EUROPEAN SYMPOSIUM ON LATE COMPLICATIONS AFTER CHILDHOOD CANCER

19–20 APRIL 2007 LUND SWEDEN

PROGRAMME AND ABSTRACT BOOK

LUND UNIVERSITY

BARNCANCER FONDEN

www.eslccc2007.com

Table of Contents

Sponsors

Welcome to Lund and Sweden

Organizing committee

Christian Moëll, chairman
christian.moell@skane.se

Veronica Bojsen
verabojsen@hotmail.com

Thomas Wiebe
thomas.wiebe@skane.se

Lars Hjorth
lars.hjorth@skane.se

Scientific committee

Hamish Wallace, chairman
hamish.wallace@luht.scot.nhs.uk

Christian Moëll
christian.moell@skane.se

Thomas Wiebe
thomas.wiebe@skane.se

Welcome to Lund – "the City of Ideas", located in the centre of the Öresund region. Lund offers a rich selection of cultural experiences, with the Cathedral, Scandinavia's most distinguished church in the Romanesque style, at centre stage.

The events are many and varied, with Lund's strong tradition of comedy and farce making its mark on many of them. In Lund a creative, dynamic and innovative cultural spirit is alive and well. Lund has charm and wit and will make you feel welcome.

ESLCCC April 19-20 2007

The continuing success of the treatment for childhood cancer is an important medical achievement. It has however become increasingly evident that some survivors may pay a considerable price for their cure.

Late effects after childhood cancer often have a gradual and subtle presentation that may involve any organ system of the body. The follow-up will often require cooperation between several different medical specialities.

The European Symposium on Late Complications after Childhood Cancer in Lund, ESLCCC 2007, is the first major European meeting to focus on several different aspects of this important and developing clinical area.

The meeting is organized from the Department of Paediatrics at the University Hospital, which has a long tradition in the follow-up of late effects after childhood cancer.

Professor Stanislaw Garwicz has pioneered research in this field and this Symposium is held in his honour on his retirement from the Division of Paediatric Oncology at the University Hospital in Lund.

Christian Moëll
On behalf of the Organizing Committee

European Symposium on Late Complications after Childhood Cancer Lund April 19–20 2007

Thursday April 19, 2007

TIME	SUBJECT	SPEAKER	ABSTRACT
09:00	Welcome	Christian Moëll	
09:10	Introduction of Morning session	Kjeld Schmiegelow	
09:20	Late effects - where do we go from here?	Daniel Green	A:01
10:00	Modifications of treatment to minimize complications, the Hodgkin experience	Guenther Schellong	A:02
10:30	*Coffee*		
11:00	Antracycline cardiotoxicity in children – What is the risk and how can we avoid it?	Leontien Kremer	A:03
11:30	Discussion	Chairman: K. Schmiegelow	
12.00	Poster viewing		
12.30	*Lunch*		
13:30	Children's Cancer Foundation 25 years	Olle Björk	
13:40	Introduction of Afternoon session	Olle Björk	
13:50	Is childhood cancer a chronic disease?	Guilio D'Angio	A:04
14:30	Presentation of selected posters 1	Christian Moëll	
	Poster C:03, page 21 Poster E:06, page 29 Poster M:02, page 45 Poster M:06, page 47	Ilse Schuitema Dalit Modan-Moses Marieke De Bruin Marianne Jarfelt	
15:00	*Coffee*		
15:30	Neurocognitive sequele after brain tumours	Jacques Grill	A:05
16:00	Neuropsychological consequences of childhood cancer	Christine Eiser	A:06
16:30	Discussion	Chairman: O.Björk	
18:30	*Welcome reception*		

Friday April 20, 2007

TIME	SUBJECT	SPEAKER	ABSTRACT
09:00	Introduction of Morning Session	Christian Moëll	
09:10	Second neoplasms and late mortality	Stanislaw Garwicz	A:07
09:50	How is the Follow-up done now?	Lars Hjorth	
10:00	Presentation of selected posters 2	Lars Hjorth	
	Poster F:01, page 34 Poster F:05, page 36 Poster F:07, page 37 Poster F:08, page 37	J. Hazelhoff Kate Absolom Francesca Fioredda Thorsten Langer	
10:30	*Coffee*		
11:00	The role of the nurse in the Follow-up clinic	Faith Gibson	A:08
11:30	Models of Follow-up after childhood cancer	Andrew Toogood	A:09
12:00	Discussion	Chairman: L. Hjorth	
12:20	*Lunch*		
13:20	Introduction of Afternoon session	Hamish Wallace	
13:30	GH deficiency after Childhood cancer – whom to treat?	Stephen Shalet	A:10
14:10	Presentation of selected posters 3	Hamish Wallace	
	Poster G:04, page 39 Poster G:09, page 42 Poster G:06, page 40 Poster G:12, page 43	Yvonne L. Giwercman Jeanette Falck Winther M.H. van den Berg Kirsi Jahnukainen	
14:40	*Coffee*		
15:10	Who is at risk of gonadal dysfunction?	Charles Sklar	A:11
15:50	Fertility preservation in young people treated for cancer	Victoria Keros	A:12
16:20	Discussion	Chairman: H. Wallace	
16:40	Presentation of Poster prize		
16:50	Closing remarks	Christian Moëll	
19:00	*Symposium dinner*		

Speakers

Olle Björk
Children´s Cancer Foundation
Barncancerfonden
Stockholm, Sweden

Giulio D´Angio
Department of Radiation Oncology
Hospital of the University
of Pennsylvania
Philadelphia, USA

Christine Eiser
The University of Sheffield
Sheffield, United Kingdom

Stanislaw Garwicz
Dept of Paediatrics
Lund University Hospital
Lund, Sweden

Faith Gibson
UCL Institute of Child Health
Great Ormond Street Hospital
for Children
London, United Kingdom

Daniel Green
Roswell Park Cancer Institute
Buffalo, New York, USA

Jacques Grill
Gustave Roussy Institute
Villejuif, France

Lars Hjorth
Dept of Paediatrics
Lund University Hospital
Lund, Sweden

Victoria Keros
Obstetrics and gynecology
Karolinska University Hospital
Stockholm, Sweden

Leontien C.M. Kremer
Pediatric Oncology
Emma Children´s Hospital
Amsterdam, Netherlands

Christian Moëll
Dept of Paediatrics
Lund University Hospital
Lund, Sweden

Guenther Schellong
University of Münster
Münster, Germany

Kjeld Schmiegelow
Pediatric Clinic
University Hospital Rigshospitalet
Copenhagen, Denmark

Stephen M. Shalet
Department of Endocrinology
Christie Hospital
Manchester, United Kingdom

Charles A. Sklar
Department of Pediatrics
Memorial Sloan-Kettering
Cancer Center
New York, USA

Andrew Toogood
University Hospital Birmingham
United Kingdom

Hamish Wallace
Royal Hospital for Sick Children
Edinburgh, United Kingdom

Useful information

BANKS
Banks are open between 10.00 and 15.00 on weekdays.

CLIMATE
The weather in Lund in April is usually nice but showers can occur.
For weather forecast please visit www.smhi.com

CERTIFICATE OF ATTENDANCE
Will be available at the registration desk on individual request.

CURRENCY
The official currency is Swedish Krona (SEK).
USD 1 = SEK 7.00 (April 2007)
EUR 1 = SEK 9.35 (April 2007)

DISCLAIMER
The Organizing Committee and Congrex Sweden AB accept no liability for injuries/losses of whatever nature incurred by participants and/or accompanying persons, nor loss of, or damage to, their luggage and/or personal belongings.

INTERNET
Wireless LAN will be available to all participants at the Symposium Venue.
You will receive your user identity and password upon registration

MEALS
Coffee and lunches are included in the registration fee and will be served daily.
Your name badge is your ticket. The lunch will be served at Akademiska Föreningen (Students' Union).

LANGUAGE
The official language of the Congress is English
(no translation facilities will be provided).

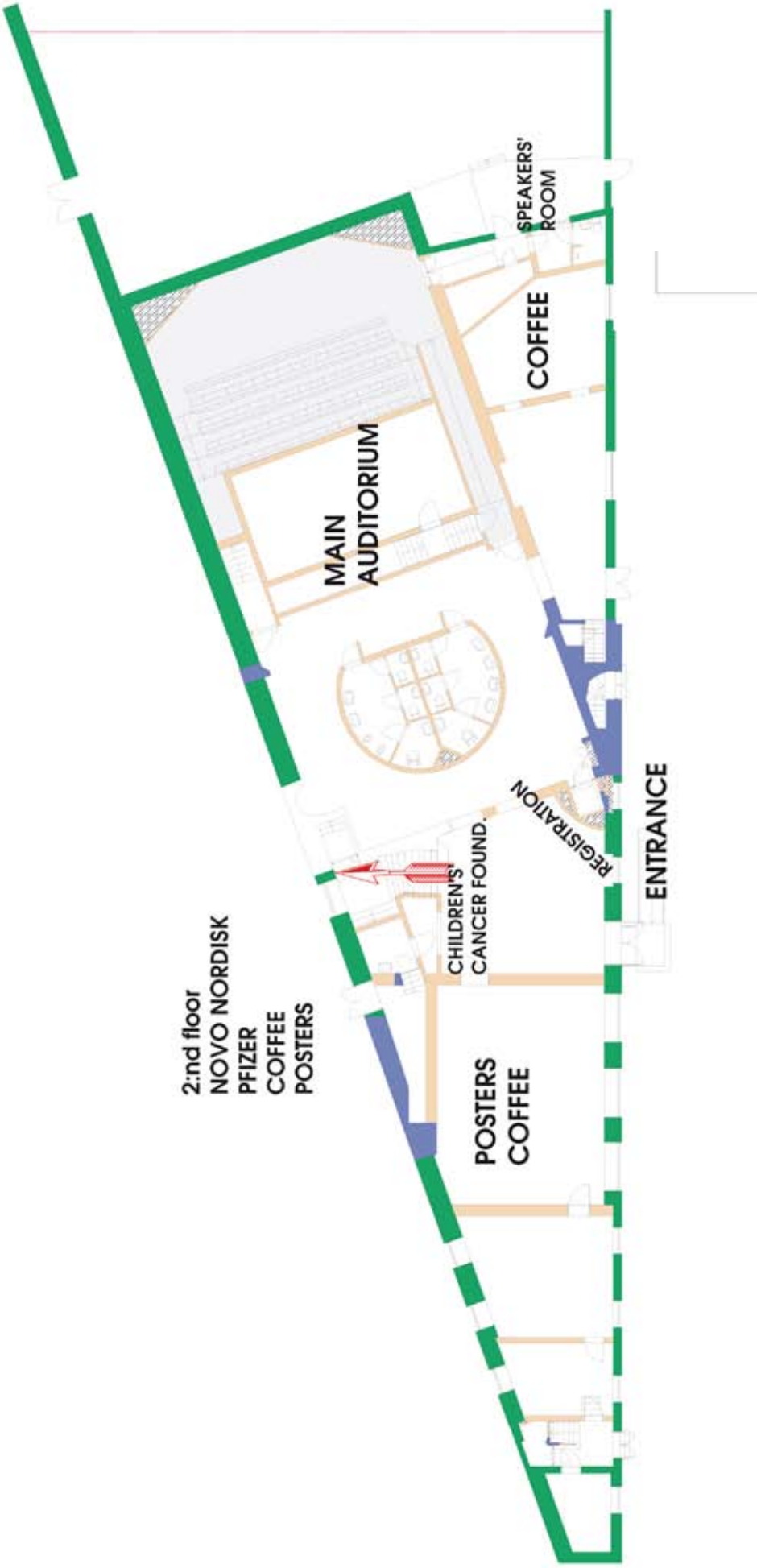
TAXI
We recommend the following taxi companies:
Taxi Skåne, Phone: +46 (0)406 330 330
Taxi Kurir, Phone: +46 (0)406 700 700
Taxi Lund, Phone: +46 (0)46 12 12 12

Social events

WELCOME RECEPTION
Thursday 19 April 18.30 at The University Building
Drinks will be served
Included in the registration fee

SYMPOSIUM DINNER
Friday 20 April 19.00 at Grand Hotel
Price/person: SEK 400

Venue Overwiev



List of participants
(2007-04-12)

A

Absolom, Kate
University of Sheffield
Department of Psychology
Western Bank
Sheffield, S10 2TP, United Kingdom

af Sandeberg, Margareta
Astrid Lindgrens Hospital
Pediatric Oncology
Karolinska University Hospital
171 76 Stockholm, Sweden

Aksnes, Liv Hege
Rikshospitalet-Radiumhospitalet Medical Centre
Cancer Clinic
Montebello
0310 Oslo, Norway

Albanese, Assunta
The Royal Marsden NHS Foundation Trust
Paediatric Oncology
Downs Road
Sutton SM2 5PT, United Kingdom

Alston, Aileen
Royal Marsden Hospital
Paediatric Endocrinology
Downs Road
Sutton SM2 5PT, United Kingdom

Amoroso, Loredana
Institut Gustave Roussy
39 Rue Camille Desmoulins
94805, France

Andersson, Christina
Gävle-Dala Barncancerförening
Sweden

Andersson, Ylva
Barncancerfonden
Box 5408
114 84 Stockholm, Sweden

Arvidson, Johan
Department of Womens and Childrens Health
Akademiska Sjukhuset
752 85 Uppsala, Sweden

B

Bashore, Lisa
Cook Children's Medical Center
Hematology/Oncology, Survivorship
901 7th Avenue, Suite 220
Fort Worth, Texas, United States

Behrendtz, Mikael
University Hospital
Department of Pediatrics
581 85 Linköping, Sweden

Berg, Rickard
Novo Nordisk Scandinavia
GHT Team, Box 50587
202 15 Malmö, Sweden

Bergsträsser, Eva
University Children's Hospital
Oncology
Steinwiesstr. 75
8032 Zürich, Switzerland

Björk, Olle
Barncancerfonden
Box 5408
114 84 Stockholm, Sweden

Björk-Eriksson, Thomas
Sahlgrenska Universitetssjukhuset
Dep of Oncology
Blå Stråket 2
413 45 Göteborg, Sweden

Blaauwbroek, Ria
University Medical Center Groningen
Paediatric Oncology
Hanzeplein 1
9700 VB Groningen, Netherlands

Bojsen, Veronica
Children's Hospital
Dept of Paediatrics
221 85 Lund, Sweden

Bokenkamp, Arend
VU Medical Center
Pediatric Nephrology
De Boelelaan 1117
1081 HV Amsterdam, Netherlands

Bolton, Jeff
Pfizer Limited
Walton Oaks
Dorking Road, Tadworth
Surrey, KT20 7NS, United Kingdom

Borgström, Birgit
Inst for Clinical Science, Karolinska Institutet
Pediatrics
Karolinska University Hospital, Huddinge
141 86 Stockholm, Sweden

Braam, Katja
VU University Medical Center
Pediatric oncology/ hematology
De Boelelaan 1117
1081 HV Amsterdam, Netherlands

Bresters, Dorine
Lumc
Wa-Kjc/Ihoba
P.O. Box 9600
2300 RC Leiden, Netherlands

Brouwer, C.A.J.
University Medical Center Groningen
Paediatric Oncology
Hanzeplein 1
9700 RB Groningen, Netherlands

Burack, Richard
Great Ormond Street Hospital
Oncology/Late Effects
26 Tempest Mead
North Weald, United Kingdom

Bökkerink, Jos
University Hospital St Radboud Nijmegen
Pediatric Hematology and Oncology
PO Box 9101
6500 HB Nijmegen, Netherlands

C

Caflisch, Ueli
Paediatric Oncology
Kinderspital
CH-6000 Luzern 16, Switzerland

Carlsson, Annelie
Dept. of Paediatrics
Lund University Hospital
221 85 Lund, Sweden

Carlsson, Göran
Astrid Lindgrens Barnsjukhus
Barnonkologen
Karolinska Universitetsjukhuset Solna
171 76 Stockholm, Sweden

Clausen, Niels
University Hospital of Aarhus at Skejby Pediatrics
Brendstrupgaardsvej
DK-8200 Aarhus N, Denmark

Cohn, Richard
Sydney Children's Hopsital
Centre for Children's Cancer and Blood Disorders
High Street, Randwick
2029 Sydney, Australia

Costa, Vitor
Baxter, Avenida da Liberdade, 103
1269-049, Portugal

D

D´Angio, Giulio
Hospital of the University of Pennsylvania
Department of Radiation Oncology
HUP, Donner 2
Philadelphia, PA 19104, United States

Dahlberg, Karin
Barn och Ungdomssjukhuset
Onkologi
221 85 Lund, Sweden

Davies, Helena
Sheffield Childrens Hospital
Western Bank
Sheffield S10 2TH, United Kingdom

De Bruin, Marieke
Netherlands Cancer Institute
Epidemiology
Plesmanlaan 121
1066CX Amsterdam, Netherlands

E

Edberg-Posse, Ebba
Kuratorskliniken
Karolinska Universitetsjukhuset, B44, Huddinge
141 86 Stockholm, Sweden

Ehrstedt, Christoffer
Uppsala University Hospital
Child Neurology
Murklevägen 15
756 46 Uppsala, Sweden

Eiser, Christine
The University of Sheffield
Sheffield S10 2TP, United Kingdom

Ek, Torben
Barnkliniken
Länssjukhuset
30185 Halmstad, Sweden

Eldeeb, Bettina
Royal Shrewsbury Hospital
Paediatric Oncology
Mytton Oak Road
Shresbury SY3 8XQ, United Kingdom

Elfving, Maria
Paediatrics
University Hospital
221 85 Lund, Sweden

Elson, Ruth
Bristol Royal Hospital for Children
Oncology Day Beds
Upper Maudlin Street
Bristol BS2 8BJ, United Kingdom

Enriquez, Raquel
Children Hospital Aarau
Pediatric Oncology
Tellstrasse
5000 Aarau, Switzerland

Eshelman, Debra
Children's Medical Center Dallas
1935 Motor Street
Dallas , TX 75235, United States

Ewers, Sven-Börje
Dep of Oncology
University Hospital
221 85 Lund, Sweden

F

Fahlén, Eva
Barncancerföreningen i Västra Sverige, Sweden

Fioredda, Francesca
Giannina Gaslini Children Hospital
Haematology-Oncology
Largo Gerolamo Gaslini 5
16134 Genova, Italy

Follin, Cecilia
Endokrin, Kraftgatan 7b
231 34 Lomma, Sweden

Forinder, Ulla
Stockholm University
Social work
106 91 Stockholm, Sweden

Fors, Hans
Barnklin NÄL
461 85 Trollhättan, Sweden

Forslund, Karin
Barncancerfonden
Box 5408
114 84 Stockholm, Sweden

Frenos, Stefano
Anna Meyer Children Hospital-Univ. of Florence
Onco-Hematology
Via Luca Giordano 13
50132, Italy

Frey, Eva
St. Anna Children´s Hospital
Oncology
Kinderspitalgasse 6
1090 Vienna, Austria

Frisk, Per
Uppsala University Children's Hospital
Women's and Children's health
751 85 Uppsala, Sweden

Frost, Britt-Marie
Uppsala University
Womens and childrens health
Akademiska Sjukhuset
751 85 Uppsala, Sweden

G

Garwicz, Stanislaw
Lund University Hospital
221 85 Lund, Sweden

Gavras, Christoforos
Ahepa University Hospital
Hematology-Oncology Unit
Votsi 12
60100 Katerini, Greece

Gibson, Faith
UCL Institute of Child Health
Great Ormond Street Hospital for Children
7th Floor Old Building Great Ormond Street
WC1N3JH London, United Kingdom

Gisselbaek, Mogens
Novo Nordisk
Baeverdalen 26
3400 Hillerod, Denmark

Giwercman, Yvonne
Lund University
Clinical Sciences
CRC, Building 91, Plan 10
205 02 Malmö, Sweden

Goldkuhl, Christina
Sahlgrenska University Hospital
Dep.of Oncology
Blå Stråket 2
413 45 Göteborg, Sweden

Green, Daniel
Roswell Park Cancer Institute
Elm & Carlton Streets
Buffalo, New York 14263, United States

Greenfield, Diana
Cancer Research Centre
University of Sheffield
Weston Park Hospital, Whitham Road
Sheffield, S10 2SJ, United Kingdom

Grill, Jacques
Gustave Roussy Institute
39 Rue C. Desmoulins
94805 Villejuif, France

Gullersbo, Malin
Barnkliniken
Universitetssjukhuset
581 85 Linköping, Sweden

H

Hakvoort-Cammel, Friederike G.A.J.
Erasmus MC-Sophia Children's Hospital
Hematology/Oncology
Dr. Molewaterplein 60
3015 GJ Rotterdam, Netherlands

Hamre, Hanne M.
Rikshospitalet-Radiumhospitalet HF
Kreftklinikken, seksjon for langtidsstudier
Montebello
0310 Oslo, Norway

Harila, Marika
Oulu University Hospital
Dept of Rehabilitation
Po Box 23
90029 Oys, Finland

Harila-Saari, Arja
Oulu University Hospital
Pediatrics, PL23
90029 OYS, Oulu, Finland

Haugan, Nils Henry
Ullevål Universitetssykehus Oslo
Barneavdeling og Poliklinikk
Kirkev.166
0407 Oslo , Norway

Haupt, Riccardo
Gaslini Children Hospital, Scientific Directorate
Largo G. Gaslini, 5
16147 Genova, Italy

Hazelhoff, Janneke
Emma Children's Hospital/Academic Medical Center
Po Box 22660
1100 DD Amsterdam, Netherlands

Hellman, Ann-Mari
Barncancerfonden
Box 5408
114 84 Stockholm, Sweden

Hengartner, Heinz
Ostschweizer Kinderspital
Hematology/Oncology
Claudiusstrasse 6
9600 St. Gallen, Switzerland

Hess, Siri Lothe
Rikshospitalet - Radiumhospitalet Medical Centre
Montebello
0310 Oslo, Norway

Hjorth, Lars
Children's Hospital, Dept of Paediatrics
221 85 Lund, Sweden

Holmer, Helene
Medicinkliniken
Centralsjukhuset
291 94 Kristianstad, Sweden

Horne, Beverly
St. James's University Hospital
Paediatric Oncology & Haematology
Beckett Street
LS9 7TF Leeds, United Kingdom

Hou, Mi
Karolinska Institute
Dept. of Woman and Child Health
Pediatric Endocrinology Unit, Q2:08
171 76 Stockholm, Sweden

I

Ishida, Yasushi
Ehime University Graduate School of Medicine
Pediatrics
Shitukawa, Touon-city
Ehime, 791-0295, Japan

J

Jahnukainen, Kirsi
Astrid Lindgren Children´s Hospital
Department of Woman and Child Health
Pediatric Endocrinology Unit, Q2:08
171 76 Stockholm, Sweden

Jakobsson, Jörgen
Novo Nordisk Scandinavia
GHT Team, Box 50587
202 15 Malmö, Sweden

Jarfelt, Marianne
The Queen Silvia Children´s Hospital
Pediatric Hematology and Oncology
Inst. of Clinical Sciences
416 85 Göteborg, Sweden

Jernberg, Birgitta
Akademiska Barnsjukhuset 95B
751 85 Uppsala, Sweden

Johannsdottir, Inga Maria Rinvoll
Rikshospitalet
Pediatric hemato-/oncology
Bekkeliveien 14B
0375 Oslo, Norway

Johansson, Magnus
Pfizer Limited, Sweden

Jonmundsson, Gudmundur
Landspitali Children's Hospital
Hringbraut
IS-101 Reykjavik, Iceland

K

Kazanowska, Bernarda
Wroclaw Medical University
Dept. of Pediatric Oncology
Bujwida 44
50-345 Wroclaw, Poland

Kepak, Tomas
University Hospital Brno
Pediatric Oncology
Cernopolni 9
625 00 Brno, Czech Republic

Keros, Victoria
Karolinska University Hospital
Obster-gyn department
K 57
141 86 Stockholm, Sweden

Kiserud, Cecilie
Rikshospitalet-Radiumhospitalet HF
Enhet for langtidsstudier
Fagområde klinisk kreftf
0310 Montebello, Oslo, Norway

Krawczuk-Rybak, Maryna
Medical University, Pediatric Oncology
Kilinskiego 1
15-089 Bialystok, Poland

Kremer, Leontien C.M.
A.M.C.
Postbox 22660
1100 DD, Amsterdam, Netherlands

L

Lafay-Cousin, Lucie
Alberta Children's Hospital, Pediatric Oncology
2888 Shaganappi Trail NW
T2T 1X4, Canada

Langer, Thorsten
University Hospital for Children and Adolescents
Late Effects Surveillance System
Loschgestr. 15
91054 Erlangen, Germany

Leiper, Alison
Haematology
Great Ormond Street Hospital
London WC1N 3JH, United Kingdom

Levitt, Gill
Oncology/Haemartology
Great Ormond St
London WC1 N 3JH, United Kingdom

Lidén, Karin
Barn- och Ungdomskliniken
Centralsjukhuset
651 85 Karlstad, Sweden

Lindgren, Maria
Akademiska Barnsjukhuset
Avd för blod och tumörsjukdomar
Ing 95
751 85 Uppsala, Sweden

