Dr. Elizabeth D. Ferucci - Alaska Native Tribal Health Consortium

Genetic Risk for RA - Role of HLA

Dr. Kiem Oen - University of Manitoba

Genetic Risk for RA - New Genetic Associations

Dr. Kathy Siminovitch - University of Toronto

The Pre-Clinical Phase of RA: Lessons from the Cree/Ojibway Population

Dr. Hani El-Gabalawy - University of Manitoba

12:30 - 1:15 Lunch and Poster Viewing - 2nd Floor Concourse, Basic Medical Sciences Building

1:15 - 2:45 **Defining the Knowledge Gaps**

Group plenary session

2:45 - 3:00 Break & Poster Viewing - 2nd floor Concourse, Basic Medical Sciences Building

3:00 - 4:00 **Small Group Sessions: Towards defining a research agenda**

Group 1: Clinical Epidemiology

Group 2: Partnership in Science, Traditional Medicine/Healing and Knowledge Translation

Group 3: Basic Research

Group 4: Ethics

Group 5: Health Care Delivery and Public Health

Group 6: Pediatric Rheumatic Diseases

4:00 - 5:00 **Consensus Building: Where do we go from here with the research agenda?**

Reports from Small Group Discussion

Plenary Discussion

5:00 - 5:30 **Concluding Remarks and Wrap Up**

Dr. Hani El-Gabalawy

Dr. Brenda Elias

Concluding Prayer

Elder Margaret Lavallee

Appendix B - Presentation Summaries

Living With Arthritis and Rheumatic Diseases

A Life with Rheumatoid Arthritis

Ms. Joyce Greene

I am a member of Lax Kw' Alaams Band – part of the Coast Tsimshian Tribal Society located on the Northwest coast of British Columbia. I am a second generation First Nation Canadian who has lived with severe rheumatoid arthritis since I was 33 years old. My family, including four siblings, my mother and an uncle all have known first-hand how severe, debilitating and mind-numbing the pain of arthritis can be.

Poor living conditions and lack of education contribute to the 27 per cent of all Canadian Aboriginal people who live with arthritis. Timely access to awareness, education, treatment and information to this forgotten segment of Canadians living with arthritis must be addressed now. Pain is pain, for all Aboriginal people living with arthritis, no matter where they live in our country. We can and we must change this NOW.

First Nations people believe that health is a balance of mind, body, emotions and spirit. It cannot be separated from other issues in a person's life, and knowledge is very important to health. Myths about arthritis, such as people being unable to live a full life, need to be dispelled. Control of the patient through self-management opens up possibilities for healing both oneself and others with arthritis.

A Collective Account of the Impact of Arthritis on INA Populations

Dr. Brenda Elias - University of Manitoba

The indigenous people of the Americas, historically and currently, have the highest incidence and prevalence of rheumatoid arthritis (RA), multi-case families, early age of onset, female sex risk, and a higher frequency of shared epitope (SE) genes in patients and their unaffected family members. Aggressive onset and severity, described as advanced disease with stage IV radiological changes, severe disease with

rheumatoid nodules and erosive disease, or disease severity marked by positive antinuclear antibody (ANA), also characterizes this population.

While many efforts generally have been directed at understanding the pathogenesis of disease, no studies have investigated the strategies developed by affected First Nations individuals to resist chronic inflammatory events.

Understanding this resistance at the social, psychological and cultural level is critical to formulate interventions in this population and other affected groups. Indeed, resistance and the power relations generated from this resistance is the power / knowledge that affected individuals require to gain some control over the unpredictable trajectory of this immunological condition.

According to Foucaudian thought, power relations are only possible among subjects who can resist and exercise contrary forces, and when we are not free to resist, we do not have power relations any more, but dominant relations.¹

To situate this field of resistance, this paper first describes the way affected First Nations women diagnosed with rheumatoid arthritis experience the disease process and its impact on their life, and concludes with the ways they have resisted the erosion of self.

An individual living with rheumatoid arthritis (RA) experiences erosive changes not just in their joints but in their lives. Fear, anger and frustration result from pain and physical limitation. Life becomes uncertain and chaotic because of the unpredictability of the disease. Sufferers lack sleep and commonly experience fear and depression. They have difficulty fulfilling their usual functions (e.g., care for children, travel, work, exercise), and fear for future disability and early death. These experiences are generational - parents worry that their children will get RA.

To disrupt the power of arthritis, First Nations women developed resistance strategies including:

- Strive to be normal (stay busy, take medications to block pain)
- Pace yourself, find your limitations and impose limits on yourself
- Self-determination, but be open to help from others
- Live day to day
- Family support (physical and emotional)
- Moving, persisting and helping others with RA to move.

¹ Dreyfus HL & Rabinow P. 1982, p. 147.

The Indigenous Person's Dilemma: Western vs. Traditional Medicine

Elder Margaret Lavallee

Traditional medicine is making a comeback in many indigenous communities. For over one hundred years, these customs were banned as part of an attempt to force Aboriginal people to adopt Western ways. The denial of traditional medicine and other customs, coupled with the removal of children from their families to attend residential schools, weakened family and community structures. In recent years, interest and involvement in traditional forms of healing has increased, their practice has been reinstated in communities and is being taught to younger generations.

Patients with chronic, debilitating conditions such as rheumatic diseases often seek both modern and traditional approaches. It is therefore important that Western and indigenous medical practitioners understand each other's ways of healing, to protect the patient against potential harms (such as drug interactions) and to expand the range of available therapies. From a collective perspective, traditional healing methods are also effective in bringing families and communities closer together.

The four traditional medicines used in communities on a daily basis:

- Weekay (like aspirin, this medicine thins the blood and is used to treat arthritis and headaches)
- Sage (treats abdominal cramps;, used in smudging ceremonies)
- Sweetgrass (a digestive; used in smudging ceremonies)
- Cedar

Unlike Western medicine, traditional modes of healing involve not just medications but also address the spiritual aspects of well-being. Healing activities involve the entire community and include dancing, sweat lodge and doctoring ceremonies. These approaches balance the individual's physical, mental, emotional and spiritual needs.

The seven healing ways used in traditional medicine – talking, laughing, yelling, sweating, crying, yawning and shaking – have been shown to have salutary physiological effects, including relieving stress and stimulating endorphin production.

Gaps in Health Care Delivery for Indigenous Peoples

Provision of Care for the Alaska Native Population

Drs. David W. Templin and Elizabeth D. Ferucci, Alaska Native Tribal Health Consortium

The challenges of delivering health care to indigenous Alaskan populations are primarily: logistics and manpower. Health care delivery is organized in four tiers: community health aides/practitioners (coordinate services in the local communities); village health clinics (primary care); small regional hospitals; the Alaska Native Medical Center (provides a full range services across the state).

Logistics are at the heart of delivering health care to Alaska Native populations. More than three-quarters of communities have no road access to a hospital and living costs are high. Because of these realities, the Alaska Native Medical Center's approach is to take the rheumatologist to the patient, rather than the reverse. Visits are made on a semi-annual schedule to assist the on-site practitioner in assessing and managing their cases. However, this is still less than desirable because, in practice, patients are seldom seen more than once a year by a rheumatologist. Ongoing management of persons with RA is also difficult because each clinic has its own formulary, so patients don't always have the option to use biologic medications.

The second challenge is manpower shortages. There are only three rheumatologists in Alaska, all of whom work in Anchorage. Two part-time rheumatologists cover the Native communities.

Responsibility for health care shifted from the federal government's Indian Health Service to tribal management in 1997. The Alaska Native Tribal Health Consortium coordinates services and the regional tribal health organizations provide primary care in the communities. Challenges remain with respect to funding, supply and retention of health care practitioners and these factors will become more acute as the high population growth rate and shift to an aging population with chronic diseases create greater demands on the system.

The Alaska Community Health Aides/Practitioners program has been operational in some form since the 1960s and is the foundation of care in the 178 village clinics. These individuals are selected by the communities and since 1998 have been formally

certified through a state-wide training program. The telehealth system in Alaska is well developed as a primary care tool, allowing for imaging and consultation to take place remotely and avoiding the need for patient travel. Since rheumatology is a hands-on practice, however, in this field telehealth has been used mainly for teleconferencing and education.

Clinical Care for INA Patients with Arthritis & Rheumatic Diseases

Dr. David Robinson - University of Manitoba

Indigenous North American (INA) populations appear to be at higher risk of several rheumatic diseases with earlier age of onset and more severe disease manifestations. Rheumatoid arthritis (RA) is an excellent example of rheumatic diseases in general. Optimum management of RA requires early diagnosis and initiation of pharmacologic treatment, multidisciplinary non-pharmacologic care, and frequent follow-up for optimization of therapy and monitoring of adverse medication effects. RA is challenging for primary care practitioners to diagnose because symptoms are vague at the early stages of disease and there is no definitive blood test. Yet, late diagnosis and/or inadequate care leads to increased damage, deformity and disability. Achieving an optimal level of care requires excellent open communication between patients, specialists, and primary care providers.

