ICORD 2012 Conference

Measures for dealing with “Intractable Diseases” -Past, Present and Future-

Chairperson: Committee for Measures of Intractable Diseases
Professor Emeritus: University of Tokyo
President Emeritus: National Center for Neurology & Psychiatry
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4th February, 2012 (University of Tokyo)
What is Intractable Disease: “Nambyo”? - Definition of “Nambyo” -
Authoritative Opinions of Specialists on the Characteristic Features of “Nambyo”

In April of 1972, the Diet formally asked the following two experts to give their opinions on “Intractable Diseases (Nambyo)” in general.

**Shigeo OKINAKA (1902~1992)**
Professor of the 3rd Department of Internal Medicine, University of Tokyo, and President of the Japanese Neurological Association.

1) Hardly (or never) recovered,
2) Unknown etiology,
3) Heavy burden on patients and family’s mind and economy

**Hirotsgu SHIRAKI (1917~2004)**
Professor of the Neuropathology, University of Tokyo, and President of Japanese Neuro-pathological Association

1) Unknown etiology
2) No established therapy
3) Chronic and progressive clinical course
In 1972, the Ministry of Health and Welfare enacted the “General Outlines for taking Measures to deal with Intractable Disease [Nambyo]” which was first established in the world. The extent of Nambyo was proposed as follows, based on the experts’ opinions.

1) Unknown etiology, Un-established therapy, and Frequent after-effects.
2) Chronic course, Heavy burdens in terms of economical, psychological and physical issues.

Attn: At this stage, there was no concept of “rareness” in the extent of Nambyo. More than 25 years was needed until “rareness” was added to the extent.
In 1995, the Ministry of Health and Welfare revised the definition of intractable diseases (Nambyo) as follows, under the suggestion of the Special Committee for Discussing the Future of “Nambyo”

1) **Etiology** is unknown --- degenerative disease etc
2) **Frequency** is low (*) --- rare disease
3) **Therapy** is not established --- hardly curable
4) **Economical, psychological and physical burdens**
   --- progressive course / necessity of heavy care
5) **Diagnostic criteria** should be established
   --- Specialists should collaborate each other

(*) : Total number of patients should be less than 50,000
Past
- short history -
1958 A case report of “after diarrheal neurological signs and symptoms,” later named Subacute Myelo-Optico-Neuropathy (SMON)

1960s SMON patients gradually and steadily increased in nation-wide fashion.

Two Streams of Measures for supporting “Nambyo”

1) SMON stream

- Diarrhea
- 2-3 weeks
- Paresthesia on feet
- Paresis on feet
- Gait disturbance
- Loss of position sense
- Visual loss
- Memory disturbance

Pyramidal tract (gait disturbance) - Lumbar cord

Posterior column (loss of position sense) - Cervical cord
1964~1970
Pandemics of SMON in Nagano, Saitama, Okayama, supports an “infection theory” of SMON. Finally in 1970, a virus research specialist reported to discover “a novel virus causing SMON”. The “infection theory” strongly hurt SMON patients.

A view of virus-origin of SMON was much strengthened

A novel type of virus was discovered from patients of SMON

6th February, 1970
ASAHI news paper
1964 A small sized research funds were raised by the MHW and others Ministries.

1969 In order to facilitate the researches on etiology of SMON, the government expanded the research funds, and launched “the Council for Nation-wide SMON Research Group”.

1970 Members of the SMON Research Group discovered that SMON is an intoxication of the most popular anti-diarrheal drug; clioquinol (trade name is “chinoform”). Chinoform was instantly announced not to use in the medical practice any more.

From the view point of welfare, the medical expenses of SMON patients were totally covered by the Government.
After the official action of the MHW in 1970, newly diagnosed SMON patients steeply went down to zero.

Action to Stop Usage of Clio-quinol on 8th September, 1970
The Success Story of SMON was a Strong Driving Force for Promoting Researches and Measures for Intractable Diseases; Nambyo

This is a “golden Triangle” in order to combat “Nambyo”
2) Another stream

1961 Start taking care of Handicapped Children by the public expenses.

1964 Nation-wide Research Group on Intractable Hepatitis was formed and financially supported by the government.

1968 Start financial support for the physical and/or mental training of Patients of the Inborn-error of Metabolism and Autistic Patients by the government.

1968 Launched the Patient Community of Muscular Dystrophy.

1969 Launched the Patient Community of SMON.

1970 Launched the Patient Community of Behcet Disease and Rheumatism.

1971 Launched the Patient Community of Collagen Diseases and Renal Diseases.

The community of patients and several members of the Diet contributed to the establishment of measures for Nambyo.
3

Present
- measures being operated today -
The Present Status of the Measures for “Nambyo”

1. Selection of “Nambyo”

130 diseases were selected as Nambyo for “special research”.
1) Unknown etiology, 2) No effective treatment,
3) Economical and psychological heavy burdens, and
4) Rareness ; number of patients are less than 500,000
Of 130 diseases, 56 diseases are the targets for being treated
with special favor in terms of medical expenses.
Recently 214 diseases were further selected as candidates of
the second group of Nambyo.