Link, Katarina
The Universityhospital in Malmö
The department of Endocrinology
205 02 Malmö, Sweden

Longhi, Alessandra
Istituto Ortopedico Rizzoli
Chemotherapy Div
Via Pupilli 1
40136 Bologna, Italy

Lundsten, Ann
Barncancerföreningen i Västra Sverige
Sweden

Lyons, Shoshanah
Royal Holloway, Univeristy of London
Department of Clinical Psychology
Egham, Surrey TW20 OBX, United Kingdom

Lähteenmäki, Päivi
Turku University Hospital
Dept of pediatrics
Po Box 52
FIN-20521 Turku, Finland

Löf, Catharina M
Karolinska Institutet, Department of Pediatrics
146 86 Stockholm, Sweden

M

Magnusson, Susanne
Dept of Oncology
Clinical Sciences
221 85 Lund, Sweden

Malmberg, Lena
Dpt. of Oncology
Onkologikliniken Centralsjukhuset
651 85 Karlstad, Sweden

Martinsson, Ulla
Onkologikliniken
Akademiska sjukhuset
751 85 Uppsala, Sweden

Mattsson, Elisabet
Public Health and Caring Sciences
Psychosocial Oncology
Uppsala Science Park
751 85 Uppsala, Sweden

Mehta, Susan
Haematology/Oncology
Great Ormond Street
London WC1N 3JH, United Kingdom

Michel, Gisela
University of Bern
Dept of Social and Preventive Medicine
Finkenhubelweg 22
3012 Bern, Switzerland

Mitchell, Anne
Wellington Hospital
Paediatrics
48B Madras Street, Kandhallah
Wellington, 6004, New Zealand

Mittal, Rakesh
Kuwait Cancer Control Centre
Medical Oncology
Post Box - 1846
Hawally – 32019, Kuwait

Modan-Moses, Dalit
The Edmond and Lily Safra Children's hospital
Pediatric Endocrinology
Tel-Hashomer, Ramat-Gan
52621, Israel

Moelgaard Hansen, Lene
Aarhus University Hospital, Skejby Sygehus
Paediatrics
Brendstrupgaardsvej 100
8200 Aarhus N, Denmark

Moëll, Christian
Children's Hospital
Dept of Paediatrics
221 85 Lund, Sweden

Moser, Andrea
University Children Hospital Graz
Pediatric Hematology/Oncology
Auenbruggerplatz 30
8036 Graz, Austria

Muszynska-Roslan, Katarzyna
Medical University
Pediatric Oncology
Waszyngtona 17
15-274 Poland

Möller, Torgil R.
Lund University Hospital
Regional Tumour Registry
Klinikgatan 22
221 85 Lund, Sweden

N

Niedzielska, Ewa
Akademia Medyczna
Klinika Hematologii i Onkologii Dzieciêcej
Wroc³aw
Bujwida 44 30-345, Poland

Nilsson, Ann-Sofie
Endokrin
Läsvägen 9
224 67 Lund, Sweden

Nussey, Stephen
St. Georges Hospital nhs trust
Endocrinology
Blackshaw Road
London SW17 OQT, United Kingdom

Nyenget, Tove
Ullevål Universitetssykehus Oslo
Barneavdeling og Poliklinikk
Kirkev.166
0407 Oslo, Norway

Nysom, Karsten
Rigshospitalet
Paediatric Haematology/Oncology
Section 4064, Blegdamsvej 9
DK-2100 Copenhagen, Denmark

O

Opperud, Vigdis
Rikshospitalet - Radiumhospitalet Medical Center
Montebello
0310 Oslo, Norway

P

Pal, Annacarin
Astrid Lindgrens Barnsjukhus
Karolinska Universitets sjukhuset
171 76 Stockholm, Sweden

Paulides, Marios
University Hospital for Children and Adolescents
Late Effects Surveillance System
Loschgestr. 15
91054 Erlangen, Germany

Pekkanen, Kirsti
Drottning Silvias Barn och Ungdomssjukhus
SU/Östra
Barncancercentrum Avd 322
416 85 Göteborg, Sweden

Petersen, Cecilia
Karolinska Institutet
Pediatric Endocrinology Unit
Astrid Lindgren Children´s Hospital, Q2:08
171 76 Stockholm, Sweden

Pettersson, Liselott
Akademiska Barnsjukhuset
Avd för Blod-och tumörsjukdomar
Ing 95
751 85 Uppsala, Sweden

Peyrl, Andreas
Novo Nordisk Pharma GmbH
Opernring 3
1010 Vienna, Austria

Postma, Aleida
University Medical Center Groningen
Pediatric Oncology
Post Box 30001
9700 RB Groningen, Netherlands

R

Radvanska, Jitka
Teaching Hospital Motol
Children Clinic Hematology and Oncology
V Uvalu 84
150 06, Czech Republic

Radvansky, Jiri
Charles University 2nd Medical Faculty
Sports Medicine
V Uvalu 84
150 00 Prague, Czech Republic

Rebholz, Cornelia Eva
Swiss Childhood Cancer Registry
Department of Social and Preventive Medicine
Finkenhubelweg 11
3012 Berne, Switzerland

Rechnitzer, Catherine
Rigshospitalet
Pediatrics
Dept of pediatric oncology 5054, Rigshospitalet
2100 Copenhagen, Denmark

Rollof, Lena
University Hospital
Pediatric Department
221 85 Lund, Sweden

Ross, Emma
Leicester Royal Infirmary
Paediatric Oncology
Infirmary Square
Leicester LE1 5WW, United Kingdom

Ruud, Ellen
Rikshospitalet
Dep. of Pediatrics
Sognsvannsveien 22
0027 Oslo, Norway

Ryalls, Michael
Royal Surrey County Hospital
Paediatrics
Egerton Road
Guildford GU2 7XX, United Kingdom

S

Schellong, Guenther
University of Münster
Germany

Schmiegelow, Kjeld
University Hospital Rigshospitalet
Pediatric Clinic
Blegdamsvej 9
2100 Copenhagen, Denmark

Schomerus, Eckhard
Klinikum Augsburg
1. Kinderklinik
Stenglinstraße 2
86156 Augsburg, Germany

Schröder, Hildegard
University Hospital
Dept.: Pediatric Oncology and Hematology
Ratzeburger Allee 160
23538 Germany

Schuitema, Ilse
Leiden University/VU University Medical Center
Maria van Hongarijelaan 4
2353 EM Leiderdorp, Netherlands

Sega-Pondel, Dorota
Wroclaw Medical University
Department of Pediatric Hematology/Oncology/BMT
ul. Bujwida 44
50-345 Wroclaw, Poland

Sehested, Astrid
Rigshospitalet
4064
Blegdamsvej 9
2100 Copenhagen Ø, Denmark

Shalet, Stephen Michael
Christie Hospital
Department of Endocrinology
Wilmslow Road
M20 4BX Manchester, United Kingdom

Sklar, Charles A.
Memorial Sloan-Kettering Cancer Center
Department of Pediatrics
23 East 20th Street, #6
10003 New York, United States

Slaby, Krystof
Charles University in Prague 2nd Medical Faculty
Department of Sports Medicine
V Uvalu 84
15006 Prague, Czech Republic

Smedler, Ann-Charlotte
Stockholm University
Dept of Psychology
106 91 Stockholm, Sweden

Stille, Jenny
Queen Silvia Children's Hospital
Centre of Pediatric Oncology
416 85 Göteborg, Sweden

Strömberg, Bo
Uppsala University Children's Hospital
Deparment of Women's and Children's Health
Uppsala Sweden
751 85 Uppsala, Sweden

Sugden, Elaine
Oxford Radcliffe Hospitals
Clinical Oncology
Churchill Hospital
Oxford OX20NA, United Kingdom

Sundberg, Kay
Uppsala Universitet, Inst.för folkhälso-och vårdvetenskap
Uppsala science Park
751 83 Uppsala, Sweden

Sunnvius, Ann
Uppsala Barncancerförening
Uppsala, Sweden

Sällfors Holmqvist, Anna
Barn- och Ungdomssjukhuset
221 85 Lund, Sweden

T

Taj, Mary
The Royal Marsden NHS Foundation Trust
Paediatric Oncology
Downs Road
Sutton SM2 5PT, United Kingdom

Teixeira, Ana
Instituto Português de Oncologia
Paediatrics
Rua Castilho, 185, 8º
1070-051 Lisboa, Portugal

Thomsen, Line
Novo Nordisk Scandinavia
ABRegion DanmarkArne Jacobsens Allé 15DK-2300
Köbenhavn SDenmark

Thorvildsen, Anne Benedicte
Rikshospitalet-Radiumhospitalet HF
Center for Shared Decision Making and Nursing Rese
Forskningsveien 2b
NO-0027 Oslo, Norway

Toogood, Andrew
University Hospital Birmingham
NHS Foundation Trust Edgbaston
Birmingham, B15 2TH, United Kingdom

Turup, Eva
Akademiska Sjukhuset
Barnonkologen
751 85 Uppsala, Sweden

U

Uhlig, Helena
Akademiska Sjukhuset
Psykosociala Enheten
Akademiska Barnsjukhuset, ing 95 NBV
751 85 Uppsala, Sweden

Urquhart, Tanya
Sheffield Childrens NHS Foundation Trust
Nursing
C Floor, Stephenson Wing, Western Bank
Sheffield, South Yorkshire, S10 2TH
United Kingdom

VW

Wahlgren, Aida
Pediatric Endocrinology Unit
Dep of Woman and Child Health
Q2:08 Astrid Lindgrens Children's Hospital
171 76 Stockholm, Sweden

Wallace, Hamish
Royal hospital for Sick Children
Consultant Paediatric Oncologist
17 Millerfield Place
Edinburgh EH9 1LF, United Kingdom

Wallenborg, Carina
Gävle-Dala Barncancerförening
Sweden

van Baalen, Manita
Erasmus University Medical Centre Sophia
van Ostadeplein 19
5151 SW Rotterdam, Netherlands

van den Berg, Marleen
VU University Medical Center
Dept. of Paediatrics
Po Box 7057
1007 MB Amsterdam, Netherlands

van den Bos, Cor
Emma Children's Hospital
Pediatric Oncology and Late Effects Study Group
Room F8-243, Po Box 22660
1100 DD Amsterdam, Netherlands

van den Heuvel-Eibrink, Marry M.
Erasmus MC-Sophia Childrens Hospital
Pediatric Oncology
P.O. Box 2060
3000 CB Rotterdam, Netherlands

van der Linden, Gerard H.M.
Erasmus University Medical Centre Sophia
Hematology/Oncology
Po Box 2060
3000 CB Rotterdam, Netherlands

van der Pal, Heleen
Academic Medical Center
Medical Oncology
Meibergdreef 9, room F4-224
1105 AZ Amsterdam, Netherlands

van der Sluis, Inge M.
Erasmus MC-Sophia Childrens Hospital
Pediatric Oncology
P.O. Box 2060
3000 CB Rotterdam, Netherlands

van Leeuwen, Flora
Netherlands Cancer Institute
Epidemiology
Plesmanlaan 121
1066CX Amsterdam, Netherlands

Vandecruys, Els
Ghent University Hospital
Pediatric Hemato-Oncology
De Pintelaan 185
9000 Ghent, Belgium

Wells, Robert
U. T. M. D. Anderson Cancer Center
Pediatrics
1515 Holcombe Blvd, Unit 87
Houston, TX 77030, United States

Wennström, Lovisa
Sahlgrenska Universitetssjukhuset
Sektionen för hematologi
2413 45 Göteborg, Sweden

Widing, Eva
Ullevål University Hospital
Dept og Paediatrics
Kierkeveien 166
0407 Oslo, Norway

Wiebe, Thomas
Children´s Hospital Dept of Paediatrics
221 85 Lund, Sweden

Wiklund, Jan-Åke
Novo Nordisk Scandinavia
GHT Team
Box 505 87
202 15 Malmö, Sweden

Winter, Anita
University Children Hospital Graz
Pediatric Hematology/ Oncology
Auenbruggerplatz 30
8036 Graz, Austria

Winther, Jeanette Falck
Danish Cancer Society
Institute of Cancer Epidemiology
Strandboulevarden 49
DK-2100 Copenhagen, Denmark

Winther, Marianne
Novo Nordisk Scandinavia
ABRegion DanmarkArne Jacobsens Allé 15
DK-2300 Köbenhavn SDenmark

Wooding, Katherine
Morriston Hospital
Morriston Swansea
SA6 6NL United Kingdom

Wynn, Belynda
Christchurch Hospital
Paediatric Department
Private Bag 4710
Christchurch, New Zealand

Z

Zaletel-Zadravec, Lorna
Institute of Oncology Ljubljana
Zaloska 2
1000 Ljubljana, Slovenia

Invited Speakers

Late Effects Of Treatment For Childhood Cancer — A:01

Green, Daniel M.
Roswell Park Cancer Institute, Department of Pediatrics, Buffalo, United States

Survival after the diagnosis of cancer in children and adolescents has become the rule. Adult survivors of childhood cancer have concerns regarding treatment effects on their longevity, fertility and offspring. The standardized mortality ratio (SMR) for male five-year survivors who participated in the Childhood Cancer Survivor Study (CCSS) was 8.5, and was 18.2 for female CCSS participants. The most frequent causes of premature mortality are the original cancer, cardiac disease and second malignant neoplasms (SMNs). Data which are population based from the Nordic countries are similar. The SMR for males was 9.2 for males and 14.6 for females.

Anthracycline antibiotics and direct cardiac irradiation cause cardiac morbidity. The risk factors for anthracycline cardiomyopathy include the cumulative dose of anthracycline received and exposure of the left ventricle to radiation. Radiation therapy can damage the cardiac valves, coronary arteries, myocardium and pericardium. Female childhood cancer survivors who were treated with > 20 Gy have a relative risk (RR) of obesity (body mass index > 30) of 2.59. The RR of obesity for males was 1.86. Obesity predisposes individuals for diabetes mellitus, hypertension and dyslipidemia, factors that will interact with known treatment effects on cardiac health. Growth hormone deficiency may underlie several of these abnormalities.

The fertility of childhood cancer survivors is impaired. The adjusted relative fertility of survivors, compared to that of their siblings was 0.85 (95% CI - 0.78 - 0.92). Fertility may be impaired by the absence of sperm and ova or abnormal uterine structure. The offspring of female CCSS participants who received pelvic irradiation were at increased risk (RR - 1.84) of weighing < 2500 grams at birth. Most chemotherapeutic agents are mutagenic. Recent studies have not identified an increased frequency of major congenital malformations, genetic disease or childhood cancer in the offspring of childhood cancer survivors.

The standardized incidence ratio (SIR) for a SMN among CCSS participants who had a median follow-up of 15.4 years after diagnosis was 6.38. The SIR reported for Nordic pediatric cancer patients who had a mean follow-up of 6.1 years after diagnosis was 3.6. Risk factors for SMNs include genetic predisposition, gender and treatment factors. Thyroid carcinoma, breast cancer, brain tumors and skin cancer are among the more frequently diagnosed radiation related SMNs. Tobacco use increases the risk of subsequent lung cancer in patients who received lung irradiation. CCSS participants reported smoking rates that were significantly lower than those of the general population. However 19% of males and 17% of females were current smokers, increasing their risks for lung disease, heart disease and SMNs. SMNs may develop after exposure to alkylating agents and topoisomerase II inhibitors.

Medical care for childhood cancer survivors must be based on accurate knowledge of the treatment exposures of the survivor and informed assessment of the survivor by medical professionals. Only 72% of CCSS participants accurately reported their diagnosis. Recall by CCSS participants of treatment with specific chemotherapeutic agents or exact radiation therapy treatment volumes is poor. Exposure specific care will be difficult unless the patient is given a physical and/or electronic record of his/her diagnosis and treatment.

Future research will be necessary to determine the most effective follow-up program for survivors. Several models, including prolonged follow-up at a cancer center, transition of care to appropriately trained physicians in a specialty setting, or transition to community physicians supported by computer based practice guidelines, have been suggested. Many current follow-up evaluations are based primarily on expert opinion. Research is necessary to document that expert opinion results in care that is cost effective and reduces morbidity and/or mortality. Such studies require large sample sizes and prolonged follow-up.

Modifications of treatment to minimise late complications after childhood cancer: The Hodgkin Lymphoma experience — A:02

Schellong, Guenther
University Children's Hospital, Haematology/Oncology, Muenster, Germany

Hodgkin's disease (HD) takes a special place amongst cancer diseases of childhood. Cure rates are very high, but long term survival goes along with a large spectrum of therapy-induced late effects. This is especially proven for the therapy concepts applied until 25 to 30 years ago, when radiotherapy was still extensively practiced and several chemotherapeutic agents were given at high cumulative doses now known to produce long-term complications. Since the 1970ies many paediatric therapy studies have tried to minimise the late consequences by treatment modifications.

1387 patients below 18 y with all disease stages were enrolled in the first 5 German-Austrian DAL-studies HD-78 to HD-90 between 1978 and 1995 by 104 centres. Following therapy extended long-term surveillance has been organised continuously into adulthood (Project HD-Late Effects). During the initial years follow-up information was provided by the participating departments. After the patients had reached adulthood the study centre established direct contact to them and/or their physicians. At the last evaluation (January 07) information was available from 78% of the patients from the last 6 years. At last information the median follow-up was 13.4 (max. 28.2) y, and median age 26.1 (max. 44.0) y. Overall survival of the total group with all treatment modifications was 95% at 10 y and 92% at 20 y.

Chemotherapy: In the general framework of combined modality treatment chemotherapy in the initial DAL-HD-studies consisted of a modification of MOPP. Mechlorethamine was replaced by doxorubicin and cyclophosphamide resulting in OPPA and COPP, respectively. The number of cycles was reduced according to the risk of disease: 2 OPPA for early stages, 2 OPPA + 2 COPP for intermediate and 2 OPPA + 4 COPP for advanced stages. Radiotherapy followed chemotherapy. Treatment results were favourable.

Late effects: The cumulative incidence of secondary leukaemias/MDS was 0.5%. Only 1 cardiomyopathy developed in 171 patients without mediastinal irradiation and without additional chemotherapy due to relapse or second malignancy, (cumulative total doxorubicin dose in all patients 160 mg/m2). By contrast, a considerably higher incidences of testicular dysfunction were detected primarily by hormonal parameters. Elevated FSH levels were noted in 40% of the examined post-pubertal male patients indicating impairment of spermatogenesis. The prevalence of abnormal findings was related to the cumulative doses of procarbazine. In the subsequent studies it was tried to eliminate procarbazine, the main gonadotoxic drug for boys, from the protocols. In a successful step etoposide was substituted for procarbazine in OPPA arriving at OEPA for boys in HD-90 and -95. This combination had no gonadotoxic effect and did not increase the risk of secondary leukaemias (cumulative incidence at 15 years 0.5%). Next, dacarbazine was substituted for procarbazine in COPP (COPDac). While the efficacy of the OEPA /COPDac regimen to control HD has already been proven in Pilot HD-2002, testicular function has to be tested in late adolescence or early adulthood. Radiotherapy: While the radiation doses were 36-40 Gy in the first study HD-78 they were stepwise reduced to 20 Gy in the subsequent studies. Extended field was changed to involved field and later to reduced involved field irradiation. Treatment results were not affected by these reductions. In GPOH-HD-95 radiotherapy was omitted in patients with complete remission after chemotherapy. This strategy was successful in terms of DFS in early, but not in intermediate and advanced stages.

Late effects: At the present time it cannot be determined whether the reduction of radiotherapy has indeed diminished the cumulative incidence of secondary solid tumours as intended. A longer follow-up of the patients from the low dose studies is needed. Preliminary data from studies with intermediate doses show some important trends.

Anthracycline cardiotoxicity in children. What is the risk and can we avoid it? A:03

Kremer, Leontien
Emma Childrens' Hospital, Pediatric Oncology, Amsterdam, Netherlands

Anthracycline-induced cardiotoxicity is a widely prevalent problem. The consequences of anthracycline-induced cardiotoxicity are extensive. First, it can cause a reduction in the amount of anthracyclines that a patient was supposed to receive and as a result, the chance of survival of that patient can be reduced. Also, it can lead to cardiac death. The risk of developing heart failure remains a lifelong threat, especially to children who have a long life-expectancy after successful antineoplastic treatment.

Several risk factors for anthracycline-induced cardiotoxicity, like a higher cumulative anthracycline dose, different anthracycline derivates, a higher anthracycline peak dose, radiation therapy involving the heart region, female sex, younger age at diagnosis, black race, additional treatment with for example cyclophosphamide or mitoxantrone and presence of trisomy 21 have been identified.

Serial monitoring of the cardiac function of children receiving anthracycline therapy allows early identification of cardiac damage. During therapy, the anthracycline dosage can then be adjusted or anthracycline therapy can be even stopped, which, hopefully, can prevent more cardiac damage to occur. Unfortunately, at the moment, there is no evidence on the most optimal way to monitor cardiac function in children treated with anthracyclines.

If cardiotoxicity could be prevented or at least be reduced, higher doses of anthracyclines could potentially be used, thereby possibly further increasing cancer survival. Extensive research has been devoted to the identification of methods or agents capable of ameliorating anthracycline-induced cardiotoxicity. The following methods for primary prevention have been identified: 1) Avoiding the use of anthracyclines in the treatment of childhood cancer, 2) The use of possible less cardiotoxic anthracycline analogues and anthracenediones, 3) Reducing the cumulative dose of anthracyclines, 4) Reducing the anthracycline peak dose, 5) Use of cardioprotective agents.

Important insight in the current state of the evidence on anthracycline cardiotoxicity is provided.

Is Childhood Cancer A Chronic Disease? A:04

D'Angio, Giulio
Department of Radiation Oncology, Philadelphia, United States

Definitions*:
1) Chronic: marked by long duration; relapsing, unremitting
2) Disease: disquiet (obsolete); disordered normal health status
*Oxford Universal Dictionary

Background: --- The Erice Conference in November 2006 was convened to address the question, "Is there such a thing as total cure of childhood cancer?" It is another way of asking whether it is a chronic disease. The consensus answer was, "No", based on both definitions. There was another issue that was very important to the long-term survivors, their representatives and the clinicians present in Erice. It was the question, "When can the patient be told he/she has been cured?" It elicited several different answers.

Discussion: --- The myriad primary and secondary effects entailed in cancer therapy include continuing dis-ease and disease in the patient. Disquiet is felt not only by members of the family, but by a wider circle that includes health care workers as well. The effects on these latter--- nurses, doctors, social workers, clinical laboratory staff, pharmacists, students, et al. --- deserve more attention and study. But is the primary cancer itself not a chronic illness? Does it never recur after a long interval? That is known to be true for certain rare entities like the mesenchymal chondrosarcoma. Recent studies indicate that late recurrence of the primary are being seen in the more common cancers, too. So when can the patient be told he/she is cured; i.e., the original cancer will never come back? Perspective --- Curing a child of cancer does not render that boy or girl immortal. He/she is subject to all the ills and misadventures of the general population. This led Easson about 60 years ago to propose his "Concept of Cure". His idea was this: the patient can be told that death from the original cancer poses no excess risk when the likelihood of dying of the primary neoplasm is not greater than the risk of death from any cause in age peers in the general population. It should be noted that, for those who survive a decade or more, second malignant neoplasms (SMNs) appear in increasing proportions among the listed causes of death; indeed, in a recent report, recurrence of the primary tumor was in second place. Some SMNs, at least, could be prevented by strongly discouraging cigarette smoking. Many of these patients are particularly vulnerable to the other damage caused by smoking depending on the curative treatments used. Impaired lung function if irradiated, is an example. The tobacco companies are targeting the 'teen and young adult population with candy-flavored cigarettes and enticing labeling; e.g., a coconut flavored product called, "Kauai Kolada". Surveillance and counseling are needed. Returning to the primary cancer, the Easson construct avoids unwonted over-optimism or pessimism on the part of individual physicians. It provides a more solid foundation on which to express an opinion when a long-term survivor asks, "Will my tumor come back to kill me?"

Conclusion: --- The question, "Is childhood cancer a chronic disease?" elicits a Talmudic answer, "Well, it depends ...."

Neurocognitive sequelae of brain tumors in children — A:05

Grill, Jacques
Gustave Roussy Institute, Pediatric and adolescent oncology, Villejuif, France

As prognosis of brain tumors is improving, concerns are growing for the quality of survival. As for other neoplasms, strategies to mitigate sequelae have been developped to minimize the use of irradiation. These strategies rely on the assumption that irradiation is the principal cause of treatment related side effects. However, surgery and chemotherapy may bring additional and substancial morbidity. In the modern age, it is of paramount importance that all the caregivers are aware of the specific sequelae associated with each treatment modality alone and in combination, before definite therapeutic decisions are made. It is now possible for some tumors like medulloblastoma to draw algorithms to predict long-term cognitive outcome based on the principal parameters that can influence IQ : age at diagnosis, interval since diagnosis and irradiation volume and dose, anatomical and neurologic damage. This later risk factor being the most important one in our later studies.