While the specific challenges in providing optimum care to indigenous North American populations with RA may vary from community to community, there are some that reoccur regularly. Access to appropriate primary care both in urban and rural or remote areas impedes early and efficient diagnosis. Follow-up and monitoring of disease activity and medication toxicity is also frequently lacking. Remoteness from specialty care presents unique challenges for transportation, drug and disease monitoring, and infusion therapies. In Canada, these issues play a role in interactions with the health care payers making timely and effective access to medications difficult. Language and cultural differences between caregivers and patients lead to ineffective communication regarding the diagnosis and its consequences, goals of treatment and the need for medication monitoring. Poor understanding of these issues on the part of patients leads to ineffective self-advocacy. These issues contribute to worse outcomes both in rheumatic diseases and in overall health.

Integration of Health Services for INA Communities

Mr. Richard Jock, Executive Director - Norway House Cree Nation, Manitoba

First Nations have had a keen interest in pursuing a holistic approach to the maintenance of health and well-being. When the parameters for transfer of health care from the federal government to First Nations' control were developed, the First Nations' proposed a very comprehensive approach as to how services would be provided (in contrast to the narrow model adopted by the federal government).

Integrated models of care are well developed internationally and have long been recommended in Canada. The Romanow Commission in 2002 proposed some of the concepts that advanced the vision of an integrated model, which were further developed by the National Aboriginal Health Organization (NAHO). The Assembly of First Nations and provincial premiers met earlier this decade to resolve how to bring First Nations to parity in health outcomes. Talks focused on integration models and, in 2004, resulted in two categories of funding being made available through the Aboriginal Health Transition Fund: adaptation funds and integration funds.

The integrated health services model developed by Norway House Health Services Inc. (NHHS) includes the following elements:

- Awareness, education and treatment services
- Empowerment of patients and the community
- Emotional, spiritual, physical and mental well-being.

NHHS is advanced in adopting health services. The community owns its own pharmacy and runs its own dental services. The only outstanding element is to integrate the federal hospital. The Alaska model, which forces government to make a decision on health care proposals within a definite timeframe, would facilitate First Nations control.

The challenges of not integrating services include:

- There is no one system to measure access and quality of services
- Unclear who is responsible for services
- No process for appeals, complaints or measurement of client satisfaction
- Service decisions are made on the basis of jurisdictional priorities rather than focussing on the patient (e.g., providing services locally vs. transporting patients)

Considerations for evolving an integrated model include:

- Common health records, integrated with provincial systems (enables the development of new assessment procedures, a case management approach and expansion of research capacity)
- Quality evaluation (health services accreditation and client satisfaction measurement)
- Unified approach to meeting the needs of the community within the community
- Parameters around the timeliness of decision-making concerning proposals need to be legislated (as in Alaska).

Discussion: Gaps in Health Care Delivery for Indigenous Peoples

The following themes emerged from the panel discussion and questions from the audience.

Traditional medicine

The importance of open communication regarding traditional medicine was stressed. Sometimes patients will forgo Western medicine in favour of traditional medicine, especially when they have chronic conditions. Many return to Western medicine later in the course of their disease, which makes it more difficult to treat. Patients are sometimes reluctant to admit that they were receiving traditional medicine, perhaps for historical reasons. Steps need to be taken to bring this out into the open, to recognize and value traditional medicine.

Health care delivery gaps - unique aspects

Rheumatic diseases present particular problems of access to care for indigenous populations living in remote communities. Frequency of specialist consultations and the number of specialists required for case management are severe compared with many other diseases. (For example, a patient with lupus may require specialists from rheumatology, nephrology, hematology, neurology and dermatology.)

The Mexican experience concurs with many of the points raised in the presentations. There are no reservations for indigenous peoples in Mexico, however the population is often located in geographically isolated communities. As in other areas, primary care practitioners are not skilled at identifying early symptoms of rheumatic diseases and, as a result, it takes an average of four years for patients to see a specialist. Underfunding by government is also a problem. Most Mexicans are covered by one of

five social security systems funded by government. Unfortunately, only certain rheumatic diseases (RA, gout and osteoarthritis) are covered in this system.

Health care system transformation

A question was raised about how to engage communities in health care improvement. Richard Jock described the Norway House approach which involved 14 working groups (comprised of community members, federal health workers, community health care workers and outsiders) each of which looked at different aspects of the integrated model. Despite this extensive consultation and engagement, however, it still took three to four years to implement the integrated model of care. Canada can learn lessons from the Alaska model - for example, tribal control is facilitated by forcing governments to make timely decisions.

Role of the family

In addition to working with patients, rheumatologists in Mexico also work with their families on logistical issues (e.g., to help patients get to appointments, assist with communication, explanations and the disease management plan).

Rheumatic diseases tend to receive a lower priority among health care providers in remote communities because acute diseases (such as heart disease, chronic renal disease, stroke) consume more of the available resources and arthritis is pushed to the side. In Alaska, if multiple family members have a particular disease, they are willing to mobilize for access to care. Manitoba is studying first degree relatives having disease and the impact on families of raised awareness of the disease. Health care providers need to be educated to understand the role of families and to include them in the patient's care plan.

Impacts of demographic change

A question was raised about the impact of urbanization of INA populations on the development of arthritis, its care and outcomes. From U.S. data it appears there has been no impact, although it may be too early to see since urbanization is a relatively recent phenomenon.

Tools to study INA populations are needed. Identifying First Nations populations is a challenge in Canada and an ethical framework for information governance is key. This would unlock data that are already available in the system.

Ethical Considerations for Research in INA Populations

Ethical Conduct for Studies in Vulnerable Populations

Dr. Danielle Bromwich - National Institutes of Health, Bethesda, MD

The concept of vulnerability is not well defined or understood in research ethics, especially as this applies to indigenous populations. This makes it difficult for researchers, sponsors and ethics review committees to know how to conduct research ethically with vulnerable populations. The purpose of this presentation, then, is to get clear on the concept of vulnerability and, in doing so, clarify ethical conduct with vulnerable populations. The special focus of this presentation is ethical conduct for studies with indigenous populations. I argue, in short, that vulnerability is not something that emerges from belonging to a specific group but, rather, is something that emerges from the characteristics of the person or the social situation in which the research is conducted. Ethical conduct requires, then, that researchers, sponsors and ethical review committees be attentive to the ways in which persons can be vulnerable in research and be attentive to the need to balance traditional and appropriate protections with fair access to the goods that can come from research participation.

From the perspective of the individual, research benefits the broader population, not necessarily the subject, thereby putting vulnerable populations at risk. Valid consent to participate in research may be problematic in certain populations, due to such factors as: competence (e.g., children), understanding (e.g., terminally ill patients), or voluntariness (e.g., prisoners).

From the collective perspective, there is a need to flag potentially vulnerable populations and to provide extra protection, but without unnecessarily limiting access to research. Although there are many types of vulnerability, social vulnerability is commonly held among INA populations. To overcome social vulnerability and to achieve a balance of power between communities and researchers, a community-based participatory research (CBPR) approach is essential at all steps in the process.

Principles developed by the Council for International Organizations of Medical Sciences (CIOMS) provide an ethical framework for CPBR, including the following:

- Collaborative partnerships
- Representation from indigenous populations

- Collaboration at all stages
- Mutual respect (for cultures and practices)
- Minimize disparities (e.g., provide training for health care personnel, help set up ERBs)
- Fair distribution of the rewards of research (e.g., intellectual property, authorship, monetary)

CBPR does not substitute for individual consent, however, and may exacerbate the potential for juridic and deferential vulnerability for those who may be liable to the authority of others, and/or who are unwilling to participate.

Canadian Guidelines: CIHR Guidelines for Research in INA Populations

Dr. Malcolm King, Scientific Director,
Institute of Aboriginal People's Health - University of Alberta
Canadian Institutes for Health Research (CIHR)

The Canadian Institutes for Health Research (CIHR) consists of 13 institutes in various health care disciplines, one of which is the Institute of Aboriginal People's Health (IAPH). The IAPH funds nine Network Environments for Aboriginal Health Research (NEARHs) across the country.

The IAPH's strategic directions for Aboriginal health research are:

1. Develop strategic regional, national and international partnerships to advance Aboriginal health research
2. Ensure inclusion and recognition of Aboriginal values and cultures in health research
3. Enhance capacity and infrastructure to advance Aboriginal health research
4. Resolve critical Aboriginal health issues
5. Facilitate and evaluate translation of Aboriginal health knowledge into policy and practice

Guidelines for Health Research Involving Aboriginal People² were adopted in 2007 and have implications for research funding related to community-based participatory research (CBPR). Several articles in the guidelines apply: for example, the expectation that researchers offer communities the option of CBPR, and support

² Available at: <http://www.cihr-irsc.gc.ca>

education and training of Aboriginal people in the community. (For a summary of the guidelines, see Section 2.1 of this report.)

Adopting these ethical requirements demands additional commitment from researchers, resources, and understanding on the part of review panels. The guidelines are intended to level the playing field and to broaden the 'ethical space' in which researchers and communities can find common ground for participation.

Individual vs. Community Consent

Chief Marcel Balfour, Chief - Norway House Cree Nation

What is a Research Collaboration Agreement and why is it needed? The imperative for research partnerships and collaborative agreements is based on indigenous, national and international law. Indigenous peoples are nations, who share a language, history, ceremonies, teachings, traditions, and laws given to us by the Creator, "who placed us here". We have traditional protocols, including treaty making, which are used for the protection of individuals and of our existence as a people.

