

整形外科・リハビリ科の診療： サリドマイド胎芽症の形態学的特徴

Two New Claimers（自分はサリドマイド胎芽症ではないか？）の問題

1. Have you seen or heard of a case with unilateral damage? from Hamburg, Germany
「片側障害のサリドマイド胎芽症はあるか」
2. Am I a thalidomider ? from Osaka, Japan
「私はサリドマイド胎芽症でしょうか」

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Dear Colleagues

I am writing to you because I have a patient who put a claim against the Conterganstiftung in order to get recognition as a thalidomider. The medical judgment is yet unclear.

She has:

1. a unilateral longitudinal dysmelia left: aplasia of the thumb, aplasia of scaphoid bone and dysplasia of trapezium bone, forearm is 3 cm shorter than the right arm, radius bone narrow.
2. a duodenal stenosis

No other defect (ENT, eyes, internal) detected. Date of birth and medical history seem to fit for a thalidomide damage.

The reason for the refusal of the medical experts is the fact that the right arm is completely normal and as far as they know there is no solid case of a strict unilateral limb damage due to congenital thalidomide exposition.

My questions to you:

- have you seen or heard of a case with unilateral damage?
- are there any publications on this topic?
- what is your opinion in this case?

Thank you very much for your help in this matter.

Best regards from Hamburg

Rudi Beyer

Dr. med. Rudolf Beyer

Conterganprechstunde Hamburg

Schön Klinik Stiftung für Gesundheit gGmbH

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Am I a thalidomider ? from Osaka, Japan

「私はサリドマイド胎芽症でしょうか？」



3

H.M 54 year-old man—
born on January 19,1962

Bilateral triphalangeal thumbs with thenar atrophy
No family history of the same anomalies. Has one kidney deficiency

両手の特徴は、両側母指三節症、母指球筋萎縮があります。片側性腎欠損があります。家族歴には同様な破格はありません。



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X-ray films showing bilateral triphalangeal thumbs

いわゆる母指が三節症になっています



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Abnormality confined only to both hands

異常は両手に限局しています



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Morphological characteristics in thalidomide embryopathy

この2症例を頭の前におき、サリドマイド胎芽症の形態学的特徴

1. Preaxial longitudinal deficiency/hypoplasia
—軸前縦列低形成
2. Almost symmetrical with a little asymmetry
—ほぼ左右対称的、少し非対称性を含む
3. Upper more commonly affected than lower limbs
—主に上肢が侵される
4. Dislocated joints and synostoses or fused bone and joints
—関節脱臼と骨や関節の癒合がある
5. Basic form and triphalangeal thumb
—基本型があり、母指三（指）節症がみられる
6. Associated visceral defects
—内部臓器の欠損を合併することがある

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Dysmelia:Thalidomide skeletal anomalies —Henkel L and Willert HG

1. 300症例のサリドマイド胎芽症児に基づいた形態パターン
2. Pre-axial longitudinal deficiency/hypoplasia
軸前縦列低形成：母指→橈骨→上腕骨の順に減数化している

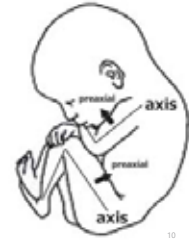


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What means pre- and post-axial ?

Axis is a central line in the limbs of the uterine fetus
軸前とか、軸後とかは、何を表しているかということ、子宮内胎児の肢位で、上下肢の中心線を軸axisと言っています。

軸前preaxial : thumb母指, radius橈骨, tibia脛骨など
軸後postaxial : little finger小指, ulna尺骨, fibula腓骨など



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On symmetrical vs. asymmetrical involvement

1. Thalidomide circulates fetus through umbilical cord
2. limb buds produced step by step right and left alternatively
resulting in almost symmetrical thalidomide anomalies with a little variation

サリドマイド薬剤は母胎から臍帯血を通じて胎児へ移行することになり、さらに胎芽期初期の肢芽形成(limb buds)には、左右同時よりむしろ左右交互に、数日に形成されると考えられる。このことから、上肢低形成には若干の左右差が生じると思われる。この2症例の右上肢は一見正常です。



Right CTS



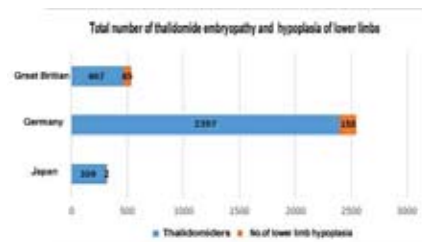
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As to dominance, Upper more commonly afflicted than lower limbs

In Great Britain, 65 out of 467 persons(14%) had lower limbs involved.
In contrast, in Japan 2 out of 309 persons(less than 1%) involved in lower limbs.