Studying the long-term results of patients treated with old-fashioned strategies can learn us a lot when choosing a given new strategy. Indeed, one can guess the late sequelae of a given modality based on the type of refinement of the treatment. In addition, any new modality has to be fully evaluated on the long-term (or with appropriate surrogates such as early MRI changes), before it can be adopted as a standard. Certainly in the future, all new protocols will need to incorporate careful evaluation of late sequelae

In addition to treatment related risk factors, age at diagnosis is a major predictor for impaired cogniotive outcome. Damage to specific structures may have a strong impact on further development of brain functions and this impact may depend on the age at which the structure is damaged. There will be critical period for each brain region, eg around two years for the cerebellum. We may need to take into account these issues for treatment planning in the future.

Finally, rehabilitation by dedicated teams is still the best garanty to lower the burden of disease and treatment-related late complications.

Neuropsychological consequences of childhood cancer — A:06

Eiser, Christine
University of Sheffield, Psychology, Sheffield, United Kingdom

Concern about the neuropsychological consequences of cancer and its treatment initially focused on treatment of acute lymphoblastic leukaemia (ALL) in children. Although the earliest reports suggested there were no identifiable effects, burgeoning work in the 1970s and 1980s pointed to intellectual deficits for many children. Younger age on diagnosis was identified as a risk factor, as was female gender. There was also much discussion about whether the deficit was a general one, or specific to certain skills. Attention and concentration were viewed as especially vulnerable.

Cranial irradiation was initially seen to be the most likely cause of any deficits, though subsequent work focused on comparisons between standard and reduced dose radiation, and later chemotherapy alone. In practice, it is clear that many factors determine neuropsychological outcomes, including treatment protocols, as well as socioeconomic and family variables.

Many issues remain. Critical is the question of the underlying cause of the condition. Two main hypotheses have been proposed. The first is that treatment disrupts elementary psychological processes such as attention or learning, and this compromises further development and acquisition of subsequent skills. The second involves a physiological process that is on-going and results in continued neuronal damage.

While the focus of research has been on identifying whether or not deficits occur, the more pressing question of remediation has received less attention. Drawing to a large extent on the brain injury rehabilitation literature, several techniques have now been described, including pharmacotherapy, cognitive remediation and ecological interventions. The latter emphasises the important role of schools and families in acknowledging the child's problems and engaging them in the child's education.

School achievement and acquistion of skills is vital for successful adult functioning, and especially so given the excellent survival rates now being achieved. Waiting until the child is a long-term survivor before considering these issues is not acceptable, and regular assessment, and associated remediation if needed, is vital.

Second malignant neoplasms and late mortality as complications after cancer in childhood and adolescence — A:07

Garwicz, Stanislaw
Division of Pediatric Oncology, Department of Pediatrics, Lund, Sweden

Second malignant neoplasms The observations that children treated for cancer are at increased risk of developing second malignant neoplasms (SMN) are not new. Starting with single case reports more than four decades ago, the literature now encompasses more than hundred publications of various size and quality. Combining elements of pediatric oncology, adult oncology, cancer epidemiology, radiobiology, legislation and statistics, every investigation of SMN must address several methodological issues, which are sometimes not readily recognizable. At the same time, when interpreting the results, readers should be aware of different approaches in different studies.

In the hospital-based studies, the standardized incidence ratio (SIR) of SMN is between 5 and 20 and the cumulative risk at 20 years of follow-up is between 3% and 12%. In the population-based studies the corresponding figures are: SIR 3.6 - 6.4 and cumulative risk 2.6% - 3.6%, compared with 0.6% expected. Absolute excess risk (AER) is between 1 and 3.5 cases of SMN per 1,000 person-years. The risk is higher in the patients treated more recently.

As SMN, bone and connective tissue tumors, breast cancer, CNS tumors and thyroid cancer have highest SIR. The interval between first and second cancer is in average more than 10 years, being shortest for leukemia and longest for breast cancer and tumors of the digestive tract as SMN. Among specific combinations of the first and second cancers, especially worrying is the high cumulative risk of breast cancer among women surviving Hodgkin lymphoma. Results of the investigations on the etiological factors in the development of SMN are partly conflicting. Genetic factors, radiation therapy, chemotherapy and possibly also relapse of the primary tumor per se, are all incriminated in increasing the risk of SMN, but their quantitative contribution is difficult to establish and it varies greatly depending on the nature of first and second cancer.

Late mortality Cumulative mortality among 5-year survivors diagnosed in sixties through eighties is 8 - 10% at 15 years after diagnosis and 12 - 14% at 25 years. Standardized mortality ratio (SMR) is about tenfold higher than in the general population. SMR is highest at 5 - 10 years after diagnosis and decreases with longer follow-up. Absolute excess risk (AER) is about 7 deaths per 1,000 person-years at risk. Cumulative mortality is higher in males than females, while SMR is higher in females, depending on lower background mortality in women. The highest percentage of deaths is observed among patients with Hodgkin lymphoma, CNS tumors and leukemia. Relapse status in the first 5 years after diagnosis, age at diagnosis, treatment era and treatment modality appear to be important prognostic indicators. The pattern of causes of death depends on primary diagnosis and varies with the lengths of follow-up. While recurrence of the primary tumor dominates greatly at shorter follow-up, second malignant neoplasms, cardiac toxicity and pulmonary complications emerge as important causes of death with longer follow-up. Since mortality continues to be excessive many years after diagnosis, further long-term follow-up of survivors of cancer in childhood and adolescence is mandatory.

What is the role of the nurse in the late effects practice/clinic? — A:08

Gibson, Faith
UCL Institute of Child Health and Great Ormond Street Hospital for Children, Centre for Nursing and Allied Health Research, London, United Kingdom

Though cure from cancer is not guaranteed, children's chances of survival have increased significantly. As a result the paediatric oncology community is focused on providing appropriate follow-up care to an increasing number of cancer survivors. However, while there is theoretical agreement about how future follow-up care should be designed and delivered the current service remains somewhat inconsistent and fragmented. There remains some uncertainty around 'whom', 'how', 'when' and 'why' in relation to follow-up care: with some tensions existing between health care professionals and young person's views. This presentation mainly addresses the 'who' factor in this debate, focusing exclusively on the role of the nurse, but within this context the 'why' will also receive some attention: drawing on both professional and service users perspectives.

Nurses can play a key role in follow-up care by: decreasing the full impact of long-lasting effects of treatment; assisting the child/young person and family to cope effectively while monitoring and treating late effects; helping them and their family gain perspective on the cancer experience so that they can be vigilant toward potential late effects. There is evidence already in existence that supports maximising the role of the nurse in follow-up care. For example, nurse-led follow-up clinics have been in place in the USA since 1983, and in the UK there is evidence that nurses have begun to take a role in long-term follow-up. However, some roles are not consistent in either approach or intentions and outcomes are rarely described, leaving posts fragile when service re-organisations take place. This presentation draws on data collected from nurses working in late effects in the UK and elsewhere with the specific aim of capturing a moment in time to describe the characteristics of this evolving role. There is a need to move beyond traditional frameworks of treatment and care that are situated in historical professional boundaries in order that we embrace enhanced cancer care for survivors.

Models of Follow Up After Childhood Cancer A:09

Toogood, Andy
University Hospital Birmingham NHS Foundation Trust, Birmingham, United Kingdom

The evolution of multidisciplinary management of malignant disease that occurs during childhood has led to improved survival into adult life. However, this success has come at a cost. In excess of 60% of survivors of childhood cancer have one or more on-going medical problem and are at risk of additional problems such as endocrine dysfunction or second malignancy. Consequently this cohort of patients require life-long follow-up in a service that provides appropriate management of the conditions the patient already suffers and surveillance for those they may develop in the future. To a certain extent long-term follow-up services have evolved out of necessity and their nature has been dependent upon local geographical arrangement of services and personnel who are willing to be involved.

The ideal service should facilitate seamless care of patients from treatment in childhood to independent living young adults. Transition between paediatric and adult services is important. Many patients are lost to follow up during this period so a robust process needs to be in place to ensure that the necessary information and the patient are moved between the two services. Each part of the service must provide education, psychological support and access to specialist facilities appropriate to the patient's age.

Further evaluation of current models is required to determine the optimal follow up strategies of this complex cohort of patients.

GH deficiency after childhood cancer – whom to treat? A:10

Shalet, Stephen, Michael
Christie Hospital NHS Trust, Endocrinology, Manchester, United Kingdom

In 1981, the first results of the experience with GH treatment were reported in 6 children who had survived a brain tumour(CBT). All responded to GH therapy, and growth rates increased to 6.0-10.1 cm during the first year. Final height outcomes in CBT survivors treated with GH were subsequently reported by various centres, with a significant proportion of children reaching final heights above the third centile. A study of the effects of spinal irradiation on final height in 79 CBT patients (not treated with GH) estimated the radiation-related spinal height loss to be at least 9 versus 7 versus 5.5cm when irradiation was given at the age of 1 versus 5 versus 10 years, highlighting the vulnerability of very young children to suffer the most severe spinal growth retardation.

Another factor, often encountered in CBT survivors, contributes to the relatively poor spinal growth response: early (although less frequent true precocious) puberty, which tends to be of normal duration. The predicted age of onset of puberty is positively correlated with the age at cranial irradiation. Both the radiation osteitis of the spine and abnormal pubertal tempo in the context of early onset contribute to the poor response of sitting height to GH treatment. Analysis of auxological data of the last 25 years of GH treatment in CBT survivors in our unit revealed a gradual improvement in final height outcome for both cranial irradiation ($r=0.5$, $p=0.03$) and craniospinal irradiation patients ($r=0.6$, $p<0.001$. The main factors contributing to that success were the improved and higher GH dosing regimes, the earlier introduction of GH treatment after completion of radiotherapy and the additional use of GnRH analogue therapy for early puberty in selected patients.. Lag times between completion of RT and initiation of GH therapy were reduced from a mean 5.8 years to 3.3 years for patients treated before versus after 1988. GnRH analogue therapy conferred additional height benefits in selected patients, although final height gains were often achieved at the expense of increased skeletal disproportion.

Who is at risk of gonadal dysfunction? A:11

Sklar, Charles
Memorial Sloan Kettering, New York, United States

Female survivors of childhood cancer are at risk of developing ovarian dysfunction. Risk factors include age at treatment, exposure to ovarian radiation and exposure to alkylating agents. A subset of survivors will suffer loss of ovarian function during or shortly after completing their treatment (referred to as acute ovarian failure [AOF]). Data from the multicenter Childhood Cancer Survivor Study (CCSS) indicated that ~6% of some 3000 female survivors developed AOF. Predominate risk factors included exposure to >1000 cGy ovarian radiation and exposure to the alkylating agents procarbazine, at any age, and cyclophosphamide, at ages >12 yrs. For females who retained ovarian function following their cancer treatment, data from the CCSS indicated that ~8% went on to develop menopause prior to age 40 yrs (referred to as premature menopause). The major risk factors for premature menopause included older attained age, exposure to ovarian radiation and any alkylating agents, and a diagnosis of Hodgkin lymphoma. For survivors treated with abdomino-pelvic radiation plus alklyating agents, the estimated cumulative incidence was 30%. Male survivors are at high risk of experiencing damage and loss of sperm producing cells. Data suggest that ~50% of male survivors develop oligo-azoospermia. While age at treatment does not appear to be a significant risk factor, exposure to >200 cGy testicular radiation and high-dose alklyating agent therapy (eg, cyclophosphamide doses > 7.5-9 gm/m2) are key risk factors for germ cell failure. Current biomarkers such as serum FSH and inhibin-B are not sensitive enough to establish fertility status in a given individual; sperm analysis is required. Leydig cell failure is much less common compared to germ cell dysfunction and is seen primarily following testicular radiation >2000 cGy.

Fertility preservation in young people treated for cancer A:12

Keros, Victoria[1]; Hovatta, Outi[2]
[1]Karolinska University Hospital- Huddinge, Obstetrics and Gynaecology, Fertility Unit, Stockholm, Sweden; [2]Karolinska University Hospital- Huddinge, Obstetrics and Gynaecology, Stockholm, Sweden

Timely diagnostics and advanced treatment of childhood cancer results in increased survival of treated patients. On the other hand, high doses of chemotherapy and radiotherapy frequently cause long term or permanent infertility due to gametes damage.

Few well-developed options for fertility preservation in young adolescent patients exist nowadays. Oocyte and embryo cryopreservation are the options for fertility preservation in women who have a partner and whose cancer treatment can be delayed. Hormonal ovarian stimulation or collection of immature oocytes has to be carried out. Collecting and cryopreservation of ejaculated, epididimal or testicular sperm should be offered for male patients with ongoing spermatogenesis. Thawed spermatozoa can be used for fertilization of the partner's eggs by intracytoplasmic sperm injection. Ovarian tissue cryopreservation is the only alternative to preserve fertility in young girls. For prepubertal boys, cryopreservation of spermatogonial stem cells within testicular tissue is an option for fertility preservation. In adult life, stored gonadal tissue can be thawed and either transplanted or matured in vitro. The harvested from patients ovarian or testicular tissue should be tested before transplantation for malignant contamination to prevent transmission of tumour cells in the treatment. Possibility for fertility preservation in young cancer patients should be discussed in a multidisciplinary team. The decision has to be made individually in each case, depending on the nature of disease, type of treatment and patient's age. Fertility preservation is important for improving the quality of life in childhood cancer survivors

Cognition, Psychology and Quality of Life

Cerebrospinal fluid tau protein level and cognitive decline in children with acute lymphoblastic leukemia. C:01

Muszynska-Roslan, Katarzyna; Protas, Piotr; Grabowska, Aleksandra; Krawczuk-Rybak, Maryna.
Medical University, Bialystok, Poland

Long-term neuropsychological complications, have been described in children after acute lymphoblastic leukemia (ALL) treatment.

The aim of the study was to assess the level of cerebrospinal fluid tau protein (a neurodegenerative marker associated with damage of neuronal axons) and to determine whether it is associated with cognitive decline in children with acute lymphoblastic leukemia. We examined 38 patients with ALL at diagnosis, after induction treatment, during consolidation and before maintenance therapy. The reference group consisted of 22 patients with clinical symptoms of cerebrospinal meningitis. In 19 patients we examined the cognitive functioning in median time 3,7 years after diagnosis.

Results: 1. Neither age nor gender had an effect on tau protein levels in both groups. 2. The mean tau protein value at diagnosis was 286.8 ±121.3 pg/ml in the study group and 297.6 ±96,8 in the reference group (norm for adults <300 pg/ml) and showed no correlation with initial leukocytosis, organomegaly at this point. 3. Dynamic analysis revealed a statistically significant increase in tau protein after induction treatment (401.8 ±140.5) as compared to its level at diagnosis [p<0.008] and later during treatment. 4. The levels of tau protein at various points of treatment did not differ statistically significantly between the groups, except for the values obtained after termination of remission induction. 5 The level of tau protein was negatively correlated with verbal abilities measured by intellectual scale.

Conclusion: Changes in tau protein level may indicate that some patients are at a greater risk of central nervous system damage. This results are cross sectional but it still suggest that the treatment may cause increase of tau protein level and decline of some of cognitive functioning. This requires further studies, also in reference to other central nervous system proteins.

Comparison of verbal and practical intelligence quotient in patients treated for childhood acute lymphoblastic leukemia with chemotherapy only C:02

Gavras, Christoforos[1]; Delinikopoulou, Eleni[2]; Adam, Anna2; Papageorgiou, Theodotis[2]; Papakonstantinou, Evgenia[3]; Abatzoglou, Grigorios[2]; Koliouskas, Dimitrios[3]; Athanassiadou, Fani[2]
[1]Ahepa University Hospital Thessaloniki Greece, Hematology-Oncology Unit, Katerini, Greece; [2]Ahepa University Hospital, Thessaloniki, Greece; [3]Ippokration University Hospital, Thessaloniki, Greece

Objective: The objective of the current study was to evaluate the long-term neurocognitive effects of chemotherapy in patients treated for childhood acute lymphoblastic leukemia (ALL) after being off treatment for at least two years.

Methods: The total number of participants was 23, 13 male and 10 female, aged from 8 to 24 years old. All had childhood ALL and had completed their treatment with chemotherapy only at least two years before. The intelligence batteries used in our study were WISC III and WAIS-R , which are universally accepted for assessing children (between 6 and 16 years old) and teenagers (above the age of 16) and adults respectively. The intelligence quotient consists of two independent subtypes of intelligence, which are the verbal and the practical one. The participants got a score for each subtype and these two scores underwent comparison in order to prove or not the existence of any statistical significant difference.

Results: The analysis of the data revealed that there is a considerable number of participants who showed a major discrepancy between the scores in the two subtypes. More specifically, 34,8% showed a difference of more than 11 points between the 2 scores which is statistically significant and 4,3% showed a major and rare difference of more than 19 points, which is regarded as abnormal and indicates the need for further research. The 60,9% of the participants showed no statistical significant differences between the scores they got.

Conclusions: From all participants, 39,1% showed a statistical significant difference between the scores they got in the two subtypes of intelligence. The performance of each participant is considered on an individual basis and personal, biological, psychological and other environmental parameters are being taken into account to evaluate the results. Therefore, a different approach is being incorporated by the therapeutic team.

Underlying mechanisms of late neurocognitive sequelae after treatment of childhood ALL C:03

Schuitema, Ilse[1]; De Sonneville, Leo[1]; Sanz-Arigita, Ernesto[2]; Barkhof, Frederik2; Van Dijk, Bob[3]; Stam, Kees[3]; Buizer, Annemieke[4]; Veerman, Anjo[4]; Van den Bos, Cor[5]

[1]Leiden University, Clinical Child and Adolescent Studies, Leiden, Netherlands; [2]VU University Medical Center, Radiology, Amsterdam, Netherlands; [3]VU University Medical Center, Clinical Neurophysiology, Amsterdam, Netherlands; [4]VU University Medical Center, Pediatric Hematology-Oncology, Amsterdam, Netherlands; [5]Academic Medical Center, Pediatric Oncology, Amsterdam, Netherlands

Objective: Cognitive functions depend on the integrity of functional networks in the brain. White matter damage can be a cause of disruption of functional networks. We are trying to find the underlying mechanisms of long-term neurocognitive sequelae after childhood ALL by assessment of functional connectivity and quality of the white matter.

Methods: Children treated according to two protocols are studied: DCLSG ALL5 (cranial irradiation plus chemotherapy (CRT+CT)) and DCLSG ALL6 (chemotherapy only (CT-only)). In a pilot-study, 14 ALL survivors (7 treated with CRT+CT, 7 treated with CT-only) and 10 healthy controls, were assessed with the Amsterdam Neuropsychological Tasks (ANT) program, structural and functional MRI (n-back task), DTI (diffusion tensor imaging, assessing white matter quality) and MEG (magneto-encephalography, assessing connectivity between brain regions). This pilot-study is being followed by a larger project assessing 175 ALL survivors (2006 - 2010). Quality of life will also be assessed.

Results pilot-study: Functional MRI showed different results for each level of the n-back task. On the 1-back level, the CT-only group shows more activity in parietal regions compared to controls. On the 2-back level, the CRT+CT group shows more activation in the dorsolateral prefrontal cortex compared to the CT-only group and controls. The CT-only group makes significantly less use of the premotor cortex than controls. On the 3-back level, the CRT+CT group still shows more activation in the dorsolateral prefrontal cortex compared to controls, but the other differences disappear. DTI revealed diffuse differences in Fractional Anisotropy values. MEG results show that both groups of ALL survivors show significantly more synchrony in the alpha-1 band than controls. Mean synchronisation likelihood is higher in the CRT+CT group than in the CT-only group.

Conclusions: These results suggest differences in neurocognitive function and functional connectivity in long-term survivors of ALL. Diffuse white matter pathology is suggested to underlie these qualitatively different functional networks.

Neuropsychological development after bone marrow transplantation at 0-3 years of age C:04

Smedler, Ann-Charlotte[1]; Winiarski, Jacek[2]

[1]Dept of Psychology, Stockholm, Sweden; [2]Karolinska institute, Huddinge Hospital, Dept of Pediatrics, Stockholm, Sweden

Background/Objective: In the face of aggressive forms of childhood leukeamia, bone marrow transplantation (BMT) may provide a chance for long-term survival. However, conditioning before transplantation involves potentially neurotoxic treatment modalities, such as total body irradiation (TBI) and cytostatic drugs. Since the immature brain is particularly vulnerable to generalized and diffuse insult, children treated at a very young age are most at risk. We have previously demonstrated that BMT, including TBI of 10 Gy in a single dose, is associated with long-term neuropsychological impairment, particularly in children treated at 3 years of age or younger. The present study investigated whether the impact is less severe when TBI is fractioned (FTBI), or replaced by the cytostatic drug busulfan (BU). Internationally available data are inconsistent and inconclusive, particularly regarding very young patients treated with BU.

Patients and Methods: Ten children treated with BMT at .4-3.5 years of age (mean age 2.0 years) according to a BU or FTBI protocol were subject to a neuropsychological assessment, at an average of 7.3 years post therapy. Eight children had received BU, and two had received FTBI. Their results were compared to a group who had received TBI in a single dose (n=10 of which 8 were historic controls; mean age at BMT 2.4 years).

Results: Compared to age-based normative data, children treated with BU tended to display deficits in visuo-spatial cognitive functioning, attention, mental speed and working memory. However, the deficits were milder and not as pervasive as was observed in the historic controls, who also suffered from pronounced motor impairment. Patients who had received fractioned irradiation had a somewhat less favourable outcome compared to the BU group.

Conclusion: BMT is associated with long-term neuropsychological deficits, calling for routine psychological follow-up and counselling. Busulfan has a less negative impact than irradiation on neuropsychological development after treatment at a very young age.

Long-term Psychosocial Support for Families of Children Who Have Undergone Allogeneic SCT C:05

Forinder, Ulla[1]*; Edberg Posse, Ebba*[2]
[1]Instutionen för socialtarbete, socialt arbete, Stockholm, Sweden; [2]Karolinska University Hospital, Huddinge, Department of Social Work, Stockholm, Sweden

Background: Stem cell transplantation (SCT)entails a major strain both on children and their families. The 60-70 % of children who make up the group of long-term survivors also have a number of late effects to contend with. These include both somatic and psychological effects that impact on the lives of these families. In an earlier study parents of SCT children expressed both concern for their children and a wish for more information as well as for more support. This knowledge resulted in prolonged psychosocial support to these families. All families attend Karolinska University Hospital, Huddinge Sweden for a yearly post-transplant follow-up were offered an appointment with the social worker at the clinic.

Objective: of this study was to evaluate the prolonged psychosocial support. How many families accepted the offered contact with the social worker? What kind of support did the families ask for? Did the meeting result in any intervention and if so of what kind?

Methods: The data that has been used is the social workers notes in the medical chart. Content analysis was used as research method.

Results: 39 of 46 families accepted the offer to have an appointment with the social worker. By analysing data the participating families were categorized into 5 groups. Each group was characterized by different criteria .The study shows that there is an ongoing need for psychosocial support many years after treatment. Time since treatment doesn't decline the need for psychosocial support but the content in the support change over time.

Conclusion: There is a need for long term support among both parents and patients after SCT. The study raise the question if the offered prolonged support is enough.

Post-traumatic Stress and Psychosocial Adjustment in Siblings of Paediatric Leukaemia Survivors C:06

Lyons, Shoshanah[1]*; Brown, Gary*[2]*; Melvin, Diane*[3]*; Leiper, Alison*[4]*.*
[1]Royal Holloway, Univeristy of London & Great Ormond Street Childrens Hospital, London, Department of Psychology, Egham, Surrey, TW20 OEX, United Kingdom; [2]Royal Holloway, Univeristy of London, Department of Psychology, Egham, Surrey, TW20 OEX, United Kingdom; [3]Great Ormond Street Childrens Hospital, Department of Psychological Medicine, London, United Kingdom; [4]Great Ormond Street Childrens Hospital, Department of Haematology and Oncology, London, United Kingdom

Background: Recent research has indicated that a model of post-traumatic stress is applicable to paediatric patients who have a diagnosis of cancer, and their mothers and fathers. However, research on the long-term sequelae of siblings of cancer survivors is limited and inconsistent, and it is not clear whether a model of post-traumatic stress also applies to siblings.

Objectives: To investigate whether siblings of childhood leukaemia survivors experience long-term post-traumatic stress symptoms (PTSS) and poor psychosocial adjustment. To identify risk factors influencing PTSS, and parental perceptions of child post-traumatic stress.

Method: 66 child and adolescent siblings of leukaemia survivors were compared with 70 control participants on measures of PTSS, anxiety, depression and self-esteem. Parents completed a measure of behavioural problems and child PTSS.

Results: 35% of siblings reported mild PTSS, and a further 35% reported moderate-to-severe PTSS, which was significantly higher than the control group. No overall differences were found between groups on measures of general adjustment, however, siblings who did not have PTSS fared better than controls on measures of depression, anxiety and low self-esteem. No demographic, individual or illness variables predicted PTSS. Parents of siblings significantly under-estimated their child's PTSS, and this was associated with the severity of sibling distress.