Western emphasis on the rights of the individual, and de-emphasis of collective rights, runs counter to indigenous approaches. This tendency of the dominant culture puts out of balance the principles on which research (and other) agreements rest.

Two years ago this month, the United Nations Assembly adopted the UN Declaration on the Rights of Indigenous Peoples, endorsing both our individual and collective rights. This necessarily drives the need for a relationship that accommodates those rights and provides for an ongoing relationship between First Nations, the research community and individual researchers.

Research can benefit communities by providing opportunities for knowledge translation, informing policy and providing evidence that can be used to improve conditions. Collaborations need to work at the local level and emphasize collective as well as individual rights in order to be effective. The priority of research, compared with other pressing socioeconomic needs in communities, is relatively low. The leadership needs to be convinced of the importance of the research to become supportive, and the principles of OCAP (ownership, control, access and possession) are essential. Bringing newcomers into the relationship network requires trust - both individually and collectively.

Local-level collaboration agreements must have these elements:

1. Be in writing (to provide certainty)
2. A statement of recognition and respect for the right to self-determination and commitment to meaningful partnerships between the First Nation and the research institute (including recognition of traditional and scientific knowledge, and intellectual property rights)
3. Prior informed consent, according to world standards
4. Involvement of indigenous partners from oversight, to staffing, to all stages of data collection, analysis and interpretation, to conclusions, recommendations and publication
5. Protection of people, lands and resources, and guarantees for reparations
6. Meeting the First Nations OCAP principles
7. Benefits and investments in the community, including a legacy for future generations
8. Mechanisms to resolve disputes.

There are many benefits of research for indigenous communities. Without solid data, the leadership is unable to advocate for improve conditions. Local agreements should enhance research efforts and are not intended to be barriers to good research relationships.

Genetic Studies in Indigenous Populations - Opportunities and Threats

Dr. James Jarvis - University of Oklahoma

Knowledge of genetic profiles can benefit patients, families and communities by informing practical steps to improve health. Therapies can be targeted to the exact protein or proteins that are responsible for the disease effects. Therapies (specific drugs and dosages) can be highly individualized, enhancing effectiveness and avoiding side-effects.

Genetic differences can have clinical consequences. For example, African Americans who receive kidney transplants were observed to have a higher rate of rejection. This was traced to the methods of donor/recipient matching that were not specific enough for this population due to genetic variations. People with different genetic profiles metabolize warfarin differently. Therefore, one size does not fit all, and we must be aware that our diagnostic tests and assessment assumptions may not apply to all

populations. The human genome project offers insights into how genetics works, which will bring new opportunities but also threats.

The perils of genetics include: the irresponsible use of biological specimens (which may be sacred to indigenous groups), stigmatization of specific peoples (for example, removing the right of tribal membership) and misuse or misinterpretation of genetic data by outsiders, which may undermine community cohesiveness and/or identity.

Another consideration is that genetics does not entirely explain the occurrence of diseases in certain populations. For example, why is the onset of diabetes earlier in indigenous populations compared with a high-risk non-indigenous population? The environment has been shown to alter one's DNA and has a huge impact on how our genes operate. Genetic information interpreted without due consideration of the impact of environmental factors on the development of disease may lead to misinformed decision making. (For example, methotrexate is not as effective in certain indigenous populations, while etanercept is more effective, yet the latter is designated by government policies as second-line therapy and patients are required to be on an ineffective medication for a year before being prescribed the biological drug.) The role played by environmental factors - both with and without predisposing genetic conditions - provides an important part of the picture.

In summary, researchers need to be extraordinarily aware of their responsibilities with respect to genetics information. Indigenous peoples need to be aware of the promise of genetics.

Ethics of Informing Indigenous Individuals of Disease Risk

Dr. Patricia Kaufert, Dhiwya Attawar, Dr. Joseph Kaufert - University of Manitoba

The ethics of research on rheumatoid arthritis in Indigenous communities was explored from the perspective of a research team in a qualitative case study. Two specific questions were addressed: (1) what are the ethical challenges of informing healthy individuals of their disease risk; and (2) in what ways does the ethical process of informing risk in a research study differ from that of providing health care? These questions were posed to members of a rheumatology research team including: clinician scientists, clinician research coordinators, research scientists, and community research workers through an initial focus group and in-depth interviews. The multiple, shifting roles of team members allowed a re-examination of the boundaries between clinical and research ethics and the principles that govern them. The practical issues faced by the team in their work revealed the complexity of

applying these principles in the uncharted territory of preclinical disease. In exploring the significance of relationships between the research team and community members in Indigenous communities, a third key question emerged from the data: what are the ethics of trust and reciprocity? Highlights of study findings are presented.

Much of the ethics of risk communication in the preclinical stage of rheumatoid arthritis centres on the ethics of not knowing enough. Knowledge of the evolving autoimmune response in asymptomatic individuals is itself evolving and incomplete. As scientists and clinicians look upstream to trace the earliest evidence of inflammatory disease, they are forced to re-evaluate the criteria for defining the onset of rheumatoid arthritis. The specificity and value of biomarkers of rheumatoid arthritis and their relationship with environmental risk factors continues to be investigated. The genetics of rheumatoid arthritis is advancing but remains complex due to the polygenic, multifactorial nature of the disease. There remains considerable uncertainty about how to apply this information clinically through contribution to early diagnosis of rheumatoid arthritis and to prediction of its course. Synthesis of new data and the translation of this information from the population level to the level of the individual are additional challenges in communicating disease risk. Given these levels of uncertainty, the dilemma arises for both clinicians and researchers as to what meaningfully to tell people.

In the debate on whether or not to disclose disease risk, the implications of sharing information that is incomplete must be considered. The potential impact of this information on the lives of healthy individuals and their families, and on the community in which they live needs to be explored. The potential harms and benefits of telling must be carefully weighed. Researchers must balance the opportunity to affirm people's understanding of their health with the wish to protect people from needless worry and anxiety about illness that may never manifest itself. Recognition of the place and contribution of the individual in ethical decision-making is also an important consideration that recognizes the rights of the individual subject to choose between knowing and not knowing. This classic ethical dilemma has become more complicated with the advent of genetic testing. Genetic information affects all family members whose rights must be balanced with the rights of individuals.

Examining the relationship between clinical ethics and research ethics is useful for understanding the roles of the treating clinician and the research scientist within professional boundaries and the approach of each discipline toward communication of risk. While acknowledging the considerable overlap between these ethical dictates,

Brody and Miller³ argue that the fundamental ethical principles governing clinical practice and clinical research - the goal of providing therapeutic benefit to individual patients and the goal of producing general medical knowledge for the benefit of future patients respectively - are different. Potential conflicts of interest in the dual role of clinical investigator thus arise. Ethical tensions between the clinical and research roles are especially apparent when decisions on treatment of rheumatoid arthritis in the early, pre-clinical phase are made. The dilemma for the researcher is that the earlier that treatment is introduced, the less the opportunity to study the natural progression of the disease. The therapeutic obligation of the clinician to the individual patient subject distinguishes this relationship from the research relationship. The clinician is therefore inclined to be cautious in discussing risk factors and biomarkers of rheumatoid arthritis that are not yet well established and in applying this information in prescribing treatment. The dilemma for the clinician is how to effectively introduce early treatment when there is hypothetically great benefit in terms of prevention but no clear guidelines to inform treatment or to accurately evaluate outcomes.

The ethics of rheumatoid arthritis in Indigenous communities encompasses the multiple dimensions of the individual, the family and the community. This discourse is embedded in the social, cultural, economic and political environment of Indigenous peoples. The data confirms the importance of recognizing the need for a relationship based ethics and for co-participatory research in Indigenous communities. Respecting the autonomy of Indigenous communities was an important part of the process of developing research agreements and partnerships. Ethics scholars working in the field of human genetic research, Bertha Knoppers and Ruth Chadwick⁴, have emphasized that complexity of interaction of genetic factors and familial and socioeconomic co-factors. This combined with the parallel expansion with public and community participation in research policy calls for additional principles including: reciprocity, mutuality, solidarity, citizen participation and universality. The principles of trust and reciprocity emerged as especially significant in the building of long-term, participatory and mutually beneficial relationships with Indigenous communities. Individual, family and community participation in the research was centred on trust. The contribution of research subjects as partners in the research process and in collaborative decision-making on treatment was recognized as integral to the process of advancing knowledge and care of rheumatoid arthritis. The commitment of the

³ Brody H, Miller FG. The clinician-investigator: unavoidable but manageable tension. *Kennedy Institute of Ethics Journal* 2003;13(4):329-346.

⁴ Knoppers BM, Chadwick R. Human genetic research: emerging trends in ethics. *Focus* 2006;4(3):416-422.

research team to the provision of ongoing, quality rheumatology care to all community members contributed also to the building of sustainable relationships.

Discussion: Ethical Considerations for Research in INA Populations

Two main themes emerged during the panel discussion that followed these presentations.

Uncertainty and disclosure

By the very nature of investigation, researchers may have an incomplete understanding of the meaning of the findings of a study. Nevertheless, if they ask, a research subject or patient should be told these results and offered an interpretation of their meaning in an understandable manner.