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Dislocated joints in shoulders and hips

Hypoplasia in humeral head and skeletal muscles around shoulder girdle
resulting in shoulder subluxation
両側上腕骨と骨頭は低形成になっており、肩関節は亜脱臼位になっている



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Hip dislocation and hypoplasia

右骨頭と臼蓋は低形成になっており、左股関節は亜脱臼位で変性が著明



Fusion of elbow

On the left, radius lacked and elbow fused in the ectromelia with club hand. Even in the ectromelia, digits over ulnar or postaxial side are almost intact.
On the right, thumb lacked

下段の左上肢は、母指、橈骨欠損、示指低形成、尺骨と上腕骨は癒合しています
上段の右上肢は、母指欠損、比較的健側で過用による手根管症候群があります



Proximal synostosis of radius and ulna

Thumbs hypoplastic

両側とも近位部で橈骨-尺骨が癒合している
母指低形成で、左は示指と癒合している



Morphological characteristics in thalidomide embryopathy

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— **基本形型と母指三指節症**
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Basic form in thalidomide embryopathy

重度から軽度のサリドマイド胎芽症の共通している、基本型は何か？

1. Basic form is not phocomelic but remaining of hands even in phocomelia
— フォコモリア（海豹症）ではなく、両手が残っていること
2. Digits over postaxial side are almost intact in phocomelia
— 軸後性の小指、環指、あるいは尺骨が残っている
3. Postaxial elements remain with lack/ hypoplasia of thumb and thenar muscles, which is basic form in thalidomide embryopathy
— 母指欠損、母指球筋低形成が基本型である



上肢低形成群の分類と頻度



Triphalangeal thumb : 母指三指節症

Last but not least, triphalangeal thumb is rare in other embryopathies, but common in thalidomiders


母指三指節症は、母指欠損であり、サリドマイド胎芽症では比較的頻度は高い



You are welcome, Professor W Angus Wallace

We are looking forward to meeting you and having your lecture on replacement of shoulder and elbow joints






The challenges of Joint Replacement for Thalidomider's Shoulders and Elbows


2nd Workshop on Thalidomide Embryopathy on 18/02/17

Prof W Angus Wallace *NHS Consultant*
 Orthopaedic (Shoulder & Elbow) Surgeon
 Nottingham University Hospital NHS Trust
 & **Mr Raymond Newman**, Harrogate Hospital




The History of Thalidomide

- Thalidomide (alpha-phthalimido-glutarimide) was developed in Germany as an anticonvulsant drug in 1957.
- Early trials failed for epilepsy treatment but showed it had sedative properties, and particularly it had one remarkable property: overdoses simply caused prolonged sleep, not death.
- Marketed in Germany in 1957 under the name Contergan.
- Marketed in the UK in April 1958 as the hypnotic Distaval, promoted on the basis that it was very safe because you could not over-dose on the drug.




Thalidomide Complications

- 2 cases of children with limb defects were shown at a paediatric meeting in Kassel, Germany by Pfeiffer in October 1960
- Wiedemann in 1961 described 13 affected children
- The Australian obstetrician William McBride and the German paediatrician - Widukind Lenz suspected a link between birth defects and the drug, a theory Lenz proved in 1961. Problems include hearing problems, heart disease and ear and facial deformities
- In the late 1950s/early 1960s >10,000 children in 46 countries were born with deformities such as phocomelia as a consequence of thalidomide use.




Thalidomide Problems

- Reduction deficiencies of the limbs = phocomelia (“seal like limbs”) or dysmelia (“congenital abnormality characterized by missing or foreshortened limbs”)
- Neurological problems
- Malformations of the eyes, ears and deafness
- Defects of the heart and kidneys and malformations of the alimentary system



Patients affected


- The only people affected were the children of mothers who took thalidomide between 1958 and 1962.
- Thalidomide was then withdrawn – however some drugs were still around till 1965.
- In 2009 there were known to be 457 surviving patients in the UK who had developed phocomelia.
- These patients are now aged between 58 and 62 and many are developing degenerative joint disease and running into serious problems with activities of daily living.




