48th Annual Meeting, 2020, Virtual One-Day Meeting

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Category: Annual ETS Meetings

Annual ETS Meetings

Tuesday September 15th from 10.00 am to 5.00 pm (CEST)

Download: ETS Invitation Letter / Flyer Register here

The ETS council regrets not being able to celebrate this year's ETS meeting in Madrid, but we are happy to partially replace it by a virtual one-day event in order for our members and collaborators to share their current findings in the field of reproductive and developmental toxicity.

Therefore, we would like to invite you all to the 1st virtual one-day event of the European Teratology Society (ETS), to be celebrated on the 15th of September online from 10:00 am to 5.00 pm (CEST).

Sign up for this exciting program, a great opportunity for sharing your knowledge with colleagues and discuss hot topics in a virtual environment.

With warmest regards, keep safe and healthy!

Arantza Muriana

Meeting Organisation

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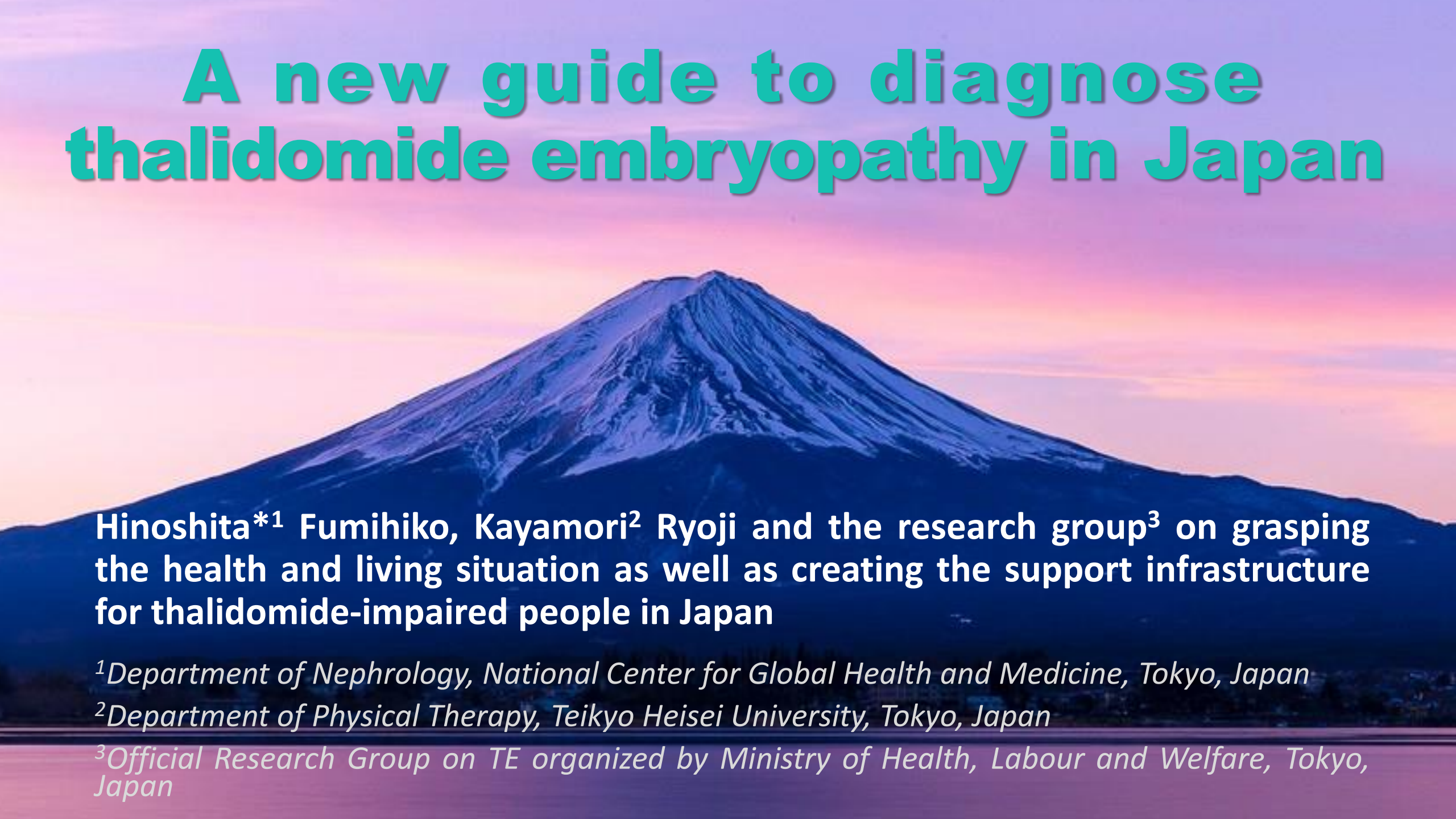
Programme Overview