There is a danger that the results of research genetics and epigenetics could be interpreted from a position of ignorance. For example, payers may use this information to promote 'blame-based medicine' and as an excuse to withhold resources, especially from those who are vulnerable.

To mitigate against these potential dangers a careful, multi-level approach to disclosure is recommended.

Community involvement in research

Research, from a consumer perspective, is very important. In regions where the prevalence of certain rheumatic diseases is high, research studies can be a catalyst for change at the individual as well as the community level. There is a desire for knowledge among individuals and communities, and social benefit derives from raising awareness and talking about a disease. Participation in research makes people feel better by being involved, and the research project can even become a health intervention in itself. It is crucial that research results are shared with the community.

The concept of community-based participatory research (CBPR) is founded on community involvement. It is hoped that, ten years from now, the rheumatic diseases research agenda will be driven by indigenous communities, not by universities. To get to this point, much work needs to be done in the areas of knowledge translation and capacity building in communities. Also, we must guard against barriers being put in place that prevent interactions between communities and researchers.

Clinical Phenotype of Rheumatic Diseases in INA Populations

Juvenile Idiopathic Arthritis in INA Children

Dr. James Jarvis - University of Oklahoma

In adults, indigenous American people have some of the highest incidence and prevalence rates of rheumatic diseases on the globe. This is equally true for indigenous American children, where the prevalence rate of polyarticular juvenile arthritis is three to five times higher than in the broader population. While these prevalence rates have generally been assumed to have a genetic basis, genetic theories fail to incorporate the unique historical and cultural experiences of indigenous American peoples in both the United States and Canada. This talk will discuss how newer studies into complex systems and new insights into epigenetics provide an opportunity to develop an historical-biological understanding of rheumatic disease in indigenous American people.

There are several factors that suggest a genetic basis for patterns of rheumatic diseases seen in indigenous populations.

- Genetic subtype distribution is very different; for example, pauciarticular JRA is more prevalent in Caucasian populations
- A greater proportion rheumatoid factor-positive
- The median age of presentation is significantly older
- There is no association with the A allele and HLA
- There are strong familial patterns of various rheumatic diseases.

However, genetic differences do not entirely explain the patterns seen, especially in familial groups. Environmental factors are also believed to play a causative role. It is known that the environment (trauma, how stress is handled, diet, deprivation, etc.) affects DNA and therefore the genes. An open question is: to what extent have generations of abuse and marginalization resulted in the genetic patterns seen today? Familial patterns can be interpreted as being epigenetic, rather than genetic in origin, as epigenetic changes are potentially heritable.

Inflammation is a complex, interrelated system. Multiple pathways operate simultaneously, so that an upset in one creates perturbations in others. Effective therapy restores the balance to a normal state. (A parallel concept to the traditional medicine approach to maintaining health and well-being.) The human genome

project may offer new ways to get at this complexity – to develop new classifications and predict response to therapy, for example. Instead of focusing on a few genes, we may be able to see networks of protective and promoting genes, and look at therapy as a means to restore balance, rather than to obliterate a few specific factors.

The model for a new vision of health must be developed that is non-linear and takes into account both genetic and environmental factors in a biological ‘systems’ approach. (For example, we should not call juvenile rheumatoid arthritis an autoimmune disease in Aboriginal children, because there is no evidence to suggest that this is its cause. Rather, it may be explained in some children as a lack of coordination between genes.) We need more complex models that incorporate these ideas and also the unique historical experiences of indigenous people.

Systemic Lupus Erythematosus in Indigenous Populations

Dr. Christine Peschken - University of Manitoba

While there is a relative paucity of literature on lupus in indigenous populations, available data demonstrate the marked variation in prevalence and phenotype of Systemic Lupus Erythematosus (SLE) between different indigenous groups. In contrast to the relatively uniform descriptions of high prevalence and severe disease for rheumatoid arthritis, prevalence, severity, and phenotype appear to differ widely depending on the population studied, echoing the heterogeneity seen worldwide in SLE. Prevalence rates vary from extraordinarily high, to much lower than expected, and disease features range from mild to severe, with or without atypical features. This makes it clear that data generated from one group cannot be generalized to North American Indigenous people as a whole.

Locally, a higher than expected prevalence rate has been established, but the phenotype and severity are less well defined, depending on the research method used. Outcomes (damage, and mortality) appear to be worse, however, the majority of this excess burden of disease is likely attributable to poverty and other socioeconomic factors. Care is complicated by higher rates of comorbidities and distance from care providers. Self assessed disease activity is high, as is self-reported depression and poor self-rated health-related quality of life. These findings illustrate the complex interaction between sociodemographic, biological, and health-related behaviours on chronic diseases. Research that further evaluates the causes of these disparate outcomes and tests interventions is urgently needed.

Undifferentiated Arthritis in the Mexican Mestizo Population

Dr. Daniel Xibille-Friedman - Mexican College of Rheumatology

Undifferentiated arthritis (UA) is much more frequent than rheumatoid arthritis(RA) and shows different characteristics. Compared with RA, the clinical presentation of UA shows the following features:

- More acute
- Less affected joints
- Less symmetric
- Oligoarthritis
- Shorter duration of stiffness.

In addition, from 30 to 50 per cent of patients with UA have evidence of preceding bacterial exposure. Some patients are positive for IgM RF and IgA RF. CCP with clinical variables can predict the course and outcomes of disease.

Like First Nations populations in Canada, Mexican Mestizos are also perceived to have severe rheumatoid arthritis but are not well studied. A comparative research study was designed with the following objectives:

- To compare the presenting features of inflammatory arthritis in three ethnic groups: Mexican Mestizos, Native American Indians / First Nations and Canadian Caucasians, including rheumatoid factor (RF) and anti-cyclical citrullinated peptide (CCP) antibody status;
- To compare the clinical outcome of patients presenting with recent onset arthritis or established rheumatoid arthritis in these populations; and
- To determine whether these differences in phenotype severity and clinical outcome were associated with human leucocyte antigen (HLA) or anti-CCP status.

Among patients presenting with early inflammatory arthritis, the results showed a comparable age at onset for the Mexican Mestizo and First Nations groups, and both presented at an earlier age compared with Canadian Caucasians. In contrast, the Mexican Mestizo group had a much greater severity disease, as measured by anti-CCP antibodies and by the number of RA criteria, than either comparator group. Clinical outcomes, measured after one year, were worse for the two indigenous populations.

After one year of follow-up, the disease activity scores (DAS) of Mexican Mestizo and First Nations were similar and both were significantly higher than the Canadian Caucasian population studied. In addition, fewer indigenous patients had achieved remission.

Similar results were shown in patients presenting with late stage arthritis and at one-year follow up. In addition, Mexican Mestizos were much less likely than either of the two comparator groups to have been treated with a disease-modifying anti-rheumatic drug (DMARD).

The increased severity of early inflammatory arthritis seen in Mexican Mestizos and First Nations is only partially explained by increased shared epitope, reduced protective antigens and anti-CCP. Further study of the influence of environmental factors, such as access to medications, on the disease process is required.

Spondyloarthropathies in British Columbia Indigenous Populations

Dr. Kevin J. Keen - University of Northern British Columbia

Rheumatic diseases in the First Nations of British Columbia are known to differ phenotypically from those in persons of solely European ancestry. This is thought to be true for the special case of the spondyloarthropathies.

Surveys for rheumatic diseases among the First Nations of British Columbia began in 1962. These First Nations communities are located along the Pacific Coast. The prevalence of ankylosing spondylitis (AS) was estimated in 1964 to be 6.2 per cent among Haida males. This estimate was based to a large degree upon radiographic evidence of sacroiliitis. Human leucocyte antigens were studied in one-sixth of the Nuxalk people of Bella Coola in 1974 and in 47 per cent of the Band List for the indigenous people of Haida Gwaii in 1975. The Nuxalk and Haida samples were 27 per cent and 54 per cent positive for HLA-B27, respectively.

In 1977, no evidence was found linking *Yersinia enterocolitica* to the prevalence of AS or reactive arthritis in the Haida. A case study in 1987 of 157 members of Nuuchahnulth, of western Vancouver Island, found no cases of either AS or psoriatic arthritis. A study published in 1991 estimated the prevalence of seronegative spondyloarthropathies (SpA) to be 11 cases per 1,000 persons among the Haida, Tlingit, and Tsimshian of the Alaskan Panhandle. A study in Alberta in 1977 among a Cree Nation found no difference in AS prevalence compared to the population of Edmonton. The Haida, Tlingit, Tsimshian, and Cree all have communities in British Columbia.

A proposal for a study to determine the prevalence of the SpA phenotypes and HLA-B27 genotypes is in the process of preparation. This will rely on clinical records held by health authorities operated by the First Nations themselves and will be conducted in coordination with the clinic staff of these health authorities. The study will begin with the Dakehl and Sekani First Nations of central British Columbia and spiral outward. The purpose of the clinical record review is to identify SpA cases for the purpose of estimating prevalences and incidences of these diseases and to determine whether there is evidence of familial clusters of disease.

Future genetic studies are to confirm HLA genotypes in SpA patients and their families. Building on this work, a genome-wide association study could be done to identify novel loci imparting heightened genetic risks for SpA.