Conclusions: Levels of PTSS, but not depression, anxiety, low self-esteem or behavioural problems were elevated in siblings of childhood leukaemia survivors. Furthermore, siblings who did not report PTSS appeared to show 'post-traumatic growth' following their experience. Thus, PTSS may be a useful model for understanding siblings' long-term adjustment to childhood cancer.

Children and adolescents health related quality of life following allogeneic Stem cell transplantation C:07

Löf, Catharina[1]; Forinder, Ulla[2]; Winiarski, Jacek[3]
[1]CLINTEC, Karolinska Institutet, Pediatrik, Stockholm, Sweden;
[2]Socialtarbete, Socialhögskolan, Sthlm Univ, Stockholm, Sweden;
[3]CLINTEC, Karolinska Institutet, Stockholm, Sweden

Objective: This study was performed during 2003 focusing on health related quality of life among children and adolescents following successful Stem cell transplantation (SCT). The aim was to explore aspects of health realted quality of life (HrQoL) both according to diagnosis, the use of a related or unrelated donor.

Methods: A total of 52 children, (age 9-22, m=15) and at least 3 years (median=8) beyond SCT for leukemia (n=31) or nonmalignant diseases, participated in a single center study of health related quality of life (HrQoL) at Karolinska University Hospital, Huddinge. 42 parents participated in the study at the same occasion. With a cross sectional design descriptive statistics, Students T-test and standard multiple regression analayses were used to asses the effect of diagnosis, donor choice, subjective and objective health on HrQoL domains in Swedish Child Health Questionnaire (SCHQ-CF87/ SCHQ-PF50).

Results: As a group we recently reported children having a good HrQoL after SCT, in comparison to a normgroup and other chronically ill children. Most children were also subjectively and objectively in good health. Children with leukemia rated a lower HrQoL score in the psychosocial area ($p<0.05$) and had a higher degree of objective late effects ($p<0.05$). Parents rated their children's HrQoL lower in both the psychosocial area and physical area if the child are diagnosed with leukemia compared to non-malignant diagnsosis ($p<0.01$). Late effects are the strongest contributor to the parents HrQoL ratings ($p<0.05$) and also had an impact on their own (parents) emotional situation. The psychosocial HrQoL area was most affected in recipients of an unrelated donor, according to child ($p<0.01$) and parent ($p<0.05$).

Conclusion: Children reason they have a good HrQoL following SCT, but their parents do not agree with this view. When interpreting paediatric HrQoL studies it is crucial to be clear who is responsible for assessing the child's HrQoL. One important clinical conclusion from the study is might be to focus healthcare resources on psychosocial support to both child and parent, especially on the group with more late-effect-related problems.

Assessment of Quality of Life and Neurocognitive Functions in Children Treated with Radiochemotherapy for Medulloblastoma or Ependymoma C:08

Winter, Anita; Spiegl, Katharina; Benesch, Martin; Passini, Andrea; Daghofer, Fedor; Moser, Andrea; Lackner, Herwig; Urban, Christian
LKH Graz, Department of Pediatrics and Adolescent Medicine, Graz, Austria

Background: To assess quality of life (QOL) and neurocognitive parameters in children who received multimodality treatment for medulloblastoma or ependymoma.

Methods: Twenty-three patients (17 males and 6 females; median age 14 years) who were treated with radiochemotherapy for medulloblastoma (n=18) or ependymoma (n=5) underwent neurocognitive and QOL testing after treatment. Median time from the end of therapy was 56 (range, 173) months. We used the German Wechsler Adult Intelligence Scales (WAIS) and German Wechsler Scales for Children (WISC), to test intelligence quotients (IQ). Additionally, the test battery included the D2 test for assessment of attention and concentration, FBT (perception and memory) and VLMT (verbal learning skills). QOL was evaluated by means of the KINDL (for patients <16 years) and EORTC-QLC-C30 (for patients >16 years), respectively.

Results: In 44% (10/23) of patients, normal IQ scores were found, whereas 52% (12/23) of patients had below-average scores, only 4% (1/23) of patients had IQ scores above-average. Intellectual skills declined with time from the end of treatment. The majority of patients scored below average for attention/concentration (65%; average, 30%; above average, 4%), for perception/memory, 65% achieved average scores, whereas 35% scored below average. QOL scores were normal or better than average in >75% of patients. No statistically significant correlation was found between neurocognitive parameters and QOL, assessed with the EORTC-QLQ-C30. In the subgroup of patients who completed the KINDL, statistically significant correlations were found between QOL and the measures of WISC, indicating a positive relation between QOL and cognitive performance.

Conclusions: The majority of patients rated their QOL as good. Our study, however, confirms a negative correlation between time since completion of treatment and intellectual skills.

Quality of life in children cancer survivors in the Czech Republic - a developmental approach (Brno QOLOP study) C:09

Kepak, Tomas[1]; Blatny, Marek[2]; Pilat, Milan[3]; Mazanek, Pavel[1]; Karova, Sarka[4]; Vlckova, Irena[1]; Jelinek, Martin[2]; Mudry, Peter[1]
[1]University Hospital Brno, Dpt. of Paediatric Oncology, Brno, Czech Republic; [2]Czech Academy of Sciences, Institute of Psychology, Brno, Czech Republic; [3]University Hospital Brno, Paediatric Psychiatry and Clinical Psychology, Brno, Czech Republic; [4]Masaryk University Brno, Institute of Psychology, Brno, Czech Republic

Background/ Objective: Along with the increasing number of childhood cancer survivors, the late effects of anticancer therapy and the associated quality of survival have got to the forefront of interest. At present, the research in the field is facing methodological problems derived primarily from a paucity of suitable measurement methods and a lack of longitudinal work.

The purpose of the project is to establish a longitudinal study of the quality of life in children surviving cancer in the Czech Republic. The methodological goal of the study is to establish methodology of measuring the quality of life that would reflect changes in the perception of the quality of life throughout the life cycle. The research purpose of the study is to identify the areas in which the quality of life in children with cancer is reduced, both in terms of objective parameters and the subjective perception of contentment.

Methods: The identification of target areas will be based on a comparison of three study populations (healthy children, children with chronic diseases other than cancer and children with cancer). During the duration of the project (4 years), at least 300 childhood cancer survivors can be expected to participate. The results of the research will be analyzed, with the intention to prepare appropriate preventive and interventional strategies that could improve the quality of life in children with cancer.

Results: In 2006 we created the original quality of life assessment (in Czech). Since November 2006 until February 2007 it has been administered to the first 16 childhood cancer survivors (age 7-18) in the framework of a pilot study qolop (Quality Of Life of Oncology Paediatric patients) at the Departement of Paediatric Oncology, Brno. We set up the project 's website (http://qolop.eu). Here we present our actual experience obtained from the pilot study.

This research is supported by the Grant Agency of the Czech Republic under No 406/07/1384

Quality of life and long-term morbidity after multimodal treatment for Ewing's sarcoma or osteosarcoma C:10

Aksnes, Liv Hege[1]; Bauer, Henrik[2]; Jebsen, Nina L.[3]; Folleraas, Gunnar1; Lernedal, Helen2; Bjork, Olle[4]; Wettergren, Lena[5]; Allert, Carin[2]; Sundby Hall, Kirsten1
[1]Rikshospitalet-Radiumhospitalet Medical Centre, Cancer Clinic, Oslo, Norway; [2]Karolinska University Hospital, Department of orthopaedics, Stockholm, Sweden; [3]Haukeland University Hospital, Department of oncology, Bergen, Norway; [4]Astrid Lindgren Children Hospital, Paediatric Cancer Research Unit, Stockholm, Sweden; [5]Uppsala University, Department of Public health and caring sciences, Uppsala, Sweden

Background: To evaluate Quality of Life (QoL), functional outcome and long-term morbidity in survivors of extremity localized Ewing's sarcoma or Osteosarcoma (EBS survivors) > 5 years after treatment.

Methods: QoL was evaluated by Short-form -36 (SF-36), Hospital Anxiety and Depression Scale (HADS), Fatigue Questionnaire (FQ) in addition to demographic data. Function was evaluated according to Musculoskeletal Tumor Society Score (MSTS score) and Toronto Extremity Salvage Score (TESS). Long-term morbidity was evaluated by objective means and questionnaires. SF-36, HADS and FQ results were compared to age and gender adjusted sample from the general population (GenPop).

Results: 133 EBT survivors (of 155 approached) over 15 years of age at time of invitation responded. 74 (56%) were males. The median age at follow up was 29 (15-57) and median years since diagnosis were 12 (6-22). 115 EBS survivors were treated for tumours in the lower extremities and 76 had limb sparing surgery (LSS). 87% were either working or still studying. The EBS survivors had significant lower scores on all the physical dimensions and one mental dimension (role emotional) of SF-36 compared to GenPop ($p<0.01$). The female EBS survivors had significant higher anxiety level ($p=0.046$), and both genders had higher total fatigue than GenPop ($p=0.004$ and 0.03, respectively). The median MSTS score was 76% (40-100) for LSS and 57% (17-90) for the amputated EBT survivors ($p<0.001$). The median TESS was 88% (58-100) for LSS and 86% (43-100) for the amputated ones.

At follow-up 36 EBS survivors had bilateral hearing loss, 8 heart failure (all<40 years of age), 5 renal failure, 3 diabetes mellitus and 8 had hypo/hyperthyroidism (all acquired during or after treatment)

Conclusions: At long-term follow up most of the EBT survivors are doing well. They have an overall good QoL, but must be prepared for a reduced physical function after treatment.

Positive and negative consequences with regard to cancer during adolescence – Experiences two years after diagnosis C:11

Mattsson, Elisabet[1]; Ringnér, Anders1; Ljungman, Gustaf[2]; von Essen, Louise[1]
[1]Public Health and Caring Sciences, Psychosocial Oncology, Uppsala, Sweden; [2]Dep of Women's and Children's Health, Paediatric Oncology, Uppsala, Sweden

Objectives: The purpose was to explore negative and positive consequences of cancer during adolescence experienced two years after diagnosis.

Methods: Two years after diagnosis thirty-eight persons, 15-21 years old, were asked two questions over the telephone: What, if anything, is bad for you due to the cancer disease? and What, if anything, is good for you due to the cancer disease? The answers were analysed by content analysis.

Results: Four categories of negative experiences were identified: a problematic body, unpleasant thoughts and feelings, outside the circle of friends, and difficulties with schoolwork. Six categories of positive experiences were identified: a more positive view of life, good self-esteem, knowledge and experience with regard to disease and hospital care, good relations, broader perspectives, and material gains.

Conclusions: Two years after diagnosis those struck by cancer during adolescence experience not only a number of negative, but also positive, consequences of the cancer disease and its treatment.

Are there any positive consequences related to surviving childhood cancer? A review of the literature C:12

Mattsson, Elisabet[1]; Lindgren, Björn[2]; von Essen, Louise[1]
[1]Public Health and Caring Sciences, Psychosocial Oncology, Uppsala, Sweden; [2]The Vårdal Institute, Lunds University, Lund, Sweden

The aim was to investigate whether there are any positive consequences related to surviving childhood cancer. A review of the literature was performed. In the first step studies with a descriptive design published 1990-2005 reporting at least one positive consequence related to surviving childhood cancer were identified through a search of the databases CINAHL, PsycINFO, and PubMed. Positive consequences were referred to three themes, according to a manifest content analysis: life values, relations to others, and relation to self. Taking these as a starting point a second search was conducted in the databases with the purpose of identifying studies with a comparative design in which variables that could be referred to these themes were investigated. The findings demonstrate that survivors of childhood cancer in most regards are similar to comparison groups with regard to life values, relations to others, and relation to self. However, friendship, marital status, parenthood, and sexuality are areas of concern for survivors of childhood cancer. The major implication for clinical care is that survivors of childhood cancer need to be followed-up by a multi-professional team.

Health-related quality of life, anxiety, and depression among adolescents and young adults with cancer: a prospective longitudinal study C:13

von Essen, Louise[1]; Mattsson, Elisabet[2]; Jörngården, Anna[3]
[1]Public Health and Caring Sciences, Psychosocial oncology, Uppsala, Sweden; [2]Uppsala University, Department of Public Health and Caring Sciences, Psychosocial oncology, Uppsala, Sweden; [3]Department of Public Health and Caring Sciences, Uppsala University, Psychocial oncology, Uppsala, Sweden

Background/Objectives: The present study sets out to add to knowledge about the development over time of health-related quality of life (HRQL), anxiety, and depression among survivors of adolescent cancer. The aim was to investigate if and how the HRQL, anxiety, and depression of a group of adolescents with cancer differ from those of a reference group shortly after diagnosis, and subsequently at six, twelve, and eighteen months after diagnosis.

Methods: Adolescents diagnosed with cancer and a reference group randomized from the general population completed the Hospital Anxiety and Deression Scale (HADS) and the two subscales Mental Health and Vitality in the Short Form 36 (SF-36) in telephone interviews.

Results: The results indicate a steady increase in psychological well-being from the time of diagnosis when the cancer patients' ratings were significantly worse than those of the general population, and onwards. The differences gradually disappeared and then were reversed, resulting in the cancer group reporting significantly better HRQL and lower levels of anxiety and depression than the reference group when 1.5 years had passed since diagnosis.

Conclusions: The adolescents faced with cancer show signs of adaptation to trauma which can be understood in relation to the theoretical framework of posttraumatic growth as well as response shift. Future research should continue to follow this development over time, to investigate if the positive effects of the cancer experience will wear off, or if it has facilitated permanent positive outcome.

What consequences of childhood cancer do young adults consider important C:14

Sundberg, Kay[1]; Björk, Olle[2]; Lampic, Claudia[3]; Wettergren, Lena[4]
[1]Folkhälso-och vårdvetenskap, Vårdvetenskap, Uppsala, Sweden; [2]Kvinnor och Barns Hälsa, Karolinska Institutet, Stockholm, Sweden; [3]Folkhälso-och vårdvetenskap, Uppsala Universitet, Uppsala, Sweden; [4]Neurobiologi, vårdvetenskap och samhälle, Karolinska Institutet, Stockholm, Sweden

Objective: The overall aim was to explore whether, and if so in what ways, long-term survivors from childhood cancer experience that their life is influenced by having had cancer.

Methods: All patients diagnosed with childhood cancer between 1985 and 1999 at Astrid Lindgren's Hospital, Karolinska University Hospital, Stockholm, were invited to participate in the study of which 253 accepted participation (response rate 72 %). Telephone interviews were conducted with participants using an extended version of The Schedule for the Evaluation of Individual Quality of Life-Direct Weighting (SEIQoL-DW). The method uses semi-structured interviews to measure individual quality of life and influence of the former disease on life. The extended version used in this study included a disease-related part. Respondents were asked: 'If you think about the fact that you have been treated for childhood cancer, what in your life is influenced, both positively and negatively by this? The respondent was allowed to mention as many aspects/areas as wanted. Each aspect/area was subsequently rated regarding how troublesome or satisfying it was perceived today on category scale. The mentioned aspects and areas influencing life today were analysed by means of content analysis.

Results: Preliminary results indicate that approximately 48% of the long-term survivors reported negative consequences and 50% reported positive consequences of having had cancer. The reported negative aspect/areas included a disruption of life, an altered body image, changed interpersonal relationships, disturbing scars and thoughts and worries. The most frequently reported positive aspect/areas were described as a life experience, personal development, improved relationships to other people, a positive outlook on life and increased empathy for others.

Conclusions: Long-term survivors who have experienced childhood cancer report numerous consequences influencing their adult life. Interestingly, positive and negative consequences were reported to the same extent.

Endocrinology, Growth and Metabolism

Thyroid function in children after hematopoietic stem cell transplantation E:01

Niedzielska, Ewa[1]; Barg, Ewa[2]; Doroszko, Adrian[3]; Sega-Pondel, Dorota[1]; Kazanowska, Bernarda[1]; Wojcik, Dorota[1]
[1]Department of Pediatric Hematology/Oncology and Bone Marrow Transplantation,Wroclaw Medical University, Wroclaw, Poland; [2]Department of Endocrinology for Children and Adolescens. Wroclaw Medical University., Wroclaw, Poland; [3]Department of Internal Medicine, Occupational Diseases and Hipertension Wroclaw Medical University, Wroclaw, Poland

Background: The success story in transplantation medicine has resulted late effects, e.g. impaired endocrine-, especially abnormal thyroid function. In this study we evaluated the thyroid function in pediatric long-term survivors of hematopoietic stem cell transplantation (HSCT).

Methods: 42 patients (24 girls and 18 boys) aged 2-20 years (median 12,5 years, mean 11,58 ± 4,95) were evaluated prospectively post transplant. The reason for HSCT were: AML (n=10), ALL (n=11), NHL (n=4), CML (n=6), MDS (n=2), carcynoma embryonale (n=2), NBL (n=3) and JMML, RMS, medulloblastoma, Ewing/PNET. These patients underwent autologous HCT (n=15), allogenic MSD-HCT (n=11), MUD-HCT (n=11) and HLA-mismatched related HCT (n=5). In three children two transplants were performed subsequently. The preparative regimens consisted of HDC/T usually BU/MEL (9); BU/CY/VP (6); BU/CY/ATG (5), VP/ATG/TBI (3), BEAM (3). Cranial irradiation (CI) prior grafting received 19 children: auto-HSCT(6) and allo-HSCT(13) and total body irradiation (TBI) in 6 patients. Endocrine function was evaluated from 3 to 104 months (median 24 months) after cessation of steroid therapy. Analysis of TSH, fT3, fT4, aTPO, TRH test was performed.

Results:
A) Hypothyroidism was found in 5 pts (2 after auto-HSCT, 3 after allo-HSCT).
B) 2 patients with hypothyroidism underwent CNS radiotherapy prior to the transplant and total body irradiation (TBI) in 1 patient.
C) 3 patients had abnormal aTPO and thyroid hormone substitution was instituted.
D) No case of hyperthyroidism was diagnosed.
E) Time from steroid therapy cessation did not influence the onset of abnormal thyroid function.

Conclusions: Children require standardized endocrine follow-up after HCT, because thyroid metabolism dysfunctions may occur frequently and worsen the quality of life posttransplant.

Abnormalities of the thyroid in long term survivors of Hodgkin's disease in childhood and adolescence E:02

Vandecruys, Els; Dhooge, Catharina; Benoit, Yves; Laureys, Genevieve
Ghent University Hosp ital, Pediatric Hemato-Oncology, Ghent, Belgium

Treatment for Hodgkin's disease (HD) is associated with a variety of thyroid abnormalities, including hypothyroidism, hyperthyroidism and thyroid neoplasms. We retrospectively studied the occurrence of thyroid abnormalities in patients who became a long term survivor after treatment of pediatric Hodgkin Lymphoma at our institution.

From February 1982 until February 2002 the diagnosis of HD has been made in 61 patients, 41 boys and 20 girls, the youngest 3 years(y) 9 months(m) and the oldest 15y6m at diagnosis. Five patients died of disease and 56 became a long term survivor. The duration of follow-up varied between 5 and 25 years.

Results: 18 out of 56 patients (32.1%) developed a thyroid abnormality, 14 subclinical hypothyroidism and 4 thyroid nodules of which 1 thyroid cancer. All patients received neck radiation (dose of radiation to the thyroid 20 Gy in 14, 30 Gy in 1 and 50 Gy in 2 patients who were treated twice) as part of the treatment. Subclinical hypothyroidism was diagnosed in 9 males and 5 females with a mean age at diagnosis of HD of 9y10m (range 4y10m - 15y6m). Hypothyroidism developed a mean of 4y6m (range 1y6m - 11y) after diagnosis of HD. All patients are receiving thyroid hormone replacement therapy. None of these patients developed a clinically apparent thyroid nodule so far. Screening ultrasonography is not routinely performed. Thyroid nodule(s) were diagnosed in 3 males and 1 female with a mean age at diagnosis of HD of 5y10 m (range 3y9m - 8y3m). Thyroid nodule(s) developed a mean of 13y1m (range 9y5m - 18y9m) after diagnosis of HD. None of these 4 patients had previously subclinical hypothyroidism. 2 patients had nodular hyperplasia, 1 patient had a thyroid adenoma and 1 patient had a papillary carcinoma. They underwent thyroid surgery (hemi or total thyroidectomy) and are currently receiving thyroid hormone replacement therapy.

Conclusion: 18 out 56 (32.1%) long term survivors of HD in childhood developed a thyroid abnormality, 14 subclinical hypothyroidism and 4 thyroid nodules of which 1 thyroid cancer. The incidence of thyroid nodules may be underestimated since screening ultrasonography is not routinely performed.

The Incidence of post radiation Hypothyroidism in children treated with chemotherapy and radiotherapy: A single institution study from Kuwait E:03

Mittal, Rakesh[1]; Al Awadi, Shafika[2]; Omar, Saharz; Mahmoud, Saadeldin[3]
[1]Kuwait Cancer Control Centre, Medical Oncology, N/A, Kuwait; [2]Kuwait Cancer Control Centre, Medical Oncology, Kuwait, Kuwait; [3]Kuwait Cancer Control Centre, Nuclear Medicine, Kuwait, Kuwait

Introduction: Having achieved long term survival for pediatric Hodgkin's disease in the range of around 90%, the focus has now shifted on the prevention of therapy related long term complications. Introduction of combined modality protocols in the mid eighties was the first step in this direction. Over the last 2 decades, there has been more and more refinement of these protocols to bring down the incidence of long term toxicity to a minimum level. Even with reduced dose, post radiotherapy (RT) long term complications are still a matter of concern. RT to neck and upper chest can lead to various long term complications including thyroid dysfunction. This could be of serious consequences particularly in growing children. This study was undertaken to find out the incidence of clinical or asymptomatic hypothyroidism in patients who were treated with combined modality therapy, and received RT to neck and upper chest.

Methodology: This is a retrospective analysis of all children with Hodgkin's Lymphoma (age 15 years or less), who were treated at out institute between January 1997 and December 2005.

Results: A total of 50 children were treated. The median age was 10 years (range 3 - 15 years). Majority of children were treated on combined modality protocol, with ABVD chemotherapy and involved field radiotherapy (IFRT). RT was given to 36 patients (72%). The dose of RT ranged from 15 to 30 Grys. Thirty four children((96%) received RT to neck and upper chest. Forty three patients (86%) achieved CR / CRU status at the end of therapy. There were 20 documented cases of hypothyroidism (55.5%). The median duration to develop hypothyroidism was 24 months (range: 5 months - 57 months). The hypothyroidism was diagnosed by persistent elevation of TSH beyond six months durations. None of the patients had symptoms of hypothyroidism. All patients who developed hypothyroidism required replacement therapy by L - Thyroixin.

Conclusion: A significant number of children developed hypothyroidism after receiving RT to neck and upper chest, which requires replacement therapy for life long. All efforts must be made to find protocols, where RT to the neck and upper chest could be avoided.

Final height and growth hormone treatment after bone marrow transplant in childhood for onco-haematological diseases E:04

Ryalls, Michael[1]; Albanese, Assunta[1]; Riva, Francesca[2]
[1]Royal Marsden Foundation Trust, Paediatrics, Sutton, United Kingdom; [2]Royal Marsden Foundation Trust, Paediatrics, Sutton, United Kingdom

Objective: To examine the endocrine and growth late effects in long term survivors to final height after BMT performed in childhood in a single centre between 1978 and 1999.

Methods: Retrospective case notes analysis of 52 patients treated at a mean age of 6.9 years with varying chemotherapeutic and fractionation schedules of TBI for BMT.

Results: There was no difference between mean height SDS at diagnosis, at BMT or mean mid parental height SDS. After BMT height SDS deteriorated to a mean final height SDS of -1.41 from -0.16. Those who did worse were aged <8 years and prepubertal at BMT, had TBI and were male. 33 of the 37 tested because of growth failure were growth hormone deficient (GHD) of whom 32 were treated with GH. In those who were GHD there was a more significant reduction in height SDS in the second year after BMT prior to GH treatment than in those who were not tested and the final height SDS in GHD patients treated with GH was -1.78 compared with -0.73 in those not tested. There was a more significant reduction in final sitting height SDS (-1.9) than final leg length SDS (-0.7) overall with GHD patients faring worse (final SH SDS -2.3 compared with -1.2 and final leg length SDS -0.96 compared with -0.04). Once GH treatment commenced the height loss to final height was the same for both groups but those receiving GH had already lost more height prior to GH commencing. GH failed to prevent continued loss of sitting height but improved the height loss in leg length.
14/21 females and 9/31 males (5/6 of whom had testicular radiotherapy) required sex hormone therapy (p=0.007) with 22/44 who had TBI and only 1/8 with chemotherapy alone having primary gonadal failure. Thyroxine treatment was required in 17/52 (32.7%) which was more likely in those who had additional cranial RT.