10:10 am	Welcome by Arantza Muriana, Nicola Powles-Glover and Steven Van Cruchten
10:30 – 12:00 pm	Short communications Chairs: Arantza Muriana & Elena Menegola
10:30 am	Screening of multi-endocrine disruptors in zebrafish María José Mazón- Biobide, Spain
10:45 am	In vitro biotransformation of proteratogens in different laboratory animal models, including the zebrafish Chloé Bars, Comparative Perinatal Development, University of Antwerp, Belgium
11:00 am	Assessment of neurodevelopmental adverse effects induced by Intrauterine growth restriction and testing of future therapies. Application in an in vitro rabbit neurosphere model Britta Kühne- GRET, INSA-UB and Toxicology Unit, Faculty of Pharmacy, University of Barcelona and BCNatal-Barcelona Center for Maternal-Fetal and Neonatal Medicine (Hospital lClínic and Hospital Sant Joan de Déu), Fetal i+D Fetal Medicine Research Center, IDIBAPS, Spain

11:15 am ✓	A new guide to diagnose thalidomide embryopathy in Japan Fumihiko Hinoshita, Department of Nephrology, National Center for Global Health and Medicine, Japan
11:30 am	ZNF48 and ZNF84 are potentially involved in the regulation of genes affected by thalidomide Thayne Kowalski, Universidade Federal do Rio Grande do Sul, Porto Alegre; 2CESUCA, Brazil
11:45 am	Challenges when designing juvenile animal studies that meet global regulatory expectations Luc De Schaepdrijver, Janssen Research & Development, Belgium
12:00 – 1:00 pm	BDRP and European Teratology Society Exchange Lecture Early Principles of Teratology: Does Karnofsky's Law Still Apply Chairs: Susan L. Makris, US Environmental Protection Agency and Nicola Suzanne Powles-Glover, AstraZeneca Dr. David Karnofsky: The First 50 Years European Teratology Society Derek R Newall, European Teratology Society Past-President Dr. David Karnofsky: Can He Rest in Peace or Do We Have a Way to Go? BDRP Alan M. Hoberman, Charles River
1:00 – 2:00 pm	Lunch

以下、午後の部は略。　書式は✓も含め一部改変。

A new guide to diagnose thalidomide embryopathy in Japan



Hinoshita*[1] Fumihiko, Kayamori[2] Ryoji and the research group[3] on grasping the health and living situation as well as creating the support infrastructure for thalidomide-impaired people in Japan

[1]Department of Nephrology, National Center for Global Health and Medicine, Tokyo, Japan

[2]Department of Physical Therapy, Teikyo Heisei University, Tokyo, Japan

[3]Official Research Group on TE organized by Ministry of Health, Labour and Welfare, Tokyo, Japan

Background

The history of thalidomide embryopathy (TE) started back in 1958. About 60 years have passed since thousands of babies, exposed in utero to thalidomide, were born with a variety of visceral disorders and birth defects such as limb deformities, phocomelia, and hearing loss or impairment.