Discussion: Clinical Phenotype of Rheumatic Diseases in INA Populations

Two major themes of discussion arose during the question period.

Historical origins of RD

Some studies have suggested that rheumatic disease existed in North America well before European contact, and some of these diseases may even have originated on this continent. However, some participants felt that this evidence is not conclusive and does not explain the patterns seen in INA populations today.

There are methodological challenges to studying historical genetic patterns in INA populations. For example, the Haida population shrunk by 90 per cent in the 1800s to just 588 in 1915 and has reconstituted to about 5,000 today. This ‘bottleneck’ has had an impact on the genetic makeup of the Haida (and other INA populations). The genetically ‘semi-isolated’ status of the Haida needs to be accounted for in the mathematical models.

Because of the relatively small population of the Haida, census surveys are possible. Similarly, in British Columbia all children with rheumatic diseases are seen by a rheumatologist based in Vancouver, therefore comparative studies involving the pediatric populations are easier to conduct.

Regarding the ethics of conducting historical genetic studies, it was noted that proper stewardship of biological samples and databases is important in maintaining or

restoring ethical relationships with indigenous groups whose rights have in the past been disregarded.

Relationship of genes to outcomes

Healthy native individuals have higher titres of autoantibodies. Although the meaning of this relationship is unknown, it suggests that both genetics and environmental factors contribute to the development and outcome of rheumatic diseases. An unpublished UK study from the 1980s showed that levels of autoantibodies correlated with socioeconomic status levels, with higher levels in lower socioeconomic strata.

Conventional research methods may need to be re-examined for studies of indigenous populations. Since phenotypes in indigenous populations are plastic, our classification criteria may not be appropriate and we may need to create our own criteria.

In all studies of INA populations, a western hemisphere approach is needed because these populations extend across borders.

Why is RA So Common in Some INA Populations?

Prevalence of Arthritis Based on Questionnaire Data

Dr. Brenda Elias - University of Manitoba

A questionnaire given to Manitoba First Nations who had stiff, painful joints showed that these symptoms are often a precursor to an official diagnosis. Other symptoms often referred to as secondary include:

- Despondency
- Fatigue
- Depression and anxiety

Depression and anxiety may be associated, along with exposure to past trauma, with hyperactivity of the hypothalamus-pituitary-adrenal axis (HPA-axis), which in turn may contribute to the pathophysiology of rheumatoid arthritis.

Those who had been told by a health care provider that they had arthritis were more often women (1.7 times as likely to have painful, stiff joints in the last year). Also, First Nations individuals who reported being depressed in the last year and to have a

history of suicidality were two times more likely to report having arthritis or rheumatism.

Among people who have stiff, painful joints but have not been diagnosed, they are more likely to be individuals 55 years or older and men (1.5 times more likely to have painful, stiff joints). They are also more likely to be individuals who experienced depression (three times more likely) or who had experienced intense anxiety (two times more likely) in the last year.

They are more likely to be individuals with a history of trauma. Individuals who have a history of suicidality are 1.6 times more likely to report having painful, stiff joints in the last year. They are also individuals who have a history of emotional, physical or sexual abuse. Other analyses have told us that individuals with these histories are more likely to be direct survivors of the residential school system or they are individuals of multigenerational exposure to the residential school system by way of their parents and grandparents.

Prevalence & Phenotype of RA in INA Populations

Dr. Elizabeth D. Ferucci - Alaska Native Tribal Health Consortium

A high prevalence of rheumatoid arthritis (RA) and severe disease has been reported in several INA populations. The objectives of this presentation are: 1) To explore the prevalence of RA in INA populations using epidemiological and administrative data sets; and 2) To define differences between INA and other populations in RA phenotype and severity.

Published literature on prevalence and severity of RA in INA populations is included. Unpublished data provided by investigators in the field are also presented.

Epidemiologic studies have demonstrated a high prevalence of RA in the Tlingit, Yakima, Pima, and Chippewa Indians. Administrative datasets support the high burden of disease in Aboriginal populations in Manitoba. Clinically the disease in INA populations is often described as severe, with early age of onset and a high prevalence of autoantibodies. Rheumatoid nodules and radiographic erosions have been described as more frequent than expected. A high frequency of large joint involvement, assessed by the Lansbury score, and more significant disability defined by Health Assessment Questionnaire (HAQ) has been demonstrated in Aboriginal people in Manitoba, as compared to non-Aboriginals with RA.

Multiple studies support the high prevalence and increased severity of RA in INA populations. These data support the need for further research investigating the causes of this health disparity.

Genetic Risk for RA - Role of HLA

Dr. Kiem Oen - University of Manitoba

In this discussion the role of human leukocyte antigen (HLA) in affecting the risk of rheumatoid arthritis (RA) in INA populations and the risk of RA antibodies as distinct from RA disease will be explored. According to the shared epitope (SE) hypothesis HLA-DRB1 alleles associated with RA share a sequence which increases RA risk. Several INA populations have high frequencies of the SE predisposing these populations as a whole to RA. The RA protection theory states that certain DQ alleles predispose to RA. SE alleles linked to susceptible DQ alleles in stable haplotypes fail to protect against RA; DERA- containing DR alleles linked to susceptible DQ's are protective. Applying this theory, several INA populations are at increased risk of RA because of high frequencies of susceptible DQ's and a lack of DERA alleles. The association of DRB1*0901, a non-SE allele, with RA in some INA populations may also be explained by linkage to susceptible DQ alleles.

That HLA may be associated with RA antibody formation rather than RA disease is supported by the following observations: antibody formation and clinical RA may be separate events as RA antibodies precede clinical RA and may be found in unaffected relatives of INA patients. CCP antibody titres are associated with HLA, high titres with SE and low titres with DR3. The association of SE is much more significant in CCP positive than CCP negative RA. In unaffected relatives of INA patients, anti-CCP may be associated with heterozygous SE and DRB1*0901. However there is no data yet comparing CCP positive individuals who develop RA versus those who don't in long-term studies.

In conclusion, genetic patterns in the general population do not necessarily mean the same thing for First Nations populations with respect to predictiveness of the course of disease or protection against disease.

Genetic Risk for RA - New Genetic Associations

Dr. Kathy Siminovitch - University of Toronto

In the past few years, we have witnessed unprecedented gains in the genetic characterization of complex genetic diseases. Nowhere is this more obvious than in the autoimmune diseases, for which newly-emergent capacity for genome-wide association analysis has enabled discovery of many of the major loci underpinning disease susceptibility. Rheumatoid arthritis (RA) has been particularly amenable to association-based genetic characterization, with at least 25 gene loci now being recognized as sites of RA risk alleles. Included among these loci are the *HLADRB1* and *PTPN22* genes, for which the specific disease-causal alleles are now known.

However, despite these major inroads in genetic definition of RA, our understanding of RA etiology remains very limited and many challenges remain in connecting the new genetic knowledge to improved patient care. The first of these challenges relates to definition of the disease-causal alleles within the newly-identified RA risk loci. Identifying these alleles may not be achievable by genetic approaches alone and is likely to require more complex and costly biologic studies as well as difficult-to-obtain human biologic samples.

Defining the clinical relevance of this genetic information is another major challenge, requiring clear understanding of the biologic and medical impact of specific disease risk alleles. Resolving these issues will be difficult, but continued advances in genetic, epidemiologic and computational tools and methods should make it possible to address both these challenges and to thereby enable new genetic understanding of RA to be translated into tangible medical benefit for affected individuals.

The Pre-Clinical Phase of RA: Lessons from the Cree/Ojibway Population

Dr. Hani El-Gabalawy - University of Manitoba

Rheumatoid arthritis (RA) is a chronic inflammatory disorder which, once established, causes progressive lifelong joint damage. Previous studies have indicated that the detection of anti-citrullinated protein antibodies (ACPA) and rheumatoid factor (RF), in the presence of disease predisposing variants of the HLA-DRB1 gene, is strongly predictive of future RA development. North American First Nations populations have some of the highest prevalence rates of RA in the world (2-5 per cent versus 1 per cent worldwide), frequent multi-case families, early age of onset, high titers of ACPA

and RF, and a high population prevalence of disease predisposing HLA-DRB1 alleles. Thus, the First Nations population is uniquely suited for studying the early events that pre-date the onset of RA.

We have established cohorts of First Nations RA patients, their first degree relatives, and unrelated community controls from several urban and rural communities. Our studies of these cohorts indicate that ACPA and/or RF are present in approximately 35 per cent of disease-free relatives, while the disease predisposing alleles of HLA-DRB1 are present in 60 to 70 per cent of the background population. We have been following this unique cohort for development of the earliest manifestations of RA, attempting to understand the gene-environment interactions that contribute to disease onset. Our study also looks at the contribution of the following environmental factors to the development of RA: smoking, parity and hormones, oral health, mineral oils and infection with proteus mirabilis.

We actively engage First Nations communities in programs aimed at increasing knowledge and understanding of RA and the benefits of early disease detection.

Discussion: Why is RA So Common in Some INA Populations?

Questions were raised across a wide spectrum of topics related to the presentations and the implications of this research.