	GH treated (+/- SD)	Non-GH treated (+/- SD)
Height SDS at BMT	-0.26 (0.84)	0.04 (0.7)
Mid Parental Height SDS	-0.13 (0.8)	0.34 (0.7)
Height SDS 1 Year Post BMT	-0.54 (0.8)	-0.18 (1.1)
Height SDS 2 Years Post BMT	-0.67 (0.8)	-0.01 (1.1)
Sitting Height SDS at GH Start	-1.03 (0.8)	-------
Final Sitting Height SDS	-2.3 (1.1)	-1.2 (0.9)
Sub Ischial Leg Length SDS at GH Start	-1.43 (0.9)	-------
Final Sub Ischial Leg Length SDS	-0.97 (1.0)	-0.04 (0.9)
Final Height SDS	-1.78 (1.1)	-0.73 (1.0)

Conclusions: GHD should be considered early in those with worse height SDS decline in the second year after BMT. Regular follow-up is needed to identify those requiring endocrine support after BMT. Reduction in sitting height SDS despite GH treatment is a major factor in loss of final height. Safety of GH needs monitoring.

Detection of growth hormone deficiency in childhood cancer survivors E:05

Ket, Jan Lucas[1]; van den Bos, C.[1]; van der Pal, HJH.[1]; Fliers, E.[2]; van Trotsenburg, AS.[3]; Heinen, RC.[1]; Caron, HN.[1]; Kremer, LCM.[1]
[1]Emma Kinderziekenhuis/AMC, Paediatric Oncology, Amsterdam, Netherlands; [2]Academic Medical Center, Endocrinology, Amsterdam, Netherlands; [3]Emma Kinderziekenhuis/AMC, Paediatric Endocrinology, Amsterdam, Netherlands

Background/ Objective: To determine the prevalence of an abnormal growth hormone (GH) reserve in a cohort of childhood cancer survivors (CCS), and the fraction of GH-deficient CCS on GH-substitution therapy. Furthermore the number of CCS where an abnormal GH-reserve could be detected by a predefined screening protocol was evaluated.

Methods: All 387 5-year CCS previously treated at the Emma Children's Hospital/ Academic Medical Center with craniofacial radiotherapy or surgery to the brain between 1966 and 1999 were retrospectively examined for GH abnormalities as reflected by serum IGF-1 level, GH-stimulation tests and GH-substitution therapy.

Results: Interval between diagnosis and last follow-up: mean 19.6 years (range 5-37). Data on GH status were available from 278 of the 387 patients (72%). In the first five years after diagnosis 76 patients underwent a GH assessment, 42 had an abnormal GH-reserve, of whom 26 received GH-substitution. After five years survival 262 of 387 patients underwent GH assessment, 202 of whom for the first time (with a mean of 16.9 years after cancer diagnosis, range 5.0 to 34.4 years). From the other 125 late survivors in follow-up 54 patients died without any GH assessment and 71 surviving patients underwent no GH assessment at all. Of all patients analyzed (n=262) 65 (25 %) had an abnormal GH-reserve, 23 of them already receiving GH-substitution. Fifty patients received GH-substitution after five years after cancer diagnosis. These CCS were detected by a screening protocol.

Conclusions: For all 387 CCS at risk the prevalence of an abnormal GH-reserve was 25%. GH-substitution therapy was given to n=76 (20%) during a median of 4.7 years (range 0.4-14.3). Fifty were detected by a screening protocol.

Endocrine late effects of pediatric cancer and its therapies - a large cohort from a single institution E:06

Modan-Moses, Dalit[1]; Pinhas-Hamiel, Orit[1]; Bielorai, Bela[2]; Waldman, Dalia[2]; Goldstein, Gal[2]; Yalon, Michal[2]; Neumann, Yoram[2]; Golan, Hana[2]; Kaplinsky, Chaim[2]; Rechavi, Gideon[2]; Toren, Amos[2]
[1]The Edmond and Lily Safra Children's Hospital, Pediatric Endocrinology, Ramat-Gan, Israel; [2]The Edmond and Lily Safra Children's Hospital, Pediatric Hematology-Oncology and BMT, Ramat-Gan, Israel

Background: Disease-free survival from childhood malignancies has improved significantly over the past few decades. Consequently, quality of life and the avoidance of long-term adverse sequelae of treatment have become major foci of interest.

Objective: To evaluate the frequency and severity of long-term endocrine sequelae of pediatric cancer and its therapies.

Methods: 505 consecutive patients of the Hemato-Oncology clinic were followed for a mean of 4.38±7.6 years. Endocrine evaluation included height and weight measurements, Tanner staging, and measurement of hormone levels.

Results: 127 (25.1%) of the patients had leukemia (ALL=78, other=49), 84 patients (16.6%) had lymphoma (Hodgkin-61, NHL-23), 145 (28.7%) patients had brain tumors, 93 (18.4%) patients had solid tumors, 15 (3%) patients had Langerhans-cell histiocytosis, and 41 (8.1%) had non-malignant hematologic diseases. 112 patients received radiotherapy either to the CNS or to the head/neck area; 85 patients had bone marrow transplantation (BMT). A total of 169 patients (33.5%) had evidence of at least one endocrinopathy. Sixty-one patients (12.1%) had thyroid malfunction: (hyperthyroidism=1, primary hypothyroidism=8, sub-clinical hypothyroidism=31, central hypothyroidism=21). Hypothroidism was related to radiation to the head/neck area, hypothalamic-pituitary lesions, or specific syndromes. 93 patients (18.4%) had evidence of gonadal dysfunction (hypergonadotrophic hypogonadism=68 patients, central hypogonadism=25 patients). 29 patients had proven GH deficiency, while 37additional patients had a decreased growth rate. As expected, GH deficiency occurred almost exclusively in patients who received cranial irradiation or had hypothlamic-pitutary lesions. Hypocortisolemia was found in 12 patients, and hyperprolcactinemia in 18.

24% of the patients were overweight (BMI>85th percentile for age). Overweight patients were significantly (p=0.002) younger than normal-weight patients.

Conclusions: Our data emphasize the importance of careful follow-up of long-term survivors of pediatric malignancey, aimed at counteracting side effects as early as possible and therefore at minimizing long-term morbidity.

Body mass index in long-term survivors of solid tumours E:07

Brouwer, C.A.J.[1]; de Vos, M.J.[1]; Vonk, J.M.[2]; Kamps, W.A.[1]; Postma, A.[1]
[1]University of Groningen and University Medical Center Groningen, Paediatric Oncology, Groningen, Netherlands; [2]University of Groningen, Epidemiology, Groningen, Netherlands

Background: Overweight is frequently diagnosed in acute lymphoblastic leukaemia (ALL) survivors, but less is known about body weight after treatment for a solid tumour. Underweight as well as overweight may be risk factors for cardiovascular disease. As treatment for solid tumours often includes potentially cardiotoxic chemotherapy and/or radiotherapy insight in the prevalence of underweight or overweight in long-term solid tumour survivors is important.

Objective: Assessment of the prevalence of under- and/or overweight after solid tumour treatment in childhood.

Patients and methods: Inclusion criteria: diagnosis of solid tumour between 1972 and 1993, age at diagnosis below 21 years, complete remission more than five years post-treatment. Height and weight for BMI were retrospectively calculated 5, 10 and 15 years post-treatment. The prevalence of overweight and underweight in the survivors was compared with reference groups using the Chi2. The relation between BMI and age at diagnosis and gender was evaluated with regression-analysis.

Results: 337 survivors (198 male) met the inclusion criteria. Cancer diagnoses were: sarcoma (n=74), blastoma (n=65), brain tumour (n=72), malignant lymphoma (n=73), Langerhans Cell Histiocytosis (n=24) and miscellaneous (n=29). The prevalence of overweight was not increased. Compared to normal, the prevalence of underweight was significantly increased in women until 10 years post-treatment, in males until 15 years post-treatment, and in survivors of blastoma, sarcoma or malignant lymphoma. There was no relation between BMI and gender or age at diagnosis.

Conclusion: In long term solid tumour survivors the prevalence of underweight was increased, whereas no increase of overweight was found.

Body mass index in long-term survivors of childhood ALL E:08

Postma, A.[1]; Wassenaar, M.[1]; Brouwer, C.A.J.[1]; Vonk, J.M.[2]; Kamps, W.A.[1]
[1]University of Groningen and University Medical Center Groningen, Paediatric Oncology, Groningen, Netherlands; [2]University of Groningen, Epidemiology, Groningen, Netherlands

Objective: To determine the prevalence of overweight in childhood acute lymphoblastic leukaemia (ALL) survivors and to assess the relation between overweight and age at diagnosis, gender or treatment with cranial irradiation (CI) and/or corticosteroids.

Patients and Methods: Body mass index (BMI) was assessed in patients in continuous complete remission of ALL who were diagnosed between 1972 and 1993 and who were treated according to the DCLSG protocols ALL 2, 3A, 5-8 or the local ALL high-risk protocol. Patients were divided into three treatment groups. Group 1 included patients who received CI and intermittent corticosteroids for two years (n = 77); group 2 included those who had intermittent corticosteroids for two years (n = 24); group 3 included patients who had two courses of corticosteroids for four weeks each (n = 47). Prevalence in overweight was compared between groups. The relation of overweight and gender or age at diagnosis was assessed by logistic regression analysis. The prevalence of overweight in the entire group was compared with the growth diagrams from the "Fourth Dutch nation-wide Survey 1997".

Results: Until five years post-diagnosis more overweight was demonstrated in group 2 survivors; afterwards we found no differences between groups. The prevalence of overweight in boys surviving more than five years after diagnosis was 17.1% at age 10 and 16.7% at age 15 (Fourth Dutch Nation-wide Survey 7.8%; Chi2 p = 0.01, and 7.7%; p = 0.07). The prevalence of overweight in girls surviving more than five years after diagnosis was 24.4% at age 10 and 28.0% at age 15 (Fourth Dutch Nation-wide Survey resp.11.8%; p = 0.03 and 9.4%; p< 0.01). Overweight correlated with age at diagnosis younger than four years but not with gender.

Conclusion: Survivors of childhood ALL are at high risk for overweight, irrespective of CI and duration of corticosteroid treatment.

Obesity in survivors of childhood malignancies E:09

Modan-Moses, Dalit[1]; Mazor-Aronovitch, Kineret[1]; Pinhas-Hamiel, Orit[1]; Bielorai, Bela[2]; Waldman, Dalia[2]; Goldstein, Gal[2]; Neumann, Yoram[2]; Golan, Hana[2]; Kaplinsky, Chaim[2]; Toren, Amos[2]
[1]The Edmond and Lily Safra Children's Hospital, Pediatric Endocrinology, Ramat-Gan, Israel; [2]The Edmond and Lily Safra Children's Hospital, Pediatric Hematology-Oncology and BMT, Ramat-Gan, Israel

Background: Increased incidence of obesity, dyslipidemia, hyperinsulinemia, and impaired glucose tolerance, as well as increased cardiovascular morbidity and mortality have been described in survivors of childhood cancer.

Objective: To evaluate the incidence of overweight and obesity in survivors of childhood cancer followed in our clinic and to identify potential risk factors.

Patients and Methods: Three hundred and forty patients (51.1% males) were prospectively evaluated in our late effects clinic. The mean age at diagnosis was 7.8 years, and the mean age at the time of evaluation was 12.4 years. 25% of our patients were treated for leukemia, 17% were treated for lymphoma, 27% had brain tumors, 21% had solid tumors, and 10% had non-malignant hematologic diseases. Eighty-six patients received radiotherapy to the CNS, and 57 patients had bone marrow transplantation (BMT).

Results: 24% of the patients were overweight (BMI>85th percentile for age), while 10.5% were obese (BMI>95th percentile). These rates are roughly twice as high as the reported rates in the pediatric population in Israel. Cranial irradiation was associated with a significantly increased incidence of obesity in survivors of brain tumors, but not in survivors of leukemia. The rates of overweight and obesity were highest in patients with brain tumors (27.6%), leukemia (29.4%), and optic glioma (38.5%). Overweight and obese patients were significantly (p=0.001) younger than normal-weight patients. This difference may reflect a difference in the distribution of diseases between the different age groups. There was no difference between males and females regarding the risk of obesity.

Conclusions: obesity is a common sequel of childhood malignancy. Since currently at least 1/1,000 young adults is a survivor of childhood malignancy, it is imperative that healthcare professionals recognize the risk of obesity and the metabolic syndrome in this population and develop strategies to enhance weight control and encourage longitudinal follow-up in order to ensure early prevention of cardiovascular disease.

Association between bone mineral density and history of fractures in childhood cancer survivors E:10

Muszynska-Roslan, Katarzyna; Konstantynowicz, Jerzy; Krawczuk-Rybak, Maryna
Medical University, Bialystok, Poland

Inability to reach peak bone mass is considered as one of causal pathways in survivors of childhood malignancy who develop osteopenia following treatment and are at risk for fractures later in their lives.

To investigate the association between bone mineral density (BMD) and history of fractures in survivors of childhood cancer, dual-energy x-ray absorptiometry was performed twice in 114 patients (70 males) who had been treated for acute lymphoblastic leukemia - ALL (43), Hodgkin disease - HD (35) and solid tumors (36). Median age at diagnosis was 8.4 years; at the consecutive examinations it was 12.8 years and 16.3 years, From 38 subjects (22 males) with a history of fractures, 32 had one whereas six had sustained repeated fractures. All fractures were results of injuries, including low-energy trauma.

Results: -For the overall group BMD Z-score for total body (-0,05 ±0,8; -0,07 ±1,0 and lumbar spine (-0,012 ±1,1; 0,03 ±0,9) were not significantly different from reference values in both examinations. -In the group reporting fractures, lower BMI, BMD total and Spine Z-score in both examinations were observed in comparison with non-fractured subjects

-The analysis in subgroups based on the diagnosis, showed the similar results, except patients treated for ALL -The BMD accretion in patients with fractures did not differ between males and females -Patients who received treatment for solid tumors had a negative association between both their BMD - total and spine (in Z-scores) and fractures ($r = -0.39$ $p<0.04$; $r = -0.4$ $p<0.01$). -The analysis in subgroups based on the time when the fracture occurred (before, during or after treatment) did not show any differences in BMDs

Conclusions: Childhood cancer survivors with history of fractures have lower BMD and represent a higher risk of osteoporosis compared with patients without fractures, (especially after treatment for solid tumors)

Normal bone mineral apparent density (BMAD) and markers of bone turnover in GH deficient (GHD) young adults of childhood acute lymphoblastic leukaemia (ALL) treated with cranial irradiation E:11

Follin, Cecilia[1]*; Link, Katarina*[2]*; Erfurth, Eva Marie*[1]
[1]Institution of clinical sciences, Department of Endocrinology, Lund, Sweden; [2]Institution of clinical sciences, Department of Endocrinology, Malmö, Sweden

Background: Adults with childhood onset GHD have reduced BMD (Bone Mineral Density). Previously, it has been shown that BMD was reduced in young adult survivors treated with cranial radiation (CRT) for childhood ALL. As ALL patients are shorter their bones will have smaller width and also be thinner, i.e. volume corrections, using BMAD is therefore preferable.

Methods: 44 former ALL patients (19-31 yr) treated with CRT (18-24 Gy) and chemotherapy with confirmed GHD (91%) or GH insufficiency, and matched controls were studied at baseline. A subgroup of 16 former ALL patients were treated with GH for 4 years and compared with the same controls as from baseline. BMAD and BMD were evaluated by DEXA and markers of bone turnover (crosslaps and osteocalcin) were analysed.

Results: Compared with controls, the former ALL patients were significantly shorter ($p < 0.001$) and had higher BMI ($p = 0.005$). Serum IGF-1 was significantly lower in the patients ($p = 0.004$). Compared to controls, BMAD was not reduced in mid radius ($p = 0.07$), femoral neck ($p > 0.3$), lumbar spine ($p = 0.19$), or total body ($p = 0.3$). A small reduction in BMD of mid radius ($p=0.06$) and total body ($p=0.05$) was recorded among the patients, but with no differences in femoral neck, lumbar spine, or in markers of bone turnover ($p=0.3$). After 4 years of GH treatment the serum IGF-1 level increased significantly ($p=0.03$), but with no difference in BMAD, at any skeletal site. Serum levels of crosslaps increased significantly ($p=0.04$) after GH treatment, but with no difference in osteocalcin levels.

Conclusions: No difference in BMAD at any skeletal sight, or in bone formation markers, was recorded in former ALL patients with GHD. After 4 years of GH treatment, BMAD was unchanged.

Assessment of bone density more than 10 years after treatment for ALL or NHL E:12

Frey, Eva; Hutter, Caroline; Kager, Leo; Helmut, Gadner
St. Anna Children's Hospital, Vienna, Austria

Background: There is rising concern about skeletal morbidity as a long-term sequela of childhood ALL and NHL. We analyzed bone mineral density (BMD) of survivors of ALL or NHL and tested whether putative risk factors such as age at diagnosis, sex or cranial irradiation had a long-term effect on bone density.

Method: We assessed the bone density of 76 patients who had been treated according to BFM protocols for either ALL (N= 67) or NHL (N= 9) in the St. Anna Children's Hospital between 1977 and 1990. DEXA measurement was undertaken in patients who were above 17.5 yrs and had been diagnosed with their condition more than ten years ago. The rationale for this late timepoint was that this group of former patients can be expected to be postpubertal and have already acquired peak bone mass. The mean age at diagnosis was 6.54 years (range: 1.3-15 years) and the mean age at time of DEXA measurement was 21.52 years (range: 17.5-33.5 years).

Results: The mean T-Score was -0.94 overall (min -3.3, max 1.13), 8 patients had a T-Score below -2. In contrast to earlier reports we did not find a significant correlation between T Scores (or Z Scores) and age at diagnosis. The mean T-Score in children aged 1-5 at time of diagnosis was -1.08 (SD 1.06), in children aged 6-10 -0.87 (SD 0.95) and those aged 11-15 at time of diagnosis -0.71 (SD 0.73). Furthermore, there was no significant difference in T scores between male and female patients (F: -0.83, SD 1.02; M: -1.02, SD 0.96). We also tested whether cranial irradiation had a negative impact on bone density and found, that there was no correlation between irradiation and bone density 10 years after diagnosis of the inital disease (+ CRX: -1.0, SD 0.89;- CRX: -0.9, SD 1.09).

Conclusions: The analysis of this patient population shows no significant correlation between bone density and age at time of diagnosis, sex, or cranial irradiation. Moreover, bone density of patients who had suffered from ALL or NHL normalizes over the years. To our knowledge, the analyzed patient cohort comprises the largest number of patients who are homogeneous regarding time after diagnosis, patient age and treatment protocol.

Occurrence of abnormal glucose metabolism i children treated with hematopoietic stem cell transplantation. Risk factor analysis E:13

Wojcik, Dorota[1]; Niedzielska, Ewa[1]; Sega-Pondel, Dorota[1]; Doroszko, Adrian[2]; Kazanowska, Bernarda[1]; Barg, Ewa[3]
[1]Department of Pediatric Hematology/Oncology and Bone Marrow Transplantation Wroclaw Medical University, Wroclaw, Poland; [2]Department of Internal Medicine, Occupational Diseases and Hipertension. Wroclaw Medical University, Wroclaw, Poland; [3]Department of Endocrinology for Children and Adolescens Wroclaw Medical University, Wroclaw, Poland

Background: Endocrine deficiencies are usual complications in children observed after hematopoietic stem cell transplantation(HSCT). This study focuses glucose metabolism in long term survivals.

Methods: In a single transplant centre we investigated: A)15 patients after auto-HSCT (7 girls, 8 boys) aged 3-20 years (average 11,62 ±5,20) for AML(5), NHL(3), NBL(3), embryonal cancer(2), medulloblastoma, Ewing/PNET; B) 27 patients after allo-HSCT (17 girls, 10 boys) aged 3-17 years (average 11,30 ±4,87). Indication for HSCT was ALL(11), AML(5), CML(6), MDS(2), NHL, JMML, RMS. Allogenic MSD-HSCT underwent(11) patients, MUD-HCT(11) and HLA-mismatched related HSCT(5). Prolonged high steroid doses (at least 28 days) received 18 children: auto-HSCT (4) and allo-HSCT (14) before, and (20) after HSCT. Analysis of IFG - Impaired Fasting Glucose (100-125 mg%),(5,6-6,9 mmol/l); IGT - Impaired Glucose Tolerance (140-199 mg%),(7,8-11 mmol/l); diabetes mellitus, homeostasis model assessment - insulin resistance (HOMA-IR) ≥ 2,5; correct HbA1c (<6,5%) and hiperinsulinemia (>10 mIU/ml), BMI (body mass index) was performed.

Results:
1)IFG was recognized in 1 pt. Glucose intolerance was found in 7 patients: in 4 treated with auto-HSCT and in 3 after allo-HSCT. All of children had correct HbA1c. 8 pts had incorrect HOMA - index.
2)In none of the children did diabetes mellitus occurred.
3)There was a statistically significant correlation between of increased HOMA-index and cytostatics: Bu (p=0,0156) and VP (p=0,0046).
4)No correlation was found between IGT and hyperinsulinism and the following parameters: sex, graft type; use of BU, MEL, VP, CY; steroid therapy before and after graft.
5)BMI was 17.80± 2.89 in the analysed group. Positive correlation was found between BMI and hyperinsulinism (p<0,035, R=0,34); BMI and hyperglycemia (p<0,0087, R=0,41); and BMI and increased HOMA-index (p<0,00112, R=0,41). No correlation was found between time from steroid therapy cessation and BMI.
Conclusions: Insulin-resistance may occur after HSCT probably due to use of some cytostatic drugs prior to- or during the preparative regimen. Further research is required to make an exact evaluation.

Hyperinsulinism; a post bone marrow transplant complication E:14

Bitar, Rana; Urquhart, Tanya; Davies, Helena
Sheffield Children's Hospital, Sheffield, United Kingdom

Background: Hyperinsulinism has been reported in post bone marrow transplant (BMT) children. This study aims to establish its prevalence and correlate it to the Body Mass Index (BMI)

Methods: This is a retrospective study. Notes for 48 patients who received BMT in a tertiary paediatric unit between year 1988 and 2005 were reviewed. These patients were followed up yearly, and results for fasting insulin (FI) and BMI were recorded at latest clinic review.

Results: 17 patients had no fasting insulin test performed on follow up. Mean age at BMT was 8.2 years (9 months - 15.5 years). 15 patients (48.3% of those who had FI performed (95% Confidence Interval (CI) = 30.1 - 67.0 %)) were diagnosed to have hyperinsulinism at 9.8 years after BMT (1.8 - 18 years). Mean body mass index for patients with normal insulin and patients with hyperinsulinism was 16.3 (95% CI = 15.8 - 18) and 17 (95% CI = 17 - 18.9) respectively. Among patients with hyperinsulinism, 10 were underweight, two normal weight, and three obese. There was no significant difference between BMI in both groups (p = 0.10).

Conclusion: Significant proportion of all followed up patients (31.25% (95%CI = 18.6 - 46.2 %)) developed hyperinsulinism, although median BMI was underweight. Long term follow up for post BMT patients and regular glucose and FI check is recommended, irrespective of BMI.

Follow-up

LATER: A nation-wide registry of 5-year survivors of childhood cancer in the Netherlands F:01

Ronckers, CM[1]; Kremer, LC[1]; van den Bos, C.[1]; Jaspers, MWM.[2]; Hazelhoff, J.[1]; Agtereek, N.[1]; Postma, A.[3]; Hakvoort-Cammel, FGAJ.[4]; Bokkerink, JPM.[5]; van Dulmen-den Broeder, E.[6]; Versluys, AB.[7]; Bresters, D.[8]; van Leeuwen, FE.[9]

[1]Emma Children's Hospital/AMC, Pediatric Oncology, Amsterdam, Netherlands; [2]Academic Medical Center, Medical Informatics, Amsterdam, Netherlands; [3]UMCG, Pediatric Oncology, Groningen, Netherlands; [4]Sophia Children's Hospital / Erasmus Medical Center, Pediatric Oncology, Rotterdam, Netherlands; [5]University Medical Center Nijmegen, Nijmegen, Netherlands; [6]Vrije Universiteit Medical Center, Pediatric Oncology, Amsterdam, Netherlands; [7]Wilhelmina Children's Hospital / UMCU, Pediatric Oncology and Hematology, Utrecht, Netherlands; [8]Leiden University Medical Center, Leiden, Netherlands; [9]Netherlands Cancer Institute, Epidemiology, Amsterdam, Netherlands

Background/objective: In view of accumulating evidence of late treatment effects in childhood cancer survivors (CCS), the need for life-long follow-up is uniformly recognized. However, the full size of the problem has not yet emerged and optimal strategies for follow-up care remain to be determined. The Dutch LATER initiative aims to set up a national registry of all 5-year CCS to support scientific research on late effects, and to enable periodic re-evaluation of evidence-based guidelines for patient care.

Methods: Representatives of five paediatric oncology centres, two centres for allogeneic haemopoietic stem cell transplantation and the DCOG, have teamed up to: (1) identify and trace the patient cohort of 5-year CCS since 1960; and (2) design a national registry for uniform data-collection. Furthermore, outpatient clinics have been started where survivors are seen by a multidisciplinary team according to uniform evidence-based guidelines.