Thalidomide Survivors by Country

(Approximate figures for 2017)

• West Germany ??? 2,700 +	• Italy	90
• United Kingdom 450	• Australia	45
• Japan 300	• Taiwan	30
• Spain 200	• USA	10
• Sweden 120		
• Canada 100		
• Brazil 100		




X-ray of a Normal Shoulder




EMed Handbook
 Emergency Medicine Centre

Upper Limb X-Rays www.emed.ie/Investigations/Xray_Limb_Upper.php



The Authors Cases

- 12 patients with phocomelia due to Thalidomide have been referred for advice because of increasing disability in their shoulders or elbows.
- These patients have had minor joint abnormalities (3 cases), moderately abnormal joints (6 cases) and grossly abnormal joints (3 cases).



RN Case Study 1 JS (Female 35 years)



- The first reported case of joint replacement in the upper limb in a phocomelia patient in the literature
- Raymond J Newman (1999) "Shoulder joint replacement for osteoarthritis in association with thalidomide-induced phocomelia", *Clinical Rehabilitation*; 13; 250-252

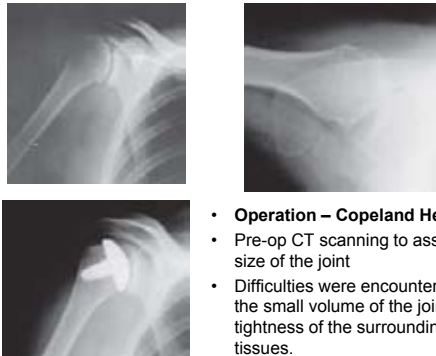


Case Study 1 JS (Female 35 years)

- 35-year-old woman presented with increasing pain and stiffness in the shoulder of her right non-dominant upper limb unresponsive to conservative treatment.
- Thalidomide-induced phocomelia of the right upper limb – short humerus solidly fused to a short bowed radius.
- Partial fusion of the humero-ulnar joint in slight flexion and the functional hand was small, with a hypoplastic little finger.
- The shoulder had no more than 45 degrees of combined forward flexion and combined abduction and with a 10 degree internal rotation contracture. All movements were painful.



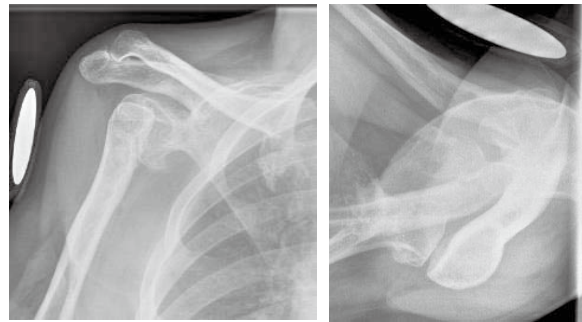
Case Study 1 JS (Female 35 years)



- Operation – Copeland Hemi 3/12/97
- Pre-op CT scanning to assess the size of the joint
- Difficulties were encountered due to the small volume of the joint and the tightness of the surrounding soft tissues.



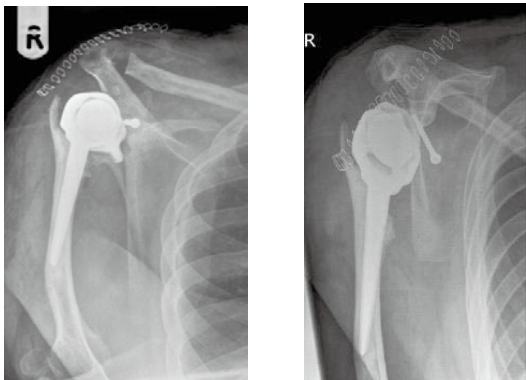
WAW Case Study 2 JW (Male 46 years) Operation 14th March 2007



WAW Case Study 2 JW (Male 46 years) A Bayley-Walker Reverse Total Shoulder Replacement



WAW Case Study 2 JW (Male 46 years) Operation 14th March 2007



WAW Case Study 2 (Male 46 years) Follow-up 15th May 2008 (14 months)



WAW Case Study 2 JW (Male 46 years)
Follow-up 15th May 2008 (14 months)



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WAW Case Study 2 JW (Male 46 years)
 Revision Op for loosening 13th September 2009 (30 months)



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WAW Case Study 2 (Male 46 years)
 Revision TSR 2009 Exam 28th May 2012 (5 years)