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at Deutsches Apotheken-Museum in Heidelberg

In fact, however, TE still continues to make history. Some specific problems remain unresolved, including new claimers for TE. Many persons with congenital birth defects have newly claimed to be thalidomiders in European countries as well as a few in Japan. New claimers have emerged with the reintroduction of thalidomide or by saying they were overlooked 50 years ago. Based on the present situation regarding new claimers for TE, a UK group showed a diagnostic algorithm for TE (DATE) in 2019*. We also felt the necessity to determine any new diagnostic criteria which are unique to Japan.

** S. Mansour, E. Baple, C.M. Hall . A Clinical Review and Introduction of the Diagnostic Algorithm for Thalidomide Embryopathy (DATE). J Hand Surg Eur 44 (1): 96-108, 2019*

Method

1) Six members were selected for the Diagnostic Criteria Development Committee of TE from the members of the Official Research Group on TE in Japan. The committee consisted of the research group head, 2 rehabilitation doctors, a radiologist, an oto-rhinolaryngologist and an ophthalmologist. The staff in charge of the Ministry of Health, Labour and Welfare also attended the committee as observers.

2) The committee met four times in 2019 to establish a guide to diagnose TE. Mr. Sato, the chairman of the Ishizue Foundation, the public interest incorporated foundation of thalidomide victims in Japan, also attended the committee as an observer for the last two meetings. We finally held a consensus meeting in which some other members of the research group and pharmaceutical companies' staff as well as thalidomide victims and general citizens participated. At the consensus meeting, a tentative guide or diagnostic flowchart to diagnose TE which had been suggested by the Diagnostic Criteria Development Committee was shown and freely discussed.

3) A tentative guide with diagnostic flowchart was made as follows:

* Each member suggested indispensable and primary conditions to diagnose TE based on objective references and past experiences as well as on radiological findings. These conditions were shown to the committee from their own specialized points of view.
* Each member also examined previous reports and documents associated with the diagnosis of TE.
* We further read and studied a diagnostic algorithm for TE (DATE) a UK group had reported in 2019 [J Hand Surg Eur 2019, 44:96–108].
* We seriously discussed how to diagnose TE at the 2nd International Symposium on TE in Tokyo held on Jul 14 and 15, 2019, where many specialists on TE got together from Germany, UK, Sweden, Switzerland, Brazil as well as Japan. There were some specialists on TE who were knowledgeable about diagnosis of TE, such as Prof. Lavinia Schuler-Faccini from Brazil, Prof. Ryoji Kayamori from Japan and Ms. Emma Baple from UK, a member of the group determining DATE.
* We also examined many congenital diseases which are similar to TE and listed for candidates for the differential diagnosis.

Diagnostic procedure

Results

New Claimers

Definite case

1) Born in 1958 to 1964
2) Mother's positive history of thalidomide intake during pregnancy
3) Congenital disorder of bilateral limbs or congenital hearing disorder, or both (See major conditions in Details)

Suspected case

Essential conditions

1) Born in 1958 to 1969; Or examined given a possible situation of TE just in case even if born after 1970
2) Mother lived in a country where thalidomide was sold during pregnancy
3) Negative family history
4) Evidence of at least one congenital disorder in upper limbs, lower limbs, face, eyes, ears and congenial hearing impairment which are typical of TE (See major conditions in Details)
5) No unilaterality of upper limb deformity

Incompatible with essential conditions above → **Exclude TE**

Check clinical characteristics and results of diagnostic imaging

Confirming 3, or more than 3, major conditions (at least 2 major conditions in addition to abnormal image findings)

Yes → **Thalidomide Embryopathy (TE)**

No

Evaluation by multiple specialists on TE

1) Differential diagnosis for similar congenital disorders
2) Genetic testing if necessary

#Prerequisite

Mother's negative history of taking specific drug such as anti-epileptic drugs causing congenital limb deformities and hearing impairment as well as of viral infection such as rubella during pregnancy

Major clinical conditions

General findings

1) Upper and lower reduction defects are longitudinal dysplasia. Preaxial longitudinal dysplasia (radial side) or hypoplasia including thumb hypoplasia is recognized in the upper limb deformity type which is often found in Japan.