2. Size of Budgets

Budgets for researches (130) ------------ 10 billion yen
Budgets for medical expenses (56) ------ 28 billion yen

3. Number of Recipients of Medical Expenses

Approximately : 700,000 --- increased by 30,000/year
Transition of Certified Recipients of “Nambyo”

Number of Recipients

Total Numbers of Recipients:
680,000 (2008) ↓ 700,000 (2010)

Fiscal Years

1974 1989 2008
A Component Ratio by each “Nambyo” in terms of Numbers and Expenses

Numbers of Recipients

Public Funds

Ulcerative Colitis

Parkinson

SLE
A transition of the total number of patients receiving chronic dialysis

More than 280,000 patients

A point of time that the patients can escape from paying their own expenses for dialysis

3631 patients

Statistics of Chronic Dialysis of Japan. (31\textsuperscript{st} December, 2008)

1972

2008
A List of “Rare and Intractable Diseases”

5,000～7,000 diseases (∗)

Definition of “Rare and Intractable Diseases” is not uniform in the world.

A List of “Rare and Intractable Diseases”

Specified Diseases Targeted for Investigation (130)

- Bone marrow fibrosis
- Temporal arteritis
- Xeroderma pigmentosum
- Fisher syndrome etc

Specified Diseases Targeted for No Charge (56)

- Lysosomal diseases
- Multiple Sclerosis
- Sarcomoidis
- Parkinson disease etc

Candidates for Specified Diseases in Future (214)

- Werner syndrome
- Hyper—IgD syndrome
- Dystonia etc
# A Transition of Medical Expenses in Japan

<table>
<thead>
<tr>
<th>Fiscal year</th>
<th>Total (trillion yen)</th>
<th>Insurance A (trillion yen)</th>
<th>Insurance B (trillion yen)</th>
<th>C (trillion yen)</th>
<th>D (trillion yen)</th>
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<td>10.0</td>
<td>8.1</td>
<td>15.5</td>
<td>1.7</td>
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</table>

A: Health insurance handled by the employer  
B: Compulsory health insurance handled by the MHW  
C: Support institutions for aged persons (older than 70) handled by the MHW  
D: Total support expenses handled by the central and/or regional government for patients of intractable diseases or disabled persons  

Ministry of Health & Welfare  
(July, 2010)
Future
-issues that should be solved or improved -
Points being Discussed in Reviewing and in Rebuilding the Measures for Nambyo

1. Nambyo should be selected equitably.
   All the intractable diseases are not managed as Nambyo.

2. The process of selection and approval of Nambyo should be fair.
   Transparency is important in every process.

3. Concrete measures for Nambyo patients should be balanced among institutions.
   Each institution has its own merits and demerits.

4. Measures for Nambyo should be carried out comprehensively.
   Not only research but various types of service are needed.

5. The institution should be stable and sustainable.
   A consideration of future generation is important.

6. Protection of Nambyo by law should be put in the field of vision.
   In order to make the institution stable, it should be protected by legislation.
Advocates to bring rare disease philanthropy under one umbrella

NORTH BETHESDA, MARYLAND—Rare diseases, defined in the US as those occurring in fewer than 200,000 people in the country, collectively affect around 10% of individuals worldwide. Yet the majority of the public can hardly name a single rare disease. As a result, most orphan disorders fall under the radar and remain poorly funded.

Patient advocacy groups are one of the primary backers of research into rare diseases. But the hundreds of disease-specific foundations and organizations out there rarely work together to raise funds, and the rare disease landscape has remained fractured and siloed.

To remedy the situation, the R.A.R.E. Project, an initiative launched in 2008 to raise awareness and accelerate the development of therapies for rare diseases, is rolling out a new platform to serve as a one-stop shop for innovative research into all 6,000-plus rare diseases.

“We’re trying to bring new people in to care about rare disease,” says Nicole Boice, founder and president of the Children’s Rare Disease Network, part of the R.A.R.E. Project. “The idea in fact is that we will stimulate foundations to think differently about funding and research,” adds R.A.R.E. Project CEO Jonathan Jacoby.

Modeled after services such as Kiva and Save the Children, where donors can precisely match their contributions to the specific project of their choice, R.A.R.E. is launching a website, called the Global Genes Fund, intended as a clearinghouse for rare disease philanthropy, where people can select projects to fund. Jacoby hopes that by bringing hundreds of research projects under one umbrella, individuals, foundations and corporations will be more likely to donate to multiple causes.

Last month, R.A.R.E. secured $50,000 for a beta version of the site, which the organization plans to make public later this year, Boice and Jacoby announced here at the Genetic Alliance annual conference on 16 July.

For projects listed on the page—which will be vetted through some as yet undefined criteria—supporters will be able to read an affected child’s personal story, the details of the study and why the research is important, among other details.

“The challenge with rare diseases is that they’re rare, and there aren’t that many families that can raise money,” says Geraldine Bliss, research chair of the Phelan-McDermid Syndrome Foundation. “A concept like [the Global Genes Fund] is really great because it allows you to reach beyond your immediate circle of support.”

“The rare disease community is large enough and deserving enough to have an effort like this and to succeed at it,” Boice says. “It’s time, it’s really time.”

Elie Dolgin