Interrelationship between psychological factors and rheumatic diseases

What interventions might help to deal with complex histories? Elder Margaret Lavalle offered that much is blamed on external traumas (such as colonization, residential schools and the 'sixties scoop'), leading to a situation where populations have become 'stuck'. It is time to acknowledge the facts and move on. At the same time, it is important to come to terms with colonization and the traumas experienced by First Nations, Inuit and Métis peoples in Canada. Beyond this, women (who are most affected by rheumatic diseases), and especially women leaders, need to know about these associations.

Research and education in the communities are needed to dispel myths and to create more knowledge about these interrelations. This needs to be done as a partnership, to include long-time patients and to bring together indigenous and non-indigenous groups to engage in dialogue.

A cautionary note was sounded that political beliefs and agendas must not be allowed to interfere with the interpretation of data collected in research. Jurisdiction of data is a concern and the potential for this type of conflict of interest must be avoided.

Genetic causes of rheumatic diseases

Some studies show that antibodies can be associated separately with the predisposition or protection to rheumatic diseases. Other cohorts (e.g., Dutch, Colombian, Mexican, Canadian) reveal different associations. No strong effects were seen when additional antibody systems were studied. It is likely that an array of genetic factors, plus environmental influences, will be predictive of disease. This complexity makes translation to the clinic very difficult.

From a consumer perspective, knowing that there is a genetic explanation of the origins of disease dispels the myth that the disease was brought on by something the individual had done. Education about the inherited aspects of disease is needed to help remove the stigma and as part of a holistic healing process for individuals and families.

Methodologic opportunities and challenges

The shift from familial studies to single nucleotide polymorphisms (SNPs) is a huge strategic change. We can now scan the entire human genome and pick out similar changes among all patients with the same disease, rather than focusing on familial patterns.

Technologies can be used in combination to pinpoint targets for therapy, although diagnosis will remain difficult despite these advances in genetics. Genome function is important, as well as its structure, in affecting disease pathways which may be common linkages between diseases.

Policy implications

While genetic profiling is fascinating to scientists, it can be a risk to the individual with respect to data security. Governments, insurers, etc. may use this data to deny services. Nevertheless, this information will become widely available, the question is: How do we put safeguards in place? Also, genome profiling is at an early stage - we don't know how to use the data yet. The U.S. has introduced new legislation to prevent genetic information from being used by insurance companies for harm.

A question was raised about the linkage between communities that participate in research and their ability to benefit from the outcomes of that research. This is clear

in the example of drug therapy, where a biological drug that is discovered and developed based on studies conducted in communities may be unaffordable to those who helped produce the knowledge. Policies of some health insurers which disallow biological drugs as first-line therapy are a concern.

Genetics and environment

RA prevalence is trending downward in the general population (although the trend for chronic inflammatory diseases is going upward in some populations). This is most likely due to public health measures (e.g., clean water) that prevent or delay the onset of disease.

Poster Presentations

Arthritis in Aboriginal Manitobans: Evidence for a High Burden of Disease

Cheryl Barnabe, Department of Medicine, University of Calgary; Brenda Elias, Department of Community Health Sciences, University of Manitoba; Judith Bartlett, Department of Community Health Sciences; Leslie Roos, Department of Community Health Sciences; Christine Peschken, Departments of Internal Medicine and Community Health Sciences, University of Manitoba.

Statement of Purpose: To evaluate the relative burden of arthritis and patterns of care in Aboriginal Manitobans, using multiple data sets to ensure a representative picture.

Methods: Arthritis burden and healthcare utilization was ascertained using 3 separate data sources. Physician claims for 3 common ICD-9 musculoskeletal diagnoses were abstracted from the Population Health Research Data Repository for First Nations (FN) Manitobans and compared to all other Manitobans. Self-reported arthritis rates were obtained from the Manitoba First Nations Regional Longitudinal Health Survey (MFN Survey), which surveyed FN persons living on-reserve. Data on ethnicity and diagnoses were abstracted from the Arthritis Centre research database, which contains records of all patients seen at the Arthritis Centre.

Results: Twice as many FN Manitobans had physician claims for rheumatoid arthritis (RA), degenerative arthritis, and unspecified arthropathy compared to all other Manitobans. MFN Survey data identified a self-reported arthritis rate of 21.0% and a RA rate of 3.0%. Data for 687 Aboriginal patients and 4135 Caucasian patients were abstracted from the Arthritis Centre database. Aboriginal patients seen in the Arthritis Centre were 2 to 4 times more likely to have a diagnosis of inflammatory disease, and less than half as likely to have noninflammatory disease.

Conclusion: The data highlight the increased burden of arthritis in Aboriginal Manitobans, and draw attention to large gaps in our knowledge of how, why, and when Aboriginals access medical care.

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Anti-CCP is a Better Predictor of Erosive Arthritis in Oklahoma Tribal Populations

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Purpose: Rheumatic diseases cause significant morbidity within American Indian populations. Oftentimes, clinical rheumatic disease presentations overlap and historically associated autoantibodies are not useful in making a diagnosis or helping assess prognosis among Oklahoma tribal members. The purpose of this study is to identify specific autoantibody associations in Oklahoma tribal populations with rheumatic disease and to help develop better diagnostic algorithms and treatment protocols for American Indian patients.

Method: Tribal-based rheumatic disease clinics were established and staffed with tribal personnel and a consulting rheumatologist. To date we have enrolled 202 Oklahoma tribal members (88 with rheumatic disease and 114 controls). Control groups of age and gender matched SLE-affected African (n=55) and European (n=55) Americans were available for comparison. Medical records were reviewed for clinical features and a rheumatologist evaluated patients for disease criteria, activity, damage and treatment. Samples were tested for: ANA and anti-dsDNA [IIF]; anti-CCP, rheumatoid factor and aPLs [ELISA] and other lupus autoantibodies. Statistical analysis was conducted using chi-square and ANOVA methods.

Results: Rheumatic diseases within the enrolled members from tribal clinics include: 35 (39%) rheumatoid arthritis patients, 14 (16%) systemic lupus erythematosus [SLE] patients, and 8 (9%) systemic sclerosis [SCL] patients. The remaining patients have a variety of rheumatic disease conditions or rheumatic disease symptoms which did not meet ACR criteria for a given disease. RA patients were over three times as likely as non-RA patients to be anti-CCP positive (48% vs 15%, $p < 0.001$) and more than twice as likely to be RF (by IgM) positive (50% vs 23%, $p = 0.011$). Moreover, by multivariate logistic regression, anti-CCP was a significantly better predictor of RA than RF ($p = 0.025$). Anti-phospholipid antibodies were also found across several different rheumatic diseases, including RA, scleroderma and SLE. Finally, precipitating levels of autoantibodies against previously unidentified antigens (UILs) were found in nearly 10% of the rheumatic disease populations.

Conclusions: Clinical presentations of rheumatic disease within Oklahoma tribal members are oftentimes overlapping and difficult to define by ACR criteria. Other autoantibodies (aPLs and UILs) are found in a variety of American Indian rheumatic disease. Anti-CCP is a better RA predictor in tribal communities and warrants changes in current diagnostic practice.

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Arthritis Prevalence and Access to Care in Three On-Reserve Communities of Aboriginal Peoples: A Total Population-Based Pilot Study

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Purpose: Identify the prevalence of functional limitations likely associated with arthritis in three on-reserve Aboriginal Peoples' communities and evaluate access to care.

Method: A household survey of all adults living in three on-reserve communities was performed using a community case-finding strategy. Band Council support was provided and public forums were held to obtain community feedback prior to survey. Surveys were administered face-to-face by three trained interviewers residing in the community. Each community member was screened for chronic joint, neck, and back pain, and functional limitations associated with arthritis. Access to health care services was recorded. Descriptive analyses were conducted.

Results: Of 536 members in these communities, 402 completed the screening interview (75%). Participants ages ranged from 19-93 yrs (mean 46), 52% female, 61% married and 23% never married. Self-report diagnosis of arthritis (excluding fibromyalgia) made by a physician or other health professional was reported in 30% of the cases (n=119/402), with 79 identifying specific type(s) of arthritis including RA (n=27), OA hip, n=24; knee, n=33; hand, n=25, neck and/or back disorder (n=18), or other (n=12). In comparison, non-age adjusted prevalence estimates reported in national surveys using the same question was 19% for off-reserve Aboriginal Peoples and 16% for non-Aboriginal Peoples. Chronic joint, neck, or back pain and functional limitations were reported by 41% (166/402). 53% (88/166) reported never having any prior injury or accident. Of these 88 individuals, 65 reported having seen a health care professional at least once for their problem: family doctor=94%; physical therapist=38%; occupational therapist=34%; rheumatologist=29%; traditional healer=20%; dietician=16%. Assistive devices were used by 51%, and 75% used medications in the past 12 months. Difficulties obtaining care needed in the past 12

months were reported by 36% (n=32/88), including wait lists (n=16), access to rheumatologists (n=13), transportation availability/costs (n=12), treatment costs (n=8), and perceived inadequate health care (n=8).

Conclusion: The prevalence of self-report arthritis in three communities of Aboriginal Peoples exceeds that reported in national surveys for off-reserve Aboriginal Peoples and non-Aboriginal Peoples. Burden of arthritis appears to be high in this population, with 41% reporting functional limitation likely attributed to arthritis. Access to care appeared to be suboptimal in this population. In future research we will attempt to determine diagnosis and explore solutions to improving access to care.