2) Hypoplasia and deformity of the limbs are basically bilateral (not always symmetric). Upper limb deformity is not unilateral.

3) No family history of similar congenital malformation.

4) Congenital hearing impairment is found, and there are multiple deformities of temporal bones, inner, middle or outer ears. Moreover, other diseases or syndromes to cause these deformities can be excluded. Crocodile tears syndrome and Duane syndrome from infancy are characteristic of TE.

Image findings

1) X-ray examination and CT reveal deficits or hypoplasia of upper limbs (humerus, radius, ulna, carlpals and finger bones), namely dysmelia. Pointed shoulder is also characteristic of TE.

2) X-ray examination, CT and MRI reveal sacrococcygeal hypoplasia.

3) X-ray examination, CT and MRI reveal that multiple vertebrae (cervical or upper thoracic vertebrae) are fused, becoming block vertebrae.

4) Ultrasonography, CT and MRI cannot identify gallbladder (gallbladder agenesis).

5) Ultrasonography, CT and MRI reveal abnormal lobulation of medial and lateral segments in the left lobe of liver.

6) CT reveals malformation in auditory organs such as in the semicircular canals, auditory ossicles, vestibule, cochlea, inner ear canal, facial canal and outer ear canal.

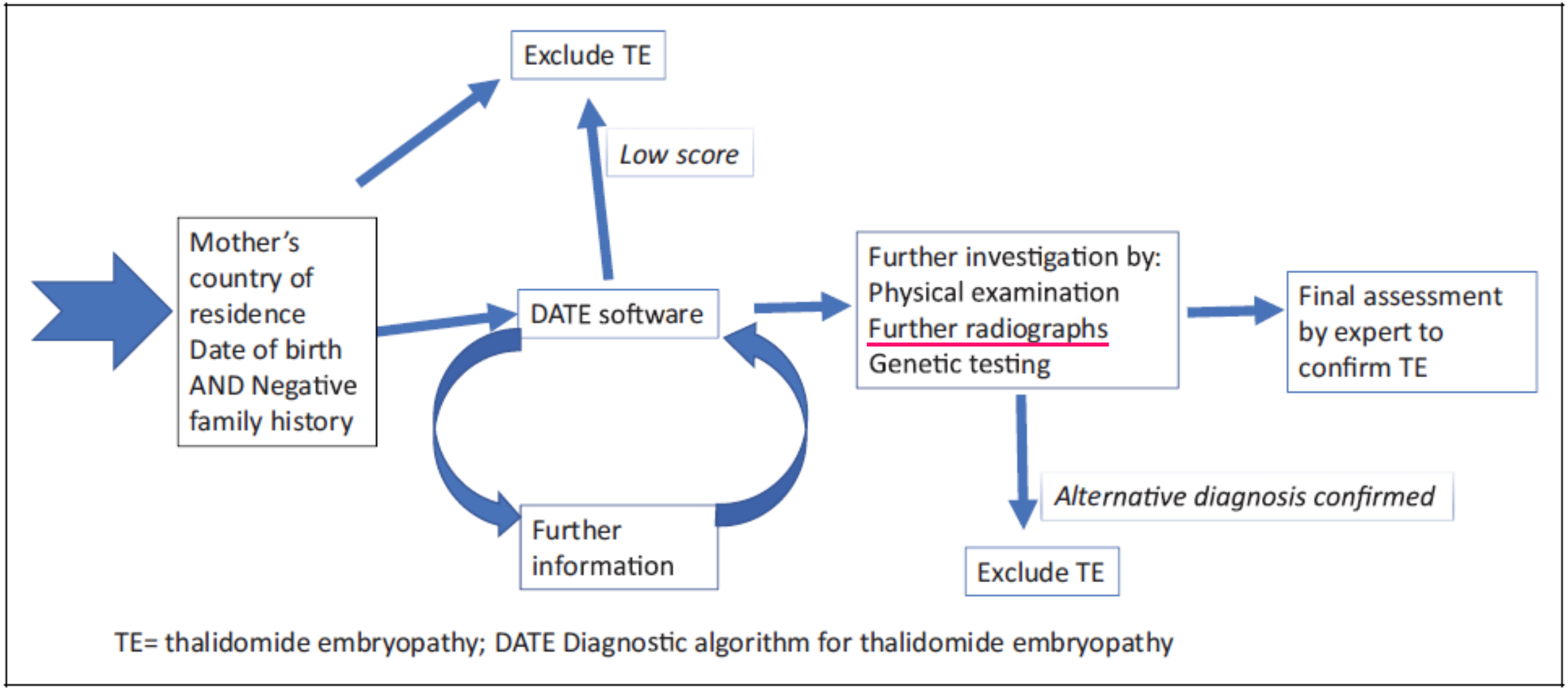
7) MRI reveals deficits or hypoplasia of cranial nerves such as auditory and facial nerves.