Results: Presently, 9500 5yr survivors have been identified. The total retrospective cohort includes approximately 10-12,000 patients with anticipated annual flow-in of 300 new 5-yr survivors. Completeness of the cohort will be achieved by linkage with hospital registries, trial databases, pathology databases, and cancer registries. A computerized national registry system is under development, using a three-phase approach. Phase I has been completed and involves the registration of patient identifiers, medical history, tumour diagnosis and detailed treatment information in a computerized system, locally installed at each participating centre. Phase 2 will include essential information of physical examination, reproductive history, and health behaviour characteristics. Phase 3 involves adverse late effects detected at the 7 outpatient clinics. Issues of confidentiality will be addressed as part of this national initiative.

Conclusions: Nationwide registries of late adverse treatment effects in CCS are crucial to provide more insight into the full extent of the problem and to provide a solid basis for evidence-based care for long-term survivors.

10 year experience from the late effects clinic in Copenhagen F:02

Rechnitzer, Catherine[1]; Sehested, Astrid[2]

[1]Late effects clinic, Dept of pediatrics, Copenhagen, Denmark; [2]Rigshospitalet, Dept of pediatrics, Copenhagen, Denmark

Background: The late effects clinic at Rigshospitalet, Copenhagen, was established in collaboration between pediatric oncologists and endocrinologists in 1995. It is open to children and adults who are at least two years from end of childhood cancer treatment including chemotherapy and/or radiotherapy and with no upper age limit so far. The first year visits include the follow-up investigations relevant to each case and according to the treatment protocol, as well as follow up of growth and pubertal development. Later on, the visits focus on symptomatic or asymptomatic late effects of chemotherapy and/or radiotherapy.

Methods: The clinic is run by pediatric oncologists in close collaboration with the many relevant specialties, e.g. endocrinologists, surgeons, pediatric neurologists or neurologists, ophthalmologists, ENT, gynecologists and fertility clinic. If a late effect is detected, symptomatic or asymptomatic, the patient is referred to the relevant specialty for further investigations and treatment. In case of multiple sequelae, the late effects clinic helps coordinating the multidisciplinary collaboration and keep up checking for other possible late effects. An individual profile (e.g. cancer diagnosis, treatment received and age at treatment) is written down for each survivor. This profile dictates the follow-up program.

Results: Up to date, app. 650 survivors have been seen at the late effects clinic, Rigshospitalet. Extremely few survivors (less than 1%) drop from follow-up before completed puberty, while after puberty less than 10% express that they don't wish to visit the clinic or don't show up. The background and late effects profile of the patients seen at the clinic will be presented.

Conclusions: The late effects clinic represents a model of follow up in places with centralized treatment of childhood cancer and rather short distance to the center. While the group of patients who received whole brain irradiation has heavy and often progressing late effects, the majority of young survivors has no or minor late effects.

ACE Educational Program: "Keys" to a Healthy Future — F:03

Eshelman, Debra[1]*; Cochran, Cindy*[1]*; Tomlinson, Gail*[2]*; Bowers, Daniel*[2]
[1]Childrens Medical Center Dallas, Center for Cancer and Blood Disorders, Dallas, United States; [2]University of Texas at Southwestern, Pediatrics, Dallas, United States

Background: Research has shown that many pediatric cancer survivors are unaware of their risk for late effects or the need for follow-up care. Additionally, survivors lack accurate, detailed information about their cancer diagnosis and its treatment, despite exceptional educational efforts by professionals in long term follow-up programs. This knowledge deficit could impact their future health since survivors will "graduate" from their treating institution, potentially incapable of conveying accurate health history information to new providers, thereby limiting interventions for early detection, prevention or ameliorization of late effects. Since 1989, the **A**fter the **C**ancer **E**xperience (ACE) Program has provided survivors a cancer treatment summary detailing important aspects of treatment. Clinicians observed that many survivors who were transitioned to adult providers for risk based care lacked significant knowledge about their cancer and unique treatment-related risk factors, even though they had received a detailed document. This observation was especially evident when survivors presented for an evaluation without a parent, and in survivors treated as very young children. In support of the Institute of Medicine's recommendation to improve awareness of late effects among childhood cancer survivors and their families, a comprehensive educational program was implemented.

Methods:

1. To describe the components of an educational program highlighting an algorithm for educating survivors.
2. To describe a component of the educational package called the ACE Navigator, a computer educational program designed around the developmental milestone of learning to drive a car, featuring the concept of a GPS navigational device to lead survivors through a "map" of their treatment including road stops at the Medical Library, Blood Bank, Laboratory, Hospital Treatment Center, and Clinic.
3. To describe the costs of a comprehensive educational program

Conclusions: After program implementation, a web-based evaluation of survivor knowledge will be designed.

Development of guidelines for follow-up of childhood cancer survivors — F:04

Kremer, Leontien[1]*; Postma, Aleida*[2]*; Hakvoort-Cammel, Friederike*[3]*; Versluys, Birgitta*[4]*; Bresters, Dorien*[5]*; Bökkerink, Jos*[6]*; van Dulmen - den Broeder, Eline*[7]*; van der Pal, Helena*[8]*; Hazelhoff, Janneke*[8]*; Ronckers, Cecile*[8]*; Braam, Katja*[7]*; van der Linden, Geert*[3]*; Blaauwbroek, Ria*[2]*; Schouten - van Meeteren, Netteke*[8]*; de Ridder-Sluiter, Hanneke*[9]*; van Dam, Evelien*[7]*; Jaspers, Monique*[10]*; van Leeuwen, Flora*[11]*; van den Bos, Cor*[8]
[1]Emma Children's Hospital/ AMC, Pediatric Oncology, Amsterdam, Netherlands; [2]Beatrix Kinderkliniek, Groningen, Netherlands; [3]ErasmusMC-Sophia, Rotterdam, Netherlands; [4]Wilhelmina Kinderziekenhuis, Utrecht, Netherlands; [5]Willem-Alexander Kinder-en Jeugdcentrum, Leiden, Netherlands; [6]UMC St Radboud Nijmegen,, Nijmegen, Netherlands; [7]VU Medisch Centrum, Amsterdam, Netherlands; [8]Emma Kinderziekenhuis/AMC, Amsterdam, Netherlands; [9]SKION, Stichting Kinderoncologie Nederland, Den Haag, Netherlands; [10]Academisch Medisch Centrum, Amsterdam, Netherlands; [11]NKI Antoni van Leeuwenhoek Ziekenhuis, Amsterdam, Netherlands

Background/ Objective: Care for childhood cancer survivors (CCS) is recognised as an important health care issue. Survivors form an unique patient group for which specialised care and sharing of knowledge and experience is needed. Until now, guidelines to standardise long-term follow-up care for CCS in The Netherlands were lacking.

Methods: Members of the Dutch Childhood Oncology Group (DCOG), including 7 academic centres, initiated the development of multidisciplinary guidelines for the follow-up of CCS. Based on clinical questions regarding the magnitude of the risk of selected late effects, the efficacy of screening and possible treatments, 16 multidisciplinary teams summarised the evidence presented in existing guidelines, systematic reviews, books, and in articles published in PubMed. Ten nationwide multidisciplinary meetings were held to define the final Dutch recommendations based on the available evidence. The summary of evidence formed the basis for extensive discussions on cost and benefit.

Results: A combined evidence-based and consensus approach was used to formulate recommendations for the optimal screening, prevention, and treatment for possible late effects. Within 2 years, 16 guidelines focussed on the follow-up of CCS were developed. These guidelines will be implemented in all participating centres in 2007. In each of the 7 centres dedicated long term follow-up clinics for CCS were started. A national database (LATER) of five-years CCS in The Netherlands was developed.

Conclusion: Development of guidelines for medical follow-up of CCS proved to be feasible on the basis of existing guidelines, available literature and discussion by experts. Because of varying local circumstances, country-specific recommendations have to be developed. Uniform recommendantions may lead to standardization and improvement of patient care and will facilitate scientific evaluation of late effects.

Follow-up after childhood cancer: Evaluation of a three-level model F:05

Absolom, Kate[1]; Eiser, Christine[2]; Greenfield, Diana[3]; Glaser, Adam[4]; Horne, Beverly[5]; Waite, Heather[5]; Urquhart, Tanya[6]; Wallace, W. Hamish B.[7]; Richard, Ross[8]; Davies, Helena[6]
[1]University of Sheffield, Psychology, Sheffield, United Kingdom; [2]University of Sheffield, Psychology, Sheffield, United Kingdom; [3]University of Sheffield, Academic Unit of Clinical Oncology, Sheffield, United Kingdom; [4]St James University Hospital, Peadiatric Oncology, Leeds, United Kingdom; [5]St James University Hospital, Peadiatric Oncology, Leeds, United Kingdom; [6]University of Sheffield, Academic Unit of Child Health, Sheffield, United Kingdom; [7]Royal Hospital for Sick Children, Department of Haematology/ Oncology, Edinburgh, United Kingdom; [8]University of Sheffield, Section of Human Metabolism, Sheffield, United Kingdom

Background: Follow-up for cancer survivors is recommended to detect recurrence; monitor late-effects; record toxicity and provide care and education. We describe our experience with a three-level model developed to guide decisions about intensity and frequency of follow-up (Wallace WHB, Blacklay A, Eiser C, et al. Developing strategies for the long term follow-up of survivors of childhood cancer. BMJ 2001;323:271-274).

Methods: One hundred and ninety eight survivors (52% male) recruited over 12-months: (mean age = 23.8 years, range = 16-39 years; mean time since diagnosis = 16.2 years, range 2.4-32.7 years) reported their number of symptoms and late-effects. Information was taken from the medical records to assign each survivor to the appropriate levels by six clinic staff independently.

Results: The survivors were assigned to level 1 (n = 8), level 2 (n = 97) and level 3 (n = 93). There were seven cases of disagreement. Level 3 survivors self-reported more symptoms and late-effects than level 2 survivors.

Conclusions: Coding was relatively simple for experienced clinic staff, although there were some disagreements for the survivors of ALL. The relationship between assigned level and self-reported symptoms and late-effects provides some evidence for validity of the model. We conclude that it is important to maintain flexibility to allow movement between levels for individual patients and that the default should always be to the higher level.

The needs of general practitioners in the follow-up of adult survivors of childhood cancer F:06

Blaauwbroek, Ria[1]; Bouma, Martijn[1]; Zwart, Nienke[1]; Postma, Aleida[1]; Kamps, Willem[1]; Meyboom-de Jong, Betty[2]
[1]University Medical Center Groningen, Paediatric Oncology, Groningen, Netherlands; [2]University Medical Center Groningen, Department of general practise, Groningen, Netherlands

Background: Long-term follow-up of childhood cancer survivors is mainly organised by paediatric oncologists and until now general practitioners (GPs) are rarely involved. To ensure life-long follow-up for all survivors, a combined effort of paediatric oncologists and general practitioners might be a solution.

We investigated the willingness of GPs, who had followed a postgraduate course on late effects of cancer treatment, to participate in a shared care model for follow-up of adult childhood cancer survivors as well as what their requirements would be in case of participation.

Methods: 358 GPs from the Northern Netherlands participated in a postgraduate course on late effects in paediatric cancer survivors. At completion of the course they were asked to fill in a 10-item questionnaire with questions on motivation to participate, requirements in case of participation and objections to participate.

Results: The response rate was 62%. Ninety six percent of the responders were ready to participate in a shared care model for follow-up and 63% felt that it was their responsibility to be in charge for childhood cancer survivors. The main requirements for participation were the availability of guidelines 63%, sufficient information about the patient's medical history (36%) and short lines for communication (45%). Fees were important for only 4% of the GPs. The main objections to participate were work burden (16%), lack of knowledge (14%) and poor communication (13%) between GP's and paediatric oncologists. Important issues for communication were easy records for exchange of information and the possibility of returning the results of the screening electronically.

Conclusion: GPs are ready to participate in the long-term follow-up of adult childhood cancer survivors if adequate guidelines and medical information is provided and communication lines are clear.

A personalized approach to the long term follow up of survivors after cancer: help from a computer system F:07

Fioredda, Francesca[1]*; Donatella, Fraschini*[2]*; Guia, Hanau*[3]*; Maura, Faraci*[3]*; Francesca, Grisolia*[3]*; Silvia, Caruso*[3]*; Marta, Pilllon*[4]*; Benedetti, G.*[5]*;Prandoni, A.*[5]*; Camnasio, R.*[5]*; Momcilo, Jankovic*[2]*; Riccardo, Haupt*[3]
[1]Giannina Gaslini Children's Hospital, Haematology-Oncology, Genova, Italy; [2]University of Milano-Bicocca, Monza, Italy; [3]Gaslini Children Hospital, , Genova, Italy; [4]University of Padua, Padua, Italy; [5]Lombard Interuniversity Consortium for automatic Data Processing, Milan, Italy

Background: monitoring people who have completed chemotherapy requires long term, standardized programs in order to identify possible secondary effects related either to primary cancer or to its treatment.

Aim of the study: to tailor the patient's follow up programs on the basis of their primary tumor and treatment with the help of a computer system.

Methods: we designed specific follow-up programs for each tumor type (oncologic follow up) or system (organ follow-up) on the basis of the available literature and on our personal experience.

Patient's data were input into the computer system at the first off-therapy visit and included demographics, anamnestic data, cancer type and stage, cumulative doses of chemotherapy and radiotherapy, complications that occurred during treatment). On the basis of the information that was input individual oncologic and organ follow up programs (are individually) were suggested by the computer system. The physician had the option to either accept or reject the tailored programs. If any unexpected results were observed during follow up, rules were defined to propose alternative timing or type of programs.

The system allows remote access via a robust secure protocol (https) according to the international ethical rules and to the severe Italian law regarding password, secure programming and privacy.

Results and conclusion: The Person Prevention Oriented Approach (PPOA) system is available as an internet browser. Security and privacy controls are strongly implemented. A total of 44 oncologic follow-up programs are now in use for patients who had been affected by leukemia , Hodgkin's and non Hodgkin's lymphomas, neuroblastoma, soft tissue and bone sarcoma The organ follow up programs allow us to monitor the heart , thyroid, lungs, liver, kidney, eye , central nervous system and immunological status. At present,the system is being used by three Italian centers and has proven its usefulness in providing homogeneous follow-up. It can be shared by multiple institutions in order to collect data even on rare outcomes.

Prospective follow-up after childhood cancer within the Late Effects Surveillance System F:08

Langer, Thorsten; Paulides, Marios; Beck, Jorn-Dirk
Late Effects Surveillance System, University Hospital for Children and Adolescents, Erlangen, Germany

Background: With better survival after childhood cancer, late effects of treatment reach socioeconomic importance. Large national prospective studies are rare in this field, especially after tumours requiring more aggressive treatment, such as sarcomas.

Methods: The Late Effects Surveillance System is a prospective longitudinal follow-up network that registers late effects of childhood cancer treatment in Germany, Austria and Switzerland since 1998. In the pilot phase, the focus was on patients after Ewing's-, soft tissue and osteosarcoma treatment within the therapy trials EICESS-92/EURO-E.W.I.N.G.-99, CWS-96/CWS-2002P and COSS-96, respectively, in cooperation with 246 hospitals and 60 general practitioners who conduct standardised follow-up locally in accordance with the LESS guidelines.

Results: Cumulative incidences for major late effects have been calculated, reaching 4.6% (27/593) of ifosfamide-treated patients for tubulopathy. A higher cumulative ifosfamide dose and age < 4 years were identified as risk factors. Anthracycline-induced cardiomyopathy was diagnosed in 3.7% (30/815) of doxorubicin-treated patients. An age <21 years was identified as a risk factor. Thyroid abnormalities were diagnosed in 15% (51/340) of examined patients and appeared even in 11% (32/289) of patients without irradiation to the head and/or neck. Irration to the head and/or neck was a risk factor, but it seems that chemotherapy also is thyreotoxic.There were no cases of HIV or hepatitis B or C infection under antineoplastic treatment (0/860).

Conclusions: Standardised risk-adapted prospective follow-up as conducted within the Late Effects Surveillance System is a successful and cost-effective strategy for the follow-up of childhood cancer survivors in a vertical network and a poweful tool for initiating secondary and tertiary preventive measures in patients at risk for major sequelae of cancer treatment.

Gonads and Fertility

Inhibin B as a marker of spermatogenesis in young male survivors of solid tumors G:01

Krawczuk-Rybak, Maryna[1]; Solarz, Elzbieta[2]; Wojtkowska, Malgorzata[2]; Wolczynski, Slawomir[2]
[1]Medical University, Pediatric Oncology, Bialystok, Poland; [2]Medical University, Bialystok, Poland

Objective: we analyzed the values of serum inhibin B in 24 boys and young men treated for different solid tumors (nephroblastoma-10, neuroblastoma -5, germinal tumors-3, RMS-4, PNET-2) using the different chemotherapy regiments; including alkylating agents (n=12), radiotherapy for abdomen (n=6).

Patients and methods: the values of inhibin B, FSH, LH, testosterone were evaluated in fifteen adolescents (seven of them were treated before puberty) and nine boys - treated and examined before puberty. Three patients diagnosed for testicular tumors, after unilateral orchiectomy, were analyzed separately. The control group was performed from 19 prepubertal and 15 pubertal boys.

Results: 1/ In 15 patients in puberty, we found lower inhibin B values (116.1ng/ml±64.35) than in control (196.53ng/ml±66.8), p=0.002 and tendency to higher FSH (8.52 IU/ml±8.8 vs 3.29 IU/ml±1.46) without the differences in LH and testosterone values. 2/ The patients (n=9) treated and examined before puberty, without radiotherapy and alkylating agents, presented normal values of all analyzed parameters. 3/ The patients treated before puberty (and examined during puberty), with chemo-and radiotherapy for abdomen, had lower inhibin B (97.08 ng/ml±44.31) than in control (p=0.006). There were no differences in FSH, LH and testosterone values. 4/ In the group treated during puberty, with the use of alkyling agents but without radiotherapy, inhibin B was slightly lowered (138.37 ng/ml±91.37, p=0.12). 5/ In all patients treated with radiotherapy for abdomen the mean values of inhibin B were lower (105.06 ng/ml±44.2) than in the group without radiotherapy (123.46ng/ml±76.6, p=009). 6/ Three patients after unilateral orchiectomy presented normal values of inhibin B and elevated values of FSH and LH. One of them achieved paternity three years after the treatment.

Conclusion:1.Radiotherapy for abdomen leads to testicular damage, independently on the time of treatment. 2. Inhibin B is sensitive marker of Sertoli cells function. 3. Leydig cell function rest essentially unaffected by treatment.

Testicular function in young men treated in childhood for Hodgkin lymphoma (HL) G:02

Krawczuk-Rybak, Maryna[1]; Solarz, Elzbieta[1]; Wojtkowska, Malgorzata[2]; Gadomski, Artur[3]; Matysiak, Michal[3]; Wolczynski, Slawomir[2]
[1]Medical University, Pediatric Oncology, Bialystok, Poland; [2]Medical University, Bialystok, Poland; [3]Medical University, Warsaw, Poland

Objective: we investigated the influence of chemo- and radiotherapy for HL during childhood on long-term gonadal function in young men depended on the age of treatment, time after cessation and clinical staging.

Patients and methods: serum concentration of inhibin B (Elisa method), FSH, LH and testosterone (immunoenzymatic methods) were determined in 21 adult patients (mean age 20.03±2.7) treated 5.91±3.7 years before for HL. Eight of them were treated before puberty (mean age 8.39±2.9), thirteen - during puberty (16.02±1.1). Control group was formed from 15 young healthy men.

Results: 1/ In all examined group we found lower values of inhibin B (50.11 ng/ml±39.5) than in control (196.53 ng/ml±66.8), p=0.0001, higher values of FSH (13.8 IU/ml±11.6 vs. 3.3 IU/ml±1.5), higher LH (4.67 IU/ml±3.65 vs.3.6 IU/ml±1.5) and normal testosterone values. 2/ We did not observe any differences in analysed parameters between the patients treated before and during puberty. 3/ Inhibin B was lower, whereas FSH and LH was higher in patients in III and IV clinical stage (treated with radiotherapy for abdomen and 3-4 protocols B-DOPA and 3-4 protocols MVPP) than in group in I and II stage (without infradiaphragmatic radiotherapy, 1-2 protocols MVPP and 2- B-DOPA). 4/ Lower inhibin B <-2SD was observed in 15/24, higher FSH - in 8/24 and higher LH -in 5/24.

Conclusion: the treatment for HL in high clinical stage causes severe, long-term testicular damage, especially - spermatogenesis, no mater the age of patients at the time of treatment.

Gonadal Function and Fertility in Male Survivors Treated for Hodgkin's disease in Iran G:03

Arjmandi Rafsanjani, Khadijeh; Vossough, Parvaneh; Faranoush, Mohammad; HedayaHedayati asl, Amir Abbas
Iran University of Medical Sciences, Tehran, Islamic Republic of Iran

Background: Overall long term disease free survival in Hodgkin's is more than 80%.Treatment for Hodgkin's disease may carry a considerable risk of sterility in male survivors. The aim of this study was to investigate the effect of chemotherapy on gonadal function of young men cured of childhood Hodgkin's disease.

Methods: Adult young males surviving of Hodgkin's disease who were 17 years old and at least 2 years after off therapy were studied in Ali Asghar Children's Hospital. Clinical evaluation for secondary sexual characteristics, semen analysis, FSH, LH, testosterone were studied in 33 survivors of Hodgkin's disease.

Results: The age at diagnosis was 5-15 years median 9 years, age at study 17-29 years median 19.The median duration off therapy was 7 years (2-20 years).All 33 patients received chemotherapy as follows: 32 patients received MOPP / ABVD 6-8 cycles,5 of whom after relapses received other protocols. One received only MOPP. 27 (81.8%) had azoospermia,2 severe oligospermia,3 oligospermia and one had normal sperm count (58000,000).All patients had normal secondary sexual characteristics. FSH, and LH in 6/33 patients were above normal. Testosterone in 3/33 was below normal.

Conclusion: The study shows that a prepubertal status does not protect the gonads from the harmful effect of chemotherapy.

Estrogen receptor β AluI single nucleotide polymorphism and the risk of azoospermia in childhood cancer survivors G:04

Giwercman, Yvonne L.[1]; Romerius, Patrik[2]; Giwercman, Aleksander[3]; Moëll, Christian[2]; Relander, Thomas[4]; Cavallin-Ståhl, Eva[4]; Wiebe, Thomas[2]
[1]Lund University, Clinical Sciences, Malmö, Sweden; [2]Lund University Hospital, Dept. of Pediatrics, Lund, Sweden; [3]Malmö University Hospital, Reproductive Medical Centre, Malmö, Sweden; [4]Lund University Hospital, Dept. of Oncology, Lund, Sweden

Background: The use of powerful therapeutic tools in childhood cancer treatment has increased the survival rates, to date exceeding 70%, and therefore, the life-quality of the survivors plays an important role. Individuals who have received identical treatment may differ in terms of semen quality, some having normal sperm counts whereas approximately 20% develop azoospermia. Sex steroids are of crucial importance for spermatogenesis and polymorphisms in genes encoding for steroids might influence the post-treatement sperm production. The androgen receptor gene (AR) CAG repeat length as well as the polymorphisms in the 5α-reductase type II (SRD5A2) gene have been shown to play a role for sperm production. Interestingly, estrogens also seem to be of importance for testicular function. The estrogen receptor β (ERβ) is expressed in Sertoli as well as in germ cells of human males. Our objective was to investigate whether polymorphisms in the AR, SRD5A2 and ERβ genes play a role for the risk of azoospermia and for the level of sperm counts in men treated for childhood cancer.

Methods: In 28 men, 18-45 years of age and diagnosed with cancer in childhood, a semen analysis and genotyping of the AR, SRD5A2 and ERβ genes in leucocyte DNA was performed. In the AR gene the polymorphic CAG and GGN repeats were analysed, whereas regions of interest were the single nucleotide polymorphism V89L in the SRD5A2 gene and the AluI and RsaI in the ERβ gene.

Results: Azoospermic men tended to have longer CAG repeats (median [range] 23[18-29] vs. 21[6-28]; p=0.17) and all men (100%) with azoospermia, presented with the ERβ AluI GA genotype, whereas the frequency was 57% in childhood cancer survivors with sperms in the ejaculate (p=0.003). The prevalence in normal population is 45%.

Conclusions: This is, to our knowledge, the first report showing a predictive value of a certain genotype for the risk of azoospermia in men treated for childhood cancer. This subgroup of childhood cancer patients could be subjects for cryopreservation of testicular tissue before treatment if our finding is confirmed in a larger study.

Gonadal function in 261 adult male survivors of childhood cancer G:05

van Casteren, Niels[1]; van der Linden, G.H.M.[2]; Hakvoort-Cammel, F.G.A.J.[2]; Dohle, G.R.[3]; Hahlen, K.[2]; van den Heuvel-Eibrink, M.M.[2]
[1]Erasmus MC, Urology/Andrology, Rotterdam, Netherlands; [2]Erasmus MC, Department of Pediatric Oncology/Hematology, Rotterdam, Netherlands; [3]Erasmus MC, Urology, Rotterdam, Netherlands

Introduction: Cytotoxic chemotherapy and radiotherapy can cause severe gonadal damage depending upon the type and cumulative dosages of drugs administered in pediatric cancer. Inhibin B has been suggested to be the strongest serum marker for spermatogenesis, but it's role as a possible marker for testicular function in large cohorts of men surviving childhood is not clear.