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WAW Case Study 2 JW (Male 46 years)
 Follow-up x-ray 30 April 2015 (8 years)



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Interview with John on 18 Feb 2017



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WAW/Gerry Williams (Philadelphia) Case Study 3
BB (Male 51 years) Operation 22 January 2012



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WAW Case Study 4 LS (Female 50 years) Clinical Problem

- Phocomelia Left arm (Rt arm not normal)
- Left arm never particularly good but could carry shopping bag
- Fell onto left arm 6 months ago
- Now arm is more wobbly and painful and nerve type neuralgia down arm
- On Examination no elbow stability i.e. elbow is wobbly in all directions
- Shoulder is also becoming painful

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WAW Case Study 4 LS (Female 50 years) X-rays Left Arm 5th January 2012



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WAW Case Study 4 LS (Female 50 years) CT 3D Reconstruction 5th Jan 2012



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WAW Case Study 4 LS (Female 50 years) Surgical Plan

- Treat the elbow instability
- Two options – Fusion or Joint replacement
- Fusion would decrease function and shorten the limb
- Total Elbow Replacement with a Discovery TER is planned
- Sizing of the Elbow for TER has been carried out.
- But operation postponed as too many risks

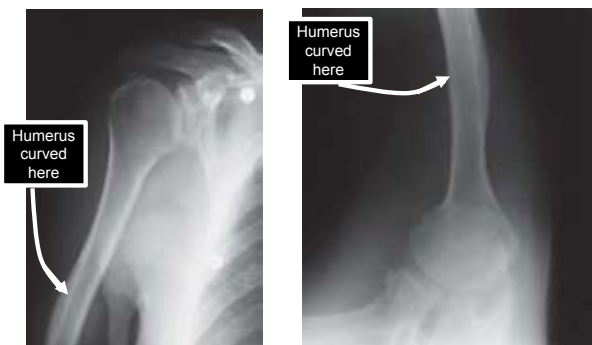
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WAW/Howard Routman Case Study 5 MG Florida (Male 49 years) Operation 13 Aug 2008

- Phocomelia both arms – Right less affected
- Painful Right Shoulder due to Osteoarthritis
- Increasing disability because of pain & limited movement in right shoulder

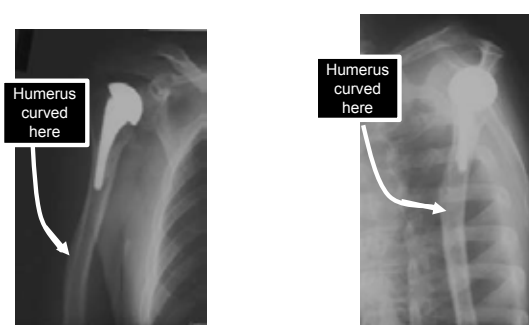
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WAW/Howard Routman Case Study 5 MG Florida (Male 49 years) Pre-op 13 Aug 2008 – bent humerus




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WAW/Howard Routman Case Study 5 MG Florida (Male 49 years) Post-op 13 Aug 2008 – bent humerus



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**WAW Case Study 6 PA Nottingham DoB 03/08/62
(Male 50 years) Op Lt 18/04/2012 Rt 13/03/2013**



NOTTINGHAM SHOULDER & ELBOW UNIT


**WAW Case Study 6 PA Nottingham DoB 03/08/62
(Male 50 years) Op Lt 18/04/2012 Rt 13/03/2013**



Bilateral Vaios Anatomic Total Shoulder Replacements


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**WAW Case Study 7 JL Nottingham DoB 20/10/1960
(Female 53 years works as a doctor)
Revision Copeland Hemi to Vaios Reverse TSR Op Rt 27/11/2013**



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**WAW Case Study 7 JL Nottingham DoB 20/10/1960
(Female 53 years works as a doctor) 2 Year Follow-up
Revision to Vaios Reverse X-rays Rt 29/11/2013 & 03/09/2015**



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Conclusions

- Phocomelia of the upper limb is a major surgical challenge
- We have learned that even the “normal” joints are abnormal in Thalidomiders – shoulders, elbows, hips and knees
- There are likely to be a significant number of these patients presenting over the next 10 years and lessons learned by those surgeons who have already treated these patients should be shared with others.

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Angus & Jackie Wallace with Prof In-Ho Jeon & Young-Sun in Korea



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The End

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