8) CT and MRI reveal microphthalmia.

Major congenital malformations to be excluded from the differential diagnosis

1) Okihiro syndrome (Duane-radial syndrome)
2) Holt-Oram syndrome
3) VATER/VACTERL association
4) Townes-Brocks syndrome
5) Thrombocytopenia-Absent Radius syndrome (TAR)
6) Fanconi anemia (Fanconi pancytopenia syndrome)
7) Roberts syndrome

Pathway for the assessment of a patient with possible TE
suggested by Mansour S, Baple E and Hall CM



J Hand Surg Eur 44 (1) : 96-108, 2019

Discussion

1) We newly determined the guide to diagnose TE, which is applied to the Japanese thalidomiders and new claimers for TE born in Japan.
2) The guide was determined based on clinical findings, past experiences, radiological findings as well as objective references. In particular, the guide for Japan is characterized by emphasizing the clinical findings and adopting **image findings of CT, MRI and ultrasonography** in addition to simple X-ray examination as major conditions.
3) We have the main flowchart for diagnosing TE, but we have neither scored the likelihood of TE nor adopted any diagnostic software in this guide for Japan, in part because we thought it is difficult to do precise grading or weighing of abnormalities and malformations in new claimers. We already know the great variety of congenital deficits or malformations in thalidomiders.
4) Finally, it was stressed that this guide is not suitable to diagnose TE in new claimers in other countries because the dose and frequency of thalidomide intake by mothers, and the race and phenotype of TE might differ in different countries.

Conclusion

The Guide to Diagnose TE was newly determined and officially published in Japan on March 31, 2020.

We believe that this guide will be used when new claimers for TE request a differential diagnosis, and that it will persistently become the cornerstone for every clinical practice, support and care as well as for research associated with TE in Japan.


Thank you for your attention

Major congenital malformations to be excluded for differential diagnosis

1) Okihiro syndrome (Duane-radial syndrome) : possible to be excluded by familial history
2) Holt-Oram syndrome: the main problem is congenital heart disease
3) VATER/VACTERL association: possible to be diagnosed by the diagnostic criteria determined by The Japan Society of Pediatric Genetics.
   Different from TE in the respect of what vertebrae abnormalities are spinal dysraphism and block vertebrae of thoracic and lumber vertebrae
4) Townes-Brocks syndrome: familiar with genetic mutation of SALL1
5) Thrombocytopenia-Absent Radius syndrome (TAR): characteristic of thrombocytopenia
6) Fanconi anemia (Fanconi pancytopenia syndrome) : characteristic of anemia
7) Roberts syndrome: main characteristic is mental retardation. difficult to make a differential diagnosis for TE in a mild case of Roberts syndrome