Material and methods: 261 male long-term survivors (median 18 years after completion of therapy), aged more than 18 years (median age 24 years) and treated for childhood cancer in our institute were studied. We assessed testicular size, patient characteristics, disease and treatment modalities, endocrinological parameters (LH, FSH, Inhibin B, SHBG and testosterone) and semen analysis. Inhibin B values are considered normal between 150 and 400 ng/l. Results of sperm analysis and endocrinological evaluation were compared with data from normospermic men (n=74, median age 33) visiting our Andrology clinic.

Results: The median value of Inhibin B in the patient group was 126 ng/l versus 176,5 ng/l in the control group (P<0,01). 151 (66%) of the survivors had Inhibin B levels below 150 ng/l compared to 19 (25%) of the normospermic controls (p<0,01). Inhibin B was strongly correlated with FSH and sperm concentration in the controls as well as in patient (p<0,01). Patients with Hodgkin Lymphoma and Sarcoma had the lowest levels of Inhibin B, respectively, 54 ng/l and 55ng/l compared to the other patient groups (p<0,05). Treatment regimes containing Procarbazine or Cyclophosphamide were significantly correlated with low Inhibin B levels compared to regimens not containing these agents (p<0,01). Age at time of diagnosis in these treatment groups did not correlate with post treatment Inhibin B levels.

Conclusion: Inhibin B can be used to asses post-treatment gonadal function. Inhibin B levels and gonadal function can be severely impaired after gonadotoxic therapy given during childhood especially after treatment for Hodgkin's lymphoma and sarcoma or regimens containing Procarbazine or Cyclophosphamide. Age at time of diagnosis is no predictor for outcome of post treatment male gonadal function.

Reproductive function, ovarian reserve and risk of premature menopause in female cancer survivors: results of a pilot study G:06

van den Berg, M.H.[1]; van Dulmen-den Broeder, E.[1]; Schats, R.[2]; Braam, K.I.[1]; van Dam, E.W.C.M.[3]; Kaspers, G.J.L.[1]; van Leeuwen, F.E.[4]; Lambalk, C.B.[2]
[1]VU University Medical Center, Dept of Paediatrics, Amsterdam, Netherlands; [2]VU University Medical Center, Dept of Obstetrics and Gynaecology, Amsterdam, Netherlands; [3]VU University Medical Center, Dept of Internal Medicine, Amsterdam, Netherlands; [4]Netherlands Cancer Institute, Dept of Epidemiology, Amsterdam, Netherlands

Objective: Aim of the pilot study was to assess the feasibility of a nationwide study on reproductive function, ovarian reserve and risk of premature menopause in female childhood cancer survivors (CCSs). Response rates of both CCSs and (sibling) controls to the different parts of the study were evaluated. Furthermore, preliminary results regarding markers of premature menopause are presented.

Methods: Seventy-three females (aged 18-45 yrs) treated for childhood cancer at the VU university medical center were approached to participate in the study, which consisted of a questionnaire, the provision of a blood sample (FSH, LH, estradiol, anti-Müllerian hormone (AMH), and inhibin A and B) and an antral follicle count (AFC) by transvaginal ultrasound. Blood sampling and AFCs were performed on cycle day 3-5 of participants with a natural cycle and on day 7 of the pill-free week for participants on oral contraceptives. Controls were contacted through participating CCSs.

Results: Of the 73 CCSs receiving the questionnaire, 62 (85%) returned it, 50 (68%) were willing to provide a blood sample and 42 (64%) agreed to a transvaginal ultrasound. Of the 34 controls who were contacted 22 completed the questionnaire, of whom 82% agreed to the provision of a blood sample and 64% to a transvaginal ultrasound. Mean age of survivors and controls was 26.3 (SD 7.3) and 27.5 (SD 6.4) years, respectively (NS). Preliminary results show no significant differences between CCSs and controls regarding endocrine and AFC values (see Table). Furthermore, a high correlation between age at diagnosis and AFC (r=-0.53; p=0.01) and between AMH and AFC (r=0.76; p<0.001) was found within the group of CCSs.

Table. Median (IQR) endocrine and AFC values of CCSs (n=31) and controls (n=12)

	FSH	LH	Estradiol	AMH	Inh. A	Inh. B	AFC
CCS	6.0 (1.9)	3.6 (3.5)	89.0 (50.0)	9.5 (10.7)	1.7 (1.6)	64.6 (40.3)	15.0 (15.0)
Controls	7.3 (2.3)	3.4 (3.4)	104.0 (63.3)	10.1 (18.6)	1.3 (2.1)	70.6 (61.5)	20.5 (15.0)
P-value	0.42	0.67	0.34	0.91	0.95	0.86	0.27

Conclusions: Given the high response rates of the pilot study, a nationwide study appears feasible in terms of patient numbers. However, a more aggressive approach towards recruitment of controls is required. Preliminary data suggest a reduced AFC in CCSs and a possible role for AMH in the determination and long-term follow-up of ovarian reserve among CCSs.

Follicular rescue in young girls treated with bone marrow transplantation G:07

Borgström, Birgit[1]; Hreinsson, Julius[2]; Keros, Victoria[2]; Rasmussen, Carsten[2]; Winiarski, Jacek[3]; Gustafsson, Britt[3]; Hovatta, Outi[2]; Fridström, Margareta[2]
[1]Inst for Clinical Science, Karolinska Institutet, Children´s Hospital, Stockholm, Sweden; [2]Karolinska Institutet, Dept of Obstetrics and Gynecology, Stockholm, Sweden; [3]Karolinska Institutet, Children´s Hospital, Stockholm, Sweden

Background: Bone marrow transplantation (BMT) has over the last 30 years saved the life of many patients suffering from lethal hematological disease. Cytostatic drugs and /or total body irradiation in different combinations and doses has been used as conditioning. Among the inevitable long term side effects infertility is frequent.

Methods: A biopsy from the ovary, taken laparascopically, was cryopreserved for the future. A small part of the biopsy was prepared for histology to get information about the condition and number of follicles. This method has been used in 17 patients from two groups. One group, 8 girls, had signs of normal ovarian function several years after BMT. Most of these girls had been treated for a non-malignant disease. The biopsy was taken at the age 13.7-17.6 years. The second group, 9 girls had the biopsy taken shortly before BMT, at the age 9.2-22 years. Most of these girls suffered from leukemia.

Results: The 8 girls post BMT had a reduced number of follicles in the biopsy. In 2 girls there were no visible follicles and in 6 girls 21-208 follicles/mm3. The 9 girls before BMT all had follicles. In 5 girls the number was normal for age, 350-1519 follicles/mm3 and in 4 there was a reduction, 18-182.

Conclusions: Cryopreservation of follicles for the future offers the possibility for fertility treatment in adult life to girls with a high risk for infertility and premature menopause after BMT. The adolescent girls with mature follicles in the biopsy have a reasonable chance for successful outcome later in life, a few successful cases have been published. In the youngest girls, with only immature primordial follicles, new treatment methods need to be developed. Also, the risk for infiltration of malignant cells in the ovary needs to be considered.

Infertility in Ewing's sarcoma female patients G:08

Longhi, Alessandra[1]; Ferrari, Stefano[2]; Ferrari, Cristina[2]; Bacci, Gaetano[2]; Mercuri, Mario[2]
[1]Istituto Ortopedico Rizzoli, Chemotherapy, Bologna, Italy; [2]Istituto Ortopedico Rizzoli, Bologna, Italy

Background: Infertility in females after chemotherapy in osteosarcoma patients have been investigated in our previous study and the incidence of permanent amenorrhea induced by treatment was 2.1% (2/92) Infertility in Ewing's sarcoma female patients is the objective of this study

Patients: 112 long term survivors female treated according to 5 different protocols from 1979 to 2005 for localized Ewing's sarcoma. Treatment was standard chemotherapy with or without Radiotherapy. In the last protocol, ISG-SSG III, poor responders received also High Dose Chemotherapy (HDCT) with PBSCR.

Results: 89 pts were interviewed, 23 couldn't be reached 29 were prepuberal at the time of chemotherapy and 60 were postpuberal Median age of all group was 15 yrs (range 1-40). Median follow up was 13 yrs (1-27). Prepuberal pts reached menarche at a median age of 13 (range 12,5 -15). 17/89 (19%) pts had permanent amenorrhea related to the treatment: 3 were prepuberal at the time of treatment and received HDCT,2 of them received also RT to pelvis. 14 patients out of 60 postpuberal had permanent amenorrhea: 6 pts received RT to the pelvis, 4 pts received HDCT (two of these had also pelvic RT) and 4 pts received no RT nor HDCT. The age of these latter pts was 28,30,35,40. 20 women delivered 32 normal babies, all except one were full term pregnancy, 1 pt had a voluntary abortion and 2 pts had spontaneous abortions both at the 7 month of gestation: 1 of this premature fetus died of congenital esofageal atresia. Besides 2 patients had 3 Second Malignant Neoplasms: a thyroid cancer and the other pts had a uterus sarcoma and a breast cancer.

Conclusions: The incidence of early menopause is higher in Ewing's sarcoma female patients (19%)compared to osteosarcoma patients (2.1%) HDCT and RT are confirmed to be the major cause of permanent amenorrhea both in prepuberal and postpuberal patients

Stillbirth and abortion following radiotherapy for childhood cancer - A population-based cohort study G:09

Winther, Jeanette Falck[1]; Boice, Jr., John D.[2]; Svendsen, Anne Louise[1]; Frederiksen, Kirsten[1]; Stovall, Marilyn[3]; Olsen, Jørgen H.[1]
[1]Danish Cancer Society, Institute of Cancer Epidemiology, Copenhagen, Denmark; [2]International Epidemiology Institute, Rockville, MD, United States; [3]The University of Texas M.D. Anderson Cancer Center, Department of Radiation Physics, Houston, United States

Background/Objective: Radiation induces germ-cell mutations in experimental animals. We assessed the risk of abortion and stillbirth in female survivors of childhood cancer in Denmark treated with radiation.

Methods: We identified 1688 female childhood cancer survivors in the national Danish Cancer Registry and 2737 sisters and 16 700 women randomly selected from the Central Population Register. Radiation doses to the ovary, uterus and pituitary gland were estimated. Pregnancy outcomes were determined from nationwide health registries, and the proportions of pregnancies among survivors that resulted in a live birth, stillbirth or abortion were compared with the equivalent proportions among the sisters and the population comparison group as proportion ratios (PR), with sisters as referent.

Results: The distributions of live births, abortions and stillbirths among 1479 pregnancies of survivors were remarkably similar to that of the comparison women. Survivors, however, had a 23% excess risk for spontaneous abortion, primarily due to a threefold increase in risk among survivors of Wilms tumour (PR, 3.0; 95% CI, 1.6-5.5) and an excess risk among survivors in general exposed to high-dose radiation to the ovaries and uterus (PR, 2.8; 95% CI 1.7-4.7). The prevalence of other types of abortions among survivors including second-trimester pregnancy terminations for foetal abnormality was similar to those among the comparison groups.

Conclusions: An increased risk for spontaneous abortion among survivors who had received abdominal irradiation was likely the result of high-dose radiation uterine damage, a non-mutagenic effect. Among those who were able to become pregnant, there was little evidence that radiation-induced germ-cell mutations led to stillbirths or abortions. These reassuring results are of importance to the cancer survivors and their families, and genetic counsellors.

Are young female cancer patients screened for ovarian dysfunction? An audit of clinical practice G:10

Greenfield, Diana[1]; Ross, Richard[2]; Absolom, Kate[3]; Eiser, Christine[3]; Coleman, Robert[4]; Hancock, Barry[4]; Snowden, John[5]; Ledger, William[6]; Davies, Helena[7]
[1]University of Sheffield, Academic Unit of Clinical Oncology, Sheffield, United Kingdom; [2]University of Sheffield, Endocrine & Reproduction, Sheffield, United Kingdom; [3]University of Sheffield, Psychology, Sheffield, United Kingdom; [4]University of Sheffield, Academic Unit of Clinical Oncology, Sheffield, United Kingdom; [5]Sheffield Teaching Hospitals NHS Trust, Haematology, Sheffield, United Kingdom; [6]University of Sheffield, Academic Unit of Reproductive and Developmental Me, Sheffield, United Kingdom; [7]University of Sheffield, Academic Unit of Child Health, Sheffield, United Kingdom

Background/Objective: Cancer therapy induced ovarian failure in women may lead to a permanent or temporary menopause resulting in menopausal symptoms and risk of osteoporosis. Screening for ovarian dysfunction is straightforward and once identified, can be managed with oestrogen replacement. The aim of this study was to audit clinical case notes of young female cancer patients who had received gonadotoxic therapy for evidence of gonadal function screening and subsequent management during active treatment and follow-up.

Patients and Methods: We audited 288 hospital clinical case notes of young women ages 38.5 years (17.9 to 50.8y, SD 8.1) with haematological cancers (n= 184); carcinomas (n=61); primitive and other cancers (n=43). Women with breast cancer were not included since oestrogen replacement therapy is currently not advised.

Results: The mean age of women at cancer diagnosis was 26.9 y (0.5 to 47y, SD 10.1) and the mean time since diagnosis was 11.1y (2.2 to 34.8y, SD 7.23). 95.1% had received chemotherapy, 68.1% radiotherapy and 63.5% had both. Case note documentation indicated that 43.4% were screened for ovarian function (gonadatrophins and/or oestradiol) at least once during or after cancer treatment. This monitoring was initiated by the: oncologist (62%); haematologist (10%); endocrinologist (14%); gynaecologist (6%); GP (3%); other (5%). Case note documentation indicated that 31.6% had or were taking hormone replacement therapy and a further 15.9% contraceptive medication.

Discussion: Evidence suggests that despite receiving gonadotoxic cancer treatment, less than half these young women were screened for ovarian failure. We advocate routine gonadal function screening for all young women receiving gonadotoxic cancer treatment.

Amh and inhibin B are valuable new markers for gonadal damage after the treatment of pediatric hodgkins lymphoma(HL) without radiotherapy G:11

van den Heuvel-Eibrink, Marry M.[1]; van Beek, Robert[1]; Weber, Rob[2]; Laven, Joop[3]; de Jong, Frank[4]; Hakvoort-Cammel, Friederike G.A.J.[1]; van der Bos, Cor[5]; Pieters, Rob[1]; de Muinck Keizer-Schrama, Sabine M.P.F.[6]
[1]Erasmus MC - Sophia Childrens Hospital, Pediatric Oncology, Rotterdam, Netherlands; [2]Erasmus MC, Andrology, Rotterdam, Netherlands; [3]Erasmus MC, Gynaecology and Obstetrics, Rotterdam, Netherlands; [4]Erasmus MC, Internal Medicine, Rotterdam, Netherlands; [5]AMC - Emma Childrens Hospital, Pediatric Oncology, Amsterdam, Netherlands; [6]Erasmus MC - Sophia Childrens Hospital, Pediatric Endocrinology, Rotterdam, Netherlands

An important long-term effect of chemotherapy is gonadal dysfunction. Aim of this study is to evaluate the gonadal long-term effects of the treatment for childhood HL with combination chemotherapy (ABVD or EBVD with/without MOPP) and to identify markers for long-term gonadal function. Eighty-six pediatric HL patients treated between 1974-1998 were included in a protocol in which RT was avoided because of the risk of serious long term side effects. All patients were in complete remission. Median follow-up was 15.5 yr. (range 5.6-30.2 yr.), median age at follow-up was 27.0 yr. (range 17.7-42.6 yr.). Follicle stimulating hormone (FSH), luteinizing hormone (LH) and inhibin B were determined in all patients.

Additionally, in men testosterone and sex hormone binding globuline (SHBG) and in women 17 β-estradiol and anti-Müllerian hormone (AMH) were determined. In 20 men semen analyses were performed. In men treated with MOPP, median FSH (16.6 U/l vs. 2.4 U/l; p<0.001) and LH (5.7 U/l vs. 2.5 U/l; p<0.001) were increased and Inhibin B (17.5 ng/l vs. 143 ng/l; p<0.001) and semen concentration (1.1*106/ml vs.49.5*106/ml; p<0.05) were decreased as compared with patients treated without MOPP. Inhibin B was strongly correlated with semen concentration (rs=0.83; p<0.001). FSH (rs=0.68; p<0.001) and inhibin B (rs=-0.68; p<0.001) were correlated with cumulative dose procarbazine. In women no significant differences in LH, FSH, inhibin B or estradiol between patients treated with or without MOPP were found, but AMH was significantly lower in patients treated with MOPP as compared to patients treated without MOPP (0.39 µg/l vs. 1.40 µg/l; p<0.01). AMH levels were correlated with cumulative dose procarbazine (rs=-0.54; p<0.01). This study shows that AMH and inhibin B are valuable new serum markers for gonadal damage after chemotherapy for pediatric HL. In men inhibin B is strongly correlated with semen concentration, whereas in women AMH detects early gonadal damage even in cases with normal LH/FSH levels.

Xenografting as an approach for fertility preservation and exploration of cancer cell contamination of testicular grafts G:12

Jahnukainen, Kirsi[1]; Hou, Mi[1]; Ehmcke, Jens[2]; Schlatt, Stefan[2]; Söder, Olle[1]
[1]Karolinska Institutet, Department of Woman and Child Health, Stockholm, Sweden; [2]University of Pittsburgh, Pittsburgh, United States

Background/ Objective: Xeno-grafting of fresh immature primate testicular tissue into nude mice leads to establishment of spermatogenesis. It therefore presents a beneficial tool for prepubertal cancer patients generating fertility options without risk of a cancer relapse. However, it is unknown whether cryopreservation maintains spermatogonial potential in primate testicular tissue or if cancer cells in the testicular graft affect the success rate of testicular tissue transplantation.

Methods: Male nude mice received eight subcutaneous grafts of either fresh juvenile rhesus monkey testicular tissue or cryopreserved tissue (24h of cryopreservation time; two concentrations of DMSO [1.4M and 0.7M], using slow uncontrolled cooling (0.5°C/min). In another experiment, Rat T-cell leukemia was employed as the source of leukemic testicular grafts which were transplanted subcutaneously into nude mice. Graft number, weight and histology were examined 5 months later or when signs of leukaemia developed.

Results: Control primate grafts showed pubertal induction of spermatogenesis to the level of B-spermatogonia and spermatocytes. Spermatogenic stem cells in juvenile testicular tissue survived cryopreservation and were able to initiate spermatogenesis when DMSO 1.4M was used as cryopreservative agent. Only few grafts with SCO tubules survived cryopreservation with DMSO 0.7M. In the second set of experiments, all mice carrying either fresh or cryopreserved testicular tissue from leukemic donors, developed generalized leukemia and/or local tumors. Rat spermatogenesis in the retrieved grafts was destroyed and leukemic infiltration was detected.

Conclusions: Our observations suggest that cryopreservation of immature primate testes is a feasible approach to maintain spermatogonial stem cells and may serve as a promising tool for fertility preservation of prepubertal boys. Grafting testicular tissue contaminated with leukemic cells results in tumor growth at the injection site. Xenografting may provide a novel strategy for simultaneous detection of malignant cell contamination and spermatogonial potential of testicular xenografts collected for fertility preservation.

Combined positive and negative flow cytometric sorting allows purification of spermatogonial stem cells from rats with Roser's rat T-cell leukemia

G:13

Hou, Mi[1]; Andersson, Margareta[2]; Zheng, Chengyun[1]; Sundblad, Anne[2]; Söder, Olle[1]; Jahnukainen, Kirsi[1]
[1]Karolinska Institute, Dept. of Woman and Child Health, Stockholm, Sweden; [2]Karolinska Institute, Dept. of Medicine, Stockholm, Sweden

Background: Infertility is one of severe late side effects of cancer treatment in boys surviving from childhood cancer. Autologous germ cell transplantation may be an efficient way to restore their fertility. The risk of reseeding contaminated tumor cells to cured patient has made germ cell purging a crucial step for preventing disease relapse.

Methods: PVG rats carrying Roser's leukemia, that resembles human acute lymphoblastic leukemia, were used as a source of testicular cells and healthy PVG rats as recipients. Ep-CAM and CD4/ MHC-Cl I were identified as specific surface markers of germ cells and leukemic cells, respectively. Testicular cells were labeled with Ep-CAM or CD4/MHC-Cl I or Ep-CAM+CD4/MHC-Cl I. This allowed flow cytometry to positively select germ cells or negatively deplete cancer cells simultaneously. The efficiency of FACS sorting was determined by intratesticular injection of 0.1x106 purged germ cells to recipients followed by FACS analysis. Aggregation of germ cells and leukemic cells was studied.

Results: Positive selection based on Ep-CAM expression reduced leukemic cell contamination and one of three recipients survived. The reduction in malignant cell contamination achieved by deletion was less pronounced. After positive selection and negative depletion leukemic cells were shown to aggregate with germ cells and resulted in contamination of the germ cell preparation. A combination of positive and negative selection prevented the transmission of leukaemia in association with transplantation, but 99.5% of cells were lost during the 4-hour sorting procedure.

Conclusions: Combined positive and negative FACS sorting allows purification of germ cells from leukemic rats. However, problems with phenotypic variations of surface markers on leukemic cells, poor cell recovery, lengthy sorting procedures and aggregation of leukemic and testicular cells limit the efficacy and safety of this approach for clinical use.

Miscellaneous

High incidence of second tumours in the cohort of the first hundred medulloblastoma long-term survivors of the Gustave Roussy Institute M:01

Amoroso, Loredana[1]; Grill, Jacques[1]; Sakiroglu, O.[1]; Raquin, Marie-Anne[1]; Habrand, JL.[2]; Sainte-Rose, Christian[3]; Lemerle, Jean[1]; Hartmann, Olivier[1]; Kalifa, Chantal[1]
[1]Institute Gustave Roussy, Paediatrics, Villejuif, France; [2]Institute Gustave Roussy, Department of Radiation Oncology, Villejuif, France; [3]Necker Sick Children's Hospital, Department of Neurosurgery, Paris, France

The risk of second tumor after brain tumor is increased compared to the normal population. Little is known about the incidence and the risk factors of second tumors in patients with medulloblastoma. We undertook a retrospective survey in all first 100 children who survived more than 5 years after the diagnosis in our institution. They were treated between 1964 and 1991 with a combination of surgery and craniospinal irradiation plus posterior fossa boost. Seventy eight children also received chemotherapy containing alkylating drugs.

All seven patients who experienced a relapse died. Forty second tumours occured in 29 patients eight to 34 years from initial diagnosis (median 21 years). Fifteen years cumulated acturial risk was 45%. Thirty-three tumors were located within the radiation field, mostly in the CNS (13 patients) and in the skin (8 patients). The interval was shorter for malignant tumors (7 years) than for benign tumors (10 years). Cancer predisposition was evidenced in 6 patients (5 Gorlin et one Li-Fraumeni syndromes). The risk of second tumor was not increased in younger children, patients receiving growth hormone replacement or higher doses of craniospinal irradiation. After treatment of their second tumor, nineteen patients were in complete remission ; nine died from the second tumour and one in a car accident.

As survival of medulloblastoma patients improves, lon-term surveillance for second tumors is required especially in the brain and on the skin. Cancer predisposition syndrome seems to be the most important predictor for second tumour in this population.

Breast cancer risk in 5-year survivors of childhood and adolescent Hodgkin's lymphoma, the influence of treatment and premature menopause M:02

De Bruin, Marieke[1]; Aleman, Berthe[2]; Sparidans, Judith[1]; van 't Veer, Mars[3]; van Leeuwen, Flora[1]
[1]Netherlands Cancer Institute, Epidemiology, Amsterdam, Netherlands; [2]Netherlands Cancer Institute, Radiotherapy, Amsterdam, Netherlands; [3]Dr. Daniel den Hoed Cancer Center, Rotterdam, Netherlands

Background: Female Hodgkin's lymphoma (HL) survivors are at increased risk of breast cancer (BC), especially those irradiated to the breast area at young ages. In adult HL-patients, chemotherapy (CT) decreases the high risk of breast cancer after radiotherapy (RT). We assessed the influence of gonadotoxic therapy on the risk of BC in survivors of childhood and adolescent HL.

Methods: We performed a cohort study in 310 women, treated for HL in the period 1965-1995 before age 21 (31% (RT), 9% CT, 60% RT+CT). We compared the incidence of BC with the general population and calculated standardized incidence ratios (SIRs) and absolute excess risks (AERs). Cox regression analyses was performed to study therapy-effects in relation to gonadotoxicity.