Correlates and characteristics of Aboriginal Canadians with arthritis and rheumatism

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Background: Arthritis and rheumatism are the most commonly reported chronic conditions among Aboriginal Canadians and prevalence estimates can be up to two times that of non-Aboriginal Canadians. The purpose of this study is to describe regional differences in characteristics and correlates of Aboriginal Canadians with arthritis.

Methods: Cross-sectional data from over 24000 individuals self-identified as Aboriginal (First Nations, Métis, Inuit) aged 15 years and over who participated in the Aboriginal Peoples Survey (APS) 2006 were used. The APS was conducted by Statistics Canada to collect information on the social and economic conditions of Aboriginal people living in Canada. Respondents were asked whether they were told by a doctor, nurse or other health professional that they have arthritis or rheumatism. Associations between arthritis and various risk factors were examined separately for the 3 territories (north) and the 10 provinces (south).

Results: Prevalence of arthritis or rheumatism in the territories was approximately 13% compared to 20% in the provinces. Arthritis is more prevalent among females than males in both the 'north' and 'south'. Almost half of Aboriginal Canadians with arthritis smoke occasionally or daily. Daily smoking was associated with 50% increased odds for arthritis in the 'south', but was not a significant factor in the 'north'. Overweight was associated with over 40% increased odds for arthritis for Aboriginals living in the 'south' compared to just 15% increased odds in the 'north'. However, obesity significantly elevated the odds for the 'north' to 50%, while more modestly increasing odds for arthritis in the 'south' to approximately 60%. 6% of Aboriginal Canadians in the 'north' and 8% of those in the 'south' report having arthritis and at

least one other chronic condition such as diabetes, heart disease, or high blood pressure. Only 12% of Aboriginals with arthritis in the ‘north’ reported consulting a health professional in the 12 months previous to the survey, compared to 19% of those in the ‘south’. Over one-third of Aboriginal Canadians with arthritis in the ‘north’ reported that traditional medicines were available to them compared to approximately 45% in the ‘south’.

Conclusions: Correlates of arthritis and rheumatism differ between Aboriginal Canadians living in the territories and provinces. Unique characteristics of those with arthritis in the ‘north’ and ‘south’ should be taken into account in the planning of prevention and treatment interventions.

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Arthritis and PBC in West Coast First Nations families: A common association or coincidence?

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Conclusions: Our study will provide an opportunity for understanding whether the arthritis reported in our patient population has a specific phenotype. A consistent phenotype may provide more information for linkage studies broadening the autoimmune syndrome associated with PBC. Our linkage studies will take into consideration genes responsible for this pattern.

Introduction: While rare for the general population, primary biliary cirrhosis (PBC) is not rare in British Columbia’s (BC) First Nations (FN) population where it is the leading indication for liver transplant and has a strong familial basis¹. Sixty percent of participants with PBC reported having arthritis in the interview done at the time of study enrollment². An 11 part questionnaire is underway to determine the phenotype of arthritis in PBC participants and their family members.

Methods: A review of all participants who self reported having ‘arthritis’ or rheumatoid arthritis is being carried out (n=38). All newly enrolled participants that respond ‘yes’ to arthritis are given the additional questionnaire, done over the phone. The questionnaire provides a focused history taking for general joint pain. Closed ended questions were used in joint diagrams, time to best improvement if morning stiffness was present and in obtaining information such as medication use and

whether a rheumatologist had been involved in the diagnosis. Open ended questions were used to explore the type of joint pain present and how it had affected their lives. As available, medical history records are being updated for all autoimmune diseases in original participants who have noted any changes to their health.

Background:

What is PBC?

- Autoimmune (AI) liver disorder, often asymptomatic in early stages. Leads to portal inflammation, cirrhosis, liver failure, transplantation/death .
- > 95% of cases have circulating AMA and up to 50% have detectable ANA.³
- Not caused by EtOH
- One of the highest concordance rates of an AI disease (63%).³
- While arthralgia can be present it is not a common presenting symptom.

Types of arthritis occurring with PBC

Rheumatoid Arthritis (prevalence 1.8-5.6%)^{2,4,5}

Commonly coexisting AI diseases that may present with arthritis:

- SLE
- Systemic Sclerosis
- Sjogrens Syndrome
- Thyroid disorders (untreated)*

No focused reports of osteoarthritis in PBC patients was available but given the average age of diagnosis in the general population (5th and 6th decade) it could be expected to be present at the prevalence of the general population. When age-standardized, arthritis is reported to be higher in Canadian Aboriginals (living off reserve) than in non Aboriginal Canadians.⁶

In our previous paper discussing genetic predisposition in our population to PBC, 63% of affected participants are from 3 nations (coastal Amer-Indian ancestry). High rates of arthritis and SLE have been reported previously in West Coast First Nations,⁷ American Indians and SE Alaskan Natives.⁸ The higher numbers of autoimmune diseases in our study population (cases and controls) compared to other PBC studies suggests an increased susceptibility to arthritis and other AI disease, however the association with PBC *per se* is unclear.

It remains to be seen whether the arthritis reported in such high rates in our population is similar to that reported in other PBC populations. First Nations patients in BC with PBC are more likely to be women, live on Vancouver Island, and are younger at referral (46.5 years vs. 54.7 years, $p=0.001$) for evaluation for transplant than the non-First Nation population.²

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A descriptive look at Manitoba's indigenous population and rheumatoid arthritis

*Gabriela Montes Aldana, Irene Smolik, PhD, Hani S. El-Gabalawy, MD.,
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Statement of Purpose: Earlier diagnosis and treatment for rheumatoid arthritis (RA) may help alleviate disease severity as well as the high economic costs associated with this disease. When considering the clinical and biological profile of patients and first-degree relatives, it is equally important to examine the self-reported socio-demographic, environmental risk and health profile of this group. This secondary analysis describes the socio-demographic-health profile and RA specific environmental risk of First Nations (FN). RA probands and first-degree relatives participated in a longitudinal study investigating the "Early Identification of Rheumatoid Arthritis in First Nations."

Methods: RA probands (RA-pro) and first-degree relatives (FDR) were recruited at the rheumatology clinic at the Health Sciences Centre in Winnipeg, and rheumatology clinics held in two northern First Nation communities. Along with a clinical exam and blood work, study participants (women and men, aged 17 years and older) were asked

to fill out a questionnaire, which included social demographic (age, sex, urban/FN community, education and marital status), RA specific environmental risk questions (smoking, pregnancy), and health profile (RA diagnosis; joint issues; medication use). A bivariate analysis was conducted using baseline data collected between September 2005 and May 2009 (overall N=377; RA pro n=121; FDR n=256).

Results: The median age of all participants at baseline visit was 37 years, with ages ranging from 17 - 79. Over half (53%) of the study population reported that they had not yet completed high school. The majority of the participants were either married (40%) or single (40%), and the rest were widowed, separated or divorced. 81% of the study population reported to have been regular smokers (past and present). The median pack-years at baseline were 4.5 years. There was some gender differences found (age, marital status, area of residence and pack years). Among women, a large percentage (88%) had been pregnant at least once, and 27% had been pregnant 3 or 4 times. Live births were also lower than expected.

Conclusions: In this study population, a high number of RA pro and FDR's were ever smokers, and the smoking rate for both groups was similar to that reported in a recent Manitoba FN regional health survey. A large number of FDR's were also experiencing pain, swelling and stiffness in their joints (59%, 38% and 49% respectively). In FN populations generally, women tend to have a higher number of pregnancies than women in the general Canadian population. In this study, a similar finding was observed. Further research, however, is required to see if the number of pregnancies has any affect on disease development. Overall, this study demonstrated that in addition to clinical and genetic data, self-reported social, demographic, health, and environmental exposure data helps to further define the onset of arthritis.

Killer immunoglobulin-like receptor (KIR) gene profiles in a Manitoban First Nation people and potential influence in disease susceptibility.

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Background: Pro-inflammatory immunity is active in fighting infections and the development of autoimmunity. Canadian Aboriginals have a greater infectious and autoimmune disease burden than non-Aboriginal populations. Though environment contributes to this statistic, recent studies indicate that genetic differences may have a critical influence in disease susceptibility and outcomes. In particular, killer immunoglobulin-like receptor (KIR) genes, present on natural killer cells and certain T

cells subsets, are associated with the progression of infectious diseases such as hepatitis C virus (HCV) and HIV. Due to their role in regulating pro-inflammatory immunity, these molecules are also associated with the onset and progression of autoimmunities including rheumatic diseases.

Methods: To investigate the possibility that KIRs influence disease outcomes in First Nation peoples, we evaluated which KIR genes were present in the peripheral blood mononuclear cells of Manitoban First Nation (predominately Ojicree, n=86) and Caucasian (n=93) individuals without known chronic viral infections. This study was performed in consultation with the Assembly of Manitoba Chiefs Health Information Research Committee and with ethic approval by the University of Manitoba. All participants provided informed consent.

Results: The First Nation cohort exhibited an enhanced prevalence of the 2D5S gene, whereas 2DL2 and 2D5S2 presence was decreased approximately 2-fold compared to the Caucasian cohort. The frequency of 2D5S3 were also diminished over 5 fold in the First Nation cohort ($p < 0.0001$). Despite a similar percentage of First Nation (95.3 %) and Caucasian (90.0 %) individuals possessing the 2DL3 gene, further analysis revealed that 2DL3 more often occurred in a homozygous manner in First Nations relative to Caucasians. When First Nation gene patterns and genotypes were compared to global reports, similarities were observed between the First Nations and indigenous peoples in Mexico and Argentina, perhaps reflecting a similar disease selection in the face of new world infections. In contrast, the Caucasian results reflected other Caucasian studies, as well as paralleling East and West Asian cohorts.

Conclusions: Of note, KIR gene profiles of the First Nation participants as compared to the Caucasians corresponded to KIR gene profiles observed in HCV clearance compared to chronicity, potentially aligning with epidemiological observations suggesting that First Nation peoples have an enhanced capacity to clear HCV infection. However, as with rheumatoid arthritis studies where the KIR gene association was population dependent, the association of these diseases with the First Nation KIR gene profile would only be able to be determined within that population or potentially with other populations that display similar profiles.

Appendix C CIHR Guidelines For Health Research Involving Aboriginal People

Summary of Articles

Article 1

A researcher should understand and respect Aboriginal world views, including responsibilities to the people and culture that flow from being granted access to traditional or sacred knowledge. These should be incorporated into research agreements, to the extent possible.

The first principle of these Guidelines is premised on a need for researchers to understand and respect Aboriginal world views, particularly when engaging in the sphere of traditional and sacred knowledge, and the corresponding responsibility that possession of such knowledge entails. Researchers should understand the broader senses of accountability in order to understand the responsibility they have when entering into a research relationship with Aboriginal people.

Article 2

A community's jurisdiction over the conduct of research should be understood and respected. This article should be read in the context of the discussion in Section 1.5, which addresses the application of this document.

Some Aboriginal communities manage and control matters dealing with health. Where this is the case, a researcher should comply with any by-laws, policies, rules or procedures adopted by the community. For example, an Aboriginal community may have its own Research Ethics Board and/or community research protocols.

Article 3

Communities should be given the option of a participatory-research approach. Genuine research collaboration is developed between researchers and Aboriginal communities when it promotes partnership within a framework of mutual trust and cooperation. Participatory research enables a range of levels and types of community participation while ensuring shared power and decision-making.

Such partnerships will help to ensure that research proceeds in a manner that is culturally sensitive, relevant, respectful, responsive, equitable and reciprocal, with regard to the understandings and benefits shared between the research partner(s) and Aboriginal community(ies).

Article 4

A researcher who proposes to carry out research that touches on traditional or sacred knowledge of an Aboriginal community, or on community members as Aboriginal people, should consult the community leaders to obtain their consent before approaching community members individually. Once community consent has been obtained, the researcher will still need the free, prior and informed consent of the individual participants.

A process to obtain the free, prior and informed consents from both the community affected and its individual participants should be undertaken sufficiently in advance of the proposed start of research activities and should take into account the community's own legitimate decision-making processes, regarding all the phases of planning, implementation, monitoring, assessment, evaluation and wind-up of a research project.

The requirement for community consent is distinct from the obligation of researchers to obtain individual consent from research participants.

Article 5

Concerns of individual participants and their community regarding anonymity, privacy and confidentiality should be respected, and should be addressed in a research agreement.

The researcher, the individual participants and the community should have a clear prior understanding as to their expectations with regard to the anonymity of the community and of the individuals participating in the research project, and the extent to which research data and results will remain confidential to the researcher.

If anonymity is not possible, or if there are necessary limitations to anonymity or confidentiality, these should be clearly communicated.

Article 6

The research agreement should, with the guidance of community knowledge holders, address the use of the community's cultural knowledge and sacred knowledge.

Article 7

Aboriginal people and their communities retain their inherent rights to any cultural knowledge, sacred knowledge, and cultural practices and traditions, which are shared with the researcher. The researcher should also support mechanisms for the protection of such knowledge, practices and traditions.

Any research involving Aboriginal people will involve the sharing of some cultural knowledge, practices and/or traditions even when these are not the subjects of the study, as they provide necessary context. The recording of knowledge, practices and traditions in any form (written notes, audio, video, or otherwise) should only be done with explicit permission and under mutually-agreed terms that are set out in advance of the research with the guidance of appropriate Elders and knowledge holders. All uses and wider dissemination of cultural knowledge, practices and traditions should also be by permission.

Article 8

Community and individual concerns over, and claims to, intellectual property should be explicitly acknowledged and addressed in the negotiation with the community prior to starting the research project.

Expectations regarding intellectual property rights of all parties involved in the research should be stated in the research agreement. Not all information and knowledge can be protected by existing intellectual property laws, given the strict eligibility criteria defining these legal rights. Understanding and communicating what does and does not qualify as intellectual property under current Canadian and international laws is the joint responsibility of the researcher and communities involved. Research with explicit commercial objectives and/or direct or indirect links to the commercial sector should be clearly communicated to all research partners.

Article 9

Research should be of benefit to the community as well as to the researcher.

A research project should lead to outcomes that are beneficial to the participating Aboriginal community and/or individual community members. Benefit sharing vis-à-vis a community should be interpreted from the community's perspective. This may include tangible and intangible benefits, including those arising from altruism.

Article 10

A researcher should support education and training of Aboriginal people in the community, including training in research methods and ethics.

Researchers should work to foster capacity building among Aboriginal people to enhance their participation in research projects and improve the overall interactions between Aboriginal governance mechanisms and public educational institutions.

Article 11.1

A researcher has an obligation to learn about, and apply, Aboriginal cultural protocols relevant to the Aboriginal community involved in the research.

Article 11.2

A researcher should, to the extent reasonably possible, translate all publications, reports and other relevant documents into the language of the community.

Article 11.3

A researcher should ensure that there is ongoing, accessible and understandable communication with the community.

Aboriginal communities often have cultural protocols involving interactions within the community. It is important that researchers learn about these and respect them.

When providing a research project report to the community, the researcher should, at a minimum, provide an executive summary in the language of the community unless the community has expressly waived this. The reports or other communications of results should use language and terminology that are readily understood by the community.

Article 12.1

A researcher should recognize and respect the rights and proprietary interests of individuals and the community in data and biological samples generated or taken in the course of the research.

Article 12.2

Transfer of data and biological samples from one of the original parties to a research agreement, to a third party, requires consent of the other original party(ies).

Article 12.3

Secondary use of data or biological samples requires specific consent from the individual donor and, where appropriate, the community. However, if the research data or biological samples cannot be traced back to the individual donor, then consent for secondary use need not be obtained from the individual. Similarly, if research data or biological samples cannot be traced back to the community, then its consent for secondary use is not required.

Article 12.4

Where the data or biological samples are known to have originated with Aboriginal people, the researcher should consult with the appropriate Aboriginal organizations before initiating secondary use.

Article 12.5

Secondary use requires REB review.

These guidelines set out basic principles for the collection, disclosure, use and transfer of data and biological samples. The details of safeguards protecting the privacy and confidentiality of data and biological samples should be negotiated as part of the research process and specified in a research agreement. Subject to the community's views on traditional or sacred knowledge, co-ownership of data between researchers and communities is recommended because the Aboriginal community and the researcher are both integral to the production of data.

If there is to be transfer of data or biological samples to a third party, this should be done only with the consent of the researcher, the individual participants and the community. If the third party is to engage in secondary use of the transferred data or biological samples, then a further consent to that use must be obtained. The consent should address how confidentiality and privacy will be respected.

In any case, secondary use of data or biological samples requires new consent unless such use is specifically agreed to in the research agreement. Notwithstanding the above, individuals retain the right to access data about themselves. In cases where the research is a governmental activity, other standards for protecting privacy may apply, flowing, for example, from the *Canadian Charter of Rights and Freedoms* or privacy legislation.

Article 13

Biological samples should be considered “on loan” to the researcher unless otherwise specified in the research agreement.

Subject to the terms of the research agreement with their community, biological samples from Aboriginal participants should be considered “on loan” to the researcher, analogous to a licensing arrangement, and this should be detailed in the research agreement.

Article 14

An Aboriginal community should have an opportunity to participate in the interpretation of data and the review of conclusions drawn from the research to ensure accuracy and cultural sensitivity of interpretation.

Research involving Aboriginal people is susceptible to misinterpretation or misrepresentation when information about the group is analyzed without sufficient consideration of other cultural characteristics that make the group distinct.

The opportunity for review of research results by the Aboriginal community should be provided before the submission of research findings for publication, to ensure that sensitive information is not inappropriately divulged to the public and that errors are corrected prior to wider dissemination.

This should not be construed as the right to block the publication of legitimate findings; rather, it refers to the community’s opportunity to contextualize the findings and correct any cultural inaccuracies.

Article 15

An Aboriginal community should, at its discretion, be able to decide how its contributions to the research project should be acknowledged. Community members are entitled to due credit and to participate in the dissemination of results.

Publications should recognize the contribution of the community and its members as appropriate, and in conformity with confidentiality agreements.

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