Results: During follow-up (median 17.5 years), 33 women developed BC (SIR 16.9 [95%CI 11.7-23.8], AER 72 per 10,000 patients per year). The risk remained high after prolonged follow-up (>25 years after treatment SIR 13.5 [6.7-24.1]). All BC's occurred among patients irradiated to the breast area. Although a trend is observed, neither CT (HR 0.8 [0.4-1.7]), nor RT to the ovaries (HR 0.3 [0.04-2.2], nor onset of menopause before age 40 (HR 0.5 [0.2-1.5]) decreased the risk of BC significantly among these patients. However, patients with <10 years of intact ovarian function after irradiation to the breast, experienced a more than 10-fold significantly lower risk of subsequent BC compared to those with >20 years of intact ovarian function (HR 0.09 [0.01-0.8]). Smoking, overweight and the use of oral contraceptives were not associated with BC.

Conclusion: The risk of BC in young survivors of HL remains elevated up to more than 25 years after treatment. Gonadotoxic therapy lowers the increased risk of BC in patients irradiated in the breast area only when menopause is induced relatively shortly after treatment.

Screening for skin cancer in survivors: to do or not to do? M:03

Braam, K.I.[1]; van den Bos, C.[2]; Wintzen, M.[1]; van Dulmen-den Broeder, E.[1]; Schouten-van Meeteren, A.Y.N.[2]; Kremer, L.C.M.[2]
[1]VU university medical center, Amsterdam, Netherlands; [2]Emma Children Hospital/Academic Medical Center, Amsterdam, Netherlands

Background/Objective: Dutch recommendations regarding screening for skin cancer in childhood cancer survivors (CCS) are not available. We determine the scientific and clinical relevance of screening for skin cancer in CCS and formulate recommendations.

Methods: A literature search was accomplished on magnitude of the risk of skin cancer in CCS and associated risk factors and the efficiency of skin cancer screening methods. Because of the high cure rates of basal cell carcinoma, we only focus on melanoma (for the Late Effect Task Force strategy of the Dutch Childhood Oncology Group, see the abstract of L.C.M. Kremer et al.).

Results: After childhood cancer the risk of skin cancer is increased. General risk factors for melanoma are: ≥50 naevi (≤20 years old), ≥4 dysplastic naevi, naevi on soles, buttocks, anterior scalp, or iris. For melanoma an odds ratio of 16.1 is observed when someone has three or more risk factors, combined with an age younger than forty. After chemotherapy CCS have an increased number of melanocytic naevi or atypical naevi compared to healthy controls. In all studies significantly more naevi were seen on palms and soles in CCS. Also radiotherapy above 15 Gray may contribute to an increased risk for malignant melanoma. Randomized- or case-control studies on screening programs have shown that routine screening for melanoma does not reduce morbidity or mortality.

Conclusions: Despite an increased risk for developing melanomas in CCS, we do not recommend special visits for screening on skin cancer during follow-up without evidence for the effectiveness of screening. Furthermore, we advise physicians to educate patients on the increased risk for melanoma.

Late Tratment Sequelae of Hodgkin Disease and Its Treatment in a Cohort of Long-Term Survivors Treated at a Single Center between 1980 and 1999 M:04

Radvanska, Jitka
Baxter Czech, Oncology, Prague, Czech Republic

Late Treatment Sequelae of Hodgkin Disease and Its Treatment in a Cohort of Long-Term Survivors Treated at a Single Center between 1980 and 1999.

Background/Objective: The aim of the study was to evaluate a wide spectrum of impairments in patients in remission for more than five years. We conducted a cross-sectional study to evaluate sequelae in patients treated between 1980 and 1999 by one of four different treatment protocols. 347 patients with Hodgkin Disease diagnosed prior to the age of 19 were treated. In 2003, 270 of them were in remission for at least 5 y. The mean age at the time of enrollment in the study was 23.9 (SD +/- 4.9) y., and the mean time in remission was 10.6 (SD +/- 3.9) y.

Methods: All patients received physical examination + immunologic, endocrine, pulmonary function and exercise testing. Mammological examination was offered to women.

Results: 32% of patients had sub-clinical hypothyroidism. Increased IgE in 29.9 % was found. Lower total T lymphocyte counts in 18.8 %, lower proportion of T-helper cells in 13.6% and a decreased CD4/ CD8 ratio in 26.2 % were found. Total cholesterol, triglycerides, HDL and LDL were checked, and 47.4% had at least one pathology. Mammogram and/or breast ultrasonography was performed in 68 women. We did not detect any case of carcinoma of the breast. Abnormal pulmonary function at least in one parameter was found in 49.7% out of 153 patients examined. Exercise stress testing did not reveal any signs of myocardial ischemia on ECG, maximal aerobic capacity was decreased more than two standard deviations of reference values in 18.9% out of 224 patients examined. Echocardiographic examination revealed hemodynamically significant heart valvular pathology in 1% of the cohort. No impairment in LVEF and no cases of cardiomyopathy were found.

Conclusions: We found a wide variety of late sequelae and yet a small incidence of serious sequelae in patients with Hodgkin Disease treated during childhood or adolescence. The potential for significant longevity in these patients emphasizes the importance of identifying and minimizing late sequelae of the treatment regimens.

Burden of disease 25 years after treatment for childhood and 'adolescent Hodgkin's lymphoma M:05

van Leeuwen, Flora[1]; Aleman, Berthe[2]; van 't Veer, Mars[3]; De Bruin, Marieke[1]
[1]Netherlands Cancer Institute, Epidemiology, Amsterdam, Netherlands; [2]Netherlands Cancer Institute, Radiotherapy, Amsterdam, Netherlands; [3]Dr. Daniel den Hoed Cancer Center, Rotterdam, Netherlands

Background: Improved survival of childhood and adolescent Hodgkin's lymphoma (HL) has been accompanied by multiple treatment-related complications. However, most studies focused only on one late effect. In this primary analysis we present the combined burden of second malignancies (SM), cardiovascular diseases (CVD) and thyroid disorders (TD) 25 years after treatment.

Methods: We performed a cohort study in 374 5-year survivors (47% male), treated for HL in the period 1965-1995 before age 21 (27% radiotherapy (RT), 3% chemotherapy (CT), 70% RT+CT) (median follow-up 20.6 years). Patients were followed from the day of first treatment to the day of diagnosis of SM, CVD, TD, death or end of follow-up. Data were collected directly from the medical records, through treating physicians and general practitioners (complete follow-up until 1-1-2002: 94%). The Kaplan-Meier method was used to calculate the combined and separate cumulative risks of SM, CVD, and TD 25 years after treatment. The Cox proportional hazards model was used to quantify the effects of different treatments, gender and age at first treatment on treatment-related complications.

Results: After a median follow-up of 20.6 years 68 first SM, 86 first CVD and 96 first TD were observed in 195 patients. The cumulative risks of SM, CVD and TD 25 years after treatment were 21%, 22% and 30% respectively. The 25-year actuarial risk to have experienced at least one of these diseases was 54%; 25-year overall survival was 76%; 25-year risk of non-HL death was 15%. The occurrence of at least one of the treatment-related complications was associated with female gender (HR 1.4 [95%CI 1.1-2.0]), increasing age at first treatment (HR 1.1 [1.0-1.1] per year) and treatment with both RT and CT vs RT only (HR 1.6 [1.2-2.2]).

Conclusion: These preliminary results suggest a very high overall burden of disease 25 years after treatment for childhood and adolescent Hodgkin's lymphoma.

Subclinical cardiac dysfunction in young adult survivors of childhood ALL revealed by exercise echocardiography M:06

Jarfelt, Marianne[1]; Kujacic, Vuk[2]; Holmgren, Daniel[1]; Bjarnason, Ragnar[3]; Lannering, Birgitta[1]
[1]Institute of Clinical Sciences, Department of Pediatrics, Göteborg, Sweden; [2]Institute of Medicine, Cardiovacular Institute, Div. of Clinical Phys, Göteborg, Sweden; [3]Institute of Clinical Sciences, Göteborg Pediatric Growth Research Center, Göteborg, Sweden

Background: Anthracyclines (AC) have highly contributed to the increased survival rate in ALL. The risk of late cardiotoxicity is probably multifactorial but total dose is a strong prognostic factor. Can patients without symptoms of cardiac disease who have received low doses of AC in early childhood be excluded from further cardiac surveillance in adulthood?

Methods: Basal evaluation with two-dimensional (2D), M-mode echocardiography and Doppler examination was performed. Thereafter echocardiography was done at maximal exercise stress and after recovery. Twenty-three young adult ALL patients in first remission treated with median 120 (120-400) mg AC/m2 before the onset of puberty and 12 healthy controls were examined. Median patient age 27 (20-31) years and median follow-up time after remission was 21 (17-27) years. Eleven patients had received cranial radiotherapy and 25% had low spontaneous GH secretion.

Results: We found highly significant differences between patients and controls in systolic function at maximal stress. The most pronounced difference was in ejection fraction at stress 59.5 (32.6-81.1) % and 77.3 (66.2-85.3) % in patients and controls respectively ($p<0.00006$). Ten out of 23 patients reduced their ejection fraction at stress compared to at rest; this was not found in any of the controls. There was also a pronounced difference in cardiac output 4.0(1.6-5.1) and 6.8(4.5-8.0) in patients and controls respectively despite no difference in heart rate ($p= 0.0002$). Systolic function was not correlated to cumulative dose of AC. Cardiovascular risk factors such as GH deficiency and a high proportion of trunk fat did not have an impact on cardiac function in this study.

Conclusions: In this study with very long follow up in a homogenous cohort of ALL survivors we found subclinical cardiac dysfunction even after low doses of AC. This motivates future follow-up of these patients.

Hypertension and prehypertension evaluation in long-term survivors of childhood and adolescent cancer: a new approach M:07

Frenos, Stefano[1]; Pollini, Iva[2]; Calabri, Giovanni[2]; Tondo, Annalisa[1]; Tamburini, Angela[1]; Tucci, Fabio[1]; Sardi, Iacopo[1]; Farina, Silvia[1]; Casini, Tommaso[1]; Veltroni, Marinella[1]; Lippi, Alma[1]; Bernini, Gabriella[1]
[1]Anna Meyer Childrens Hospital, Onco-hematology, Florence, Italy; [2]Anna Meyer Childrens Hospital, Cardiology Unit, Florence, Italy

Background: Childhood cancer, which occurs in approximately 1 out of 350-400 children and adolescents, is no longer an almost uniformly fatal disease. It was been estimated that approximately 1 of 500 young adults (20-35 years of age) having had a diagnosis of cancer as children or adolescents. Unfortunately, two-thirds of these survivors have at least one late effect, mostly from treatment. Hypertension as a late effect following childhood and adolescent cancer (CAAC) has received little attention and the risk of hypertension is considered to be either questionable or no more frequent than for the general population. Nevertheless, an increased incidence between these patients has been observed in some recent study. It is now widely accepted that cardiovascular health originates in childhood. So, the blood pressure(BP) control became essential in long-term survivors of CAAC.

Methods: Diagnosis of hypertension is critically dependent on accurate BP measurement. Systolic and diastolic BP are usually measured by an occasionally auscultatory measurement, with a properly calibrated and validated aneroid sphygmomanometers with an appropriate-sized cuff that fit the patient's arm. Nevertheless this method has many limits. To date automated PB measurement is the only one accurate method and offers multiple advantages in achieving high-quality BP determinations by reducing observer errors. The most commonly used form is 24-h ambulatory PB measurement(ABPM) but in literature there aren't any works that have used this method in long-term survivors of childhood and adolescent cancer. ABPM has been the primary tool to identify the deficiencies of office BP determination in the diagnosis of hypertension and prehypertension. ABPM showed that there were patients with white-coat hypertension and more recently patients with masked hypertension (normal office blood pressure and elevated 24 hour ABPM).

Conclusion To minimize observer and subject errors that commonly occur in clinical BP measurement and to improve the diagnosis of this important late effect of cancer therapy we suggest that ABPM should be used in all survivor of CAAC.

Cardiac damage after treatment of childhood cancer M:08

Velensek Prestor, Veronika[1]; Mazic, Uros[2]; Jereb, Berta[3]; Zaletel Zadravec, Lorna[1]
[1]University Children Hospital, Div. of Pediatric Hematology and Oncology, Ljubljana, Slovenia; [2]University Medical Center, Pediatric Cardiology, Ljubljana, Slovenia; [3]Oncology Institut, Ljubljana, Slovenia

The purpose of the study was to determine the frequency of late effect on the heart of childhood cancer survivors in Slovenia and to identify groups at the highest and lowest risk.

Included in the study were 211 survivors, treated 1968 - 1998 at ages of less than 18 years. All were over 18 years and at least 5 years after end of treatment. The observation time was 5 - 32, average 16 years. Fifty-nine had been treated surgically, 191 had received chemotherapy, 166 radiation, in 56 of whom the heart had been within the field of radiation. The total radiation dose with the area of the heart was between 10-42 Gy, average 28 Gy. Chemotherapy with anthracyclines had been given to 146 patients, to the total dose of 50-620 mg/m2, average 247 mg/m2. Antracyclines together with alkylating agents had been given to 136 patients. Thirty-three children had been treated with anthracyclines and radiation to the heart area. The cardiological diagnostic methods included history, physical examination, electrocardiogram (ECG), electrocardiographic exercise testing on a bycicle ergometer and echocardiography. Descriptive and univariant analysis (chi square test) as well as multivariant analysis (decision tree) were used for data analysis.

Our analysis showed abnormalities in the structure and function of the heart in 53% of survivors. They were all asymptomatic. However, in 2 of these, cardiac death occured.

The period time of treatment (1989-1998) emerged as an important risk factor for any injury to the heart (73% of survivors). Among survivors treated earlier are at the highest risk those with Hodgkins lymphoma treated with radiation above 30 Gy and those treated for sarcoma. At the lowest risk for injury of the heart are those treated for brain tumors and those with other malignancies treated with low total dose of anthracyclines.Among specific forms of heart injury, patients treated with large doses of anthracyclines or concomitant alkylating agents are at highest risk of systolic function defect and enlarged heart chambers and those treated with anthracyclines are at highest risk of diastolic function defect. Radiation to the heart area correlated to the valve injury.

Tetanus and diphtheria antibody levels in patients after sarcoma treatment: A report from the Late Effects Surveillance System M:09

Paulides, Marios[1]; Stohr, Wolfgang[1]; Bielack, Stefan[2]; Klingebiel, Thomas[3]; Jurgens, Heribert[4]; Beck, Jorn-Dirk[1]; Langer, Thorsten[1]
[1]Late Effects Surveillance System, University Hospital for Children and Adolescents, Erlangen, Germany; [2]COSS/EURAMOS Trial Centre, Olgahospital Department of Pediatrics 5, Stuttgart, Germany; [3]CWS Trial Centre, University Hospital for Pediatrics III, Frankfurt, Germany; [4]EURO-E.W.I.N.G. Trial Centre, University Hospital for Children and Adolescents, Munster, Germany

Background: It is known that antineoplastic treatment may induce secondary immunodeficiency. However, there has been a lack of prospective studies after childhood cancer treatment. Aim of this study is to investigate lack of immunity against vaccine-preventable diseases after childhood sarcoma treatment.

Methods: Since 1998, the Late Effects Surveillance System (LESS) of the German Society for Paediatric Oncology and Haematology (GPOH) prospectively registers late effects in soft tissue-, osteo- and Ewing's sarcoma patients of all ages treated within the therapy trials EICESS-92/EURO-E.W.I.N.G.-99, CWS-96/CWS-2002P, COSS-96 in Austria, Germany and Switzerland. The follow-up is conducted locally in accordance with the LESS guidelines. According to these guidelines, antibody levels are to be examined at four weeks and six months after end of antineoplastic treatment to determine immunity against vaccine-preventable diseases. Ten hospitals within the LESS network participated in data collection for this analysis, for which antibody levels against diphtheria and tetanus were used, as there are well-defined guidelines by the Robert-Koch Institute for protective antibody level values.

Results: There were 47 eligible relapse-free patients <21 years of age (31 male, 16 female), of whom 10 had been treated for osteosarcoma, 12 for Ewing's and 25 for soft tissue sarcoma. Median age at diagnosis was 9.6 (interquartile range: 4.4-14.7) years. In 27.6% (13/47) of patients there were no protective antibody levels (<0.1 IU/ml) against diphtheria and/or tetanus. In multivariate analysis, treatment had no effect on antibody levels, similar to tumour type and time of examination after treatment end. Younger patients had significantly lower antibody levels against tetanus (p=0.0132) and girls had significantly lower antibody levels against diphtheria (p=0.0421).

Conclusions: Lack of protective antibody levels against tetanus and/or diphtheria is frequent after childhood sarcoma treatment. Prospective surveillance of immunity and, if indicated, re-immunization is necessary in patients treated for childhood cancer.

Serum Cystatine C as a screening method in follow-up for late effects of malignancy on renal function M:10

Braam, K.I.[1]; Laarman, C.[1]; Stoffel-Wagner, B.[2]; Bouman, A.[3]; Kors, W.A.[1]; Kaspers, G.J.L.[1]; Bökenkamp, A.[1]
[1]VU university medical center, Pediatrics, Amsterdam, Netherlands; [2]University of Bonn, Clinical biochemistry, Bonn, Germany; [3]VU university medical center, Clinical biochemistry, Amsterdam, Netherlands

Background: In screening for childhood cancer late effects serum creatinine and 51CrEDTA are commonly used markers for estimating glomerular filtration rate (GFR). However, serum creatinine lacks diagnostic sensitivity for the detection of mild to moderate renal failure and 51CrEDTA clearance is too cumbersome for daily practice. Cystatin C has been shown to be a simple and robust endogenous marker of GFR, which is particularly useful in the detection of incipient renal failure.

Aim of the study: To compare serum cystatin C with the creatinine-based Schwartz-formula in children in the follow-up of renal disease and/or malignancy.

Methods: 84 children (median age 10.5, range 0.2 to 21; gender 30f, 54m) who needed assessment of renal function for malignancy (n=33) or kidney disease (n=51) participated in this study. Serum cystatin C was measured using a particle-enhanced immunonephelometric assay, creatinine by modified kinetic Jaffé reaction. From these measurements, cystatin C-based (GFRcys - calculated according to Filler et al) and creatinine-based (GFRSchwartz) estimates of GFR were calculated. Single injection inulin clearance was done as the gold standard.

Results: Mean (±SD) cystatin C was 1.13 ± 0.5 mg/l, creatinine 83 ± 38 µmol/l. GFR was 74 ± 26 ml/min/1.73m2, GFRcys 94 ± 33 ml/min/1.73m2, GFRSchwartz 90 ± 29 ml/min/1.73m2. 46% of the patients had mildly reduced GFR (i.e. 60 - 90 ml/min/1.73m2). GFRcys detected these patients with 33% sensitivity, 89% specificity. The positive predictive value was 72%, the negative predictive value 61%. For GFRSchwartz, the respective values were lower (i.e. 28%, 64%, 41% and 51%).

Conclusions: These data suggest that in daily practice, a cystatin C-based equation for the calculation of GFR is superior to the commonly used Schwartz-GFR, in particular in patients with mild-moderate renal failure. Therefore, cystatin C should complement creatinine measurements in the follow-up for late effects of malignancy on renal function.

Elevated liver enzymes two years after hematopoietic stem cell transplantation in children: prevalence and etiology M:11

Bresters, Dorine[1]; van Gils, Ilse[1]; Dekker, Friedo[2]; Lankester, Arjan[1]; Bredius, Robbert[1]; Schweizer, Joachim[3]
[1]LUMC, WA-KJC/Immunology, Hemato/Oncology and BMT (IHO-BA), Leiden, Netherlands; [2]LUMC, Epidemiology, Leiden, Netherlands; [3]LUMC, WA-KJC/Pediatric Gastroenterology and Nutrition, Leiden, Netherlands

Background: In previous studies the prevalence of elevated liver enzymes late after hematopoetic stem cell transplantation (SCT) varied from 40 to 58%. Etiology includes viral hepatitis, iron overload, auto-immune hepatitis and/or chronic graft versus host disease (cGvHD) in a majority of these patients, but in some etiology remains unclear.

Aim of the study: was to establish the prevalence and etiology of elevated liver enzymes in children surviving long term after SCT in a country with a low prevalence of HBV and HCV among blood donors.

Methods: This is a single center retrospective study. AST and ALT values from before SCT until 2 years after SCT, age, sex, diagnosis, type of transplant, conditioning regimen and post-transplant complications involving the liver (veno-occlusive disease, acute/chronic GvHD, viral reactivation) were collected in all children transplanted between 1980 and 2002.

Results: 290 of 455 patients who underwent SCT were alive at least 2 years after SCT. Median age in survivors was 7.1 years and the majority were transplanted for a hematological malignancy (57.6%) with bone marrow (95.5%) of a matched sibling donor (66.6%). The conditioning regimen included TBI in 58.5% of the patients.

AST and ALT were assessed at 2 years after SCT in 216 patients and values were above normal in 53 (24.5%). In 17 patients (7.9%) AST and/or ALT value was at least twice the upper limit of normal. In 13 of 17 patients etiology could be established and included iron overload in 6, chronic hepatitis C in 2 and cGvHD in 4. HCV seropositivity (tested after 1992) occurred in 3 patients, but chronic hepatitis B was not present in any of our patients.

Conclusions: The prevalence of abnormal liver enzymes after SCT in our center is lower than reported in previous studies. Chronic hepatitis C was found in only 5.7% of patients with elevated liver enzymes. Longer follow-up is needed to establish the clinical relevance of elevated liver enzymes late after SCT.

Continuing recovery of neurologic symptoms even after very long term follow-up in Kinsbourne syndrome M:12

van Hemsbergen, M.; Catsman-Berrevoets, C.E.; Aarsen, F.K.; Hakvoort-Cammel, F.G.A.J.; van den Heuvel-Eibrink, M.M.
Erasmus MC- Sophia Childrens Hospital, Rotterdam, Netherlands

Introduction: Kinsbourne syndrome, also known as 'dancing eyes - dancing feet syndrome' or 'opsoclonus-myoclonus syndrome' (OMS) is a well described but rare neurologic syndrome, which is highly associated with neuroblastoma. The characteristic symptoms are rapid, involuntary, irregular conjugate eye movements (opsoclonus), myoclonic jerking of the limbs and trunk, ataxia and behavioral disturbance (2, 3) and the disease has a sub acute onset. The exact etiology and pathogenesis of OMS is not yet clear, but the current suggestion is that it is immune-mediated. Data on very long-term follow-up of these patients is not available so far.

Patients and methods. The purpose of our study was to investigate the course of recovery and very long-term outcome (med. > 10 years) in all 9 patients treated for OMS from 1989 until 2000 in our institute. The results include data on medical, neurological and oncologic follow up, as well as radiological evaluation and a Quality of Life assessment(Tacqol) in a longitudinally survey.

Results. In 4 out of 9 patients in this study a NBL was found. Five children showed showed signs of bulbar dysfunction, including dysarthria. Two children lost speech completely. All children had behavioural problems. All children were treated with either Prednison, ACTH, gammaglobulines or a combination. During follow up we saw a very slow continuing improvement of neurologic symptoms in all patients. Especially the three main symptoms, ataxia, opsoclonus and myoclonus improved after starting therapy and rather strikingly, kept improving even 10 years of foloow-up. 7/9 children had a severe mental retardation at the latest point of evaluation. At follow-up, a significant improvement of motor skills (p=0,043) and the autonomy scale was found all still below the normal population average. Physical function, positive emotions and negative emotions however were, although low, within the range of the normal population.

Permanent hair loss after radiotherapy in children and adolescents M:13

Sugden, Elaine[1]; Oxford, Sarah[2]; Shine, Brian[3]; Graham, Andrea[1]
[1]Oxford Radcliffe Hospitals, Clinical Oncology, Oxford, United Kingdom; [2]Oxford Brookes University, Oxford, United Kingdom; [3]Oxford Radcliffe Hospitals, Clinical Biochemistry, Oxford, United Kingdom

Background/objective: Hair loss is a feared side effect of cancer treatment. Hair is expected to regrow after chemotherapy but after radiotherapy areas of permanent hair loss are common. This is a continuing cause of concern for children, adolescents and adults. The radiosensitive scalp hair follicles lie 0.5 to 1mm below the skin surface and are irradiated as the radiation beam enters and leaves the head. We investigated the relationship between the total dose of radiation (in small daily amounts) and permanent hair loss. We could not find this information in the literature.

Methods: We developed a visually graded scoring system for hair loss. All patients known to us who had received radiotherapy involving scalp hair more than 6 months before the study were invited for assessment (Oxford Ethics study no A99.001). Photographs and diagrams indicated the pattern of hair loss. This was then related to scalp radiation dose which was estimated from review of treatment plans.

Results: From the 50 patients assessed ninety nine areas of scalp were scored. No clinically detectable permanent hair loss was seen when the total dose to the scalp was below 20 Gy (in 2 Gy fractions). Between 30 and 40Gy, permanent loss became more likely, hair was present but thinned. After doses of 50Gy or above, 80% had easily detectable and 50% total or virtually total, hair loss. The relationship between dose and permanent hair loss was highly significant (p=0.0001).

Conclusion: Children and young adults surviving brain tumours are often left with the embarrassment of patches of complete or virtually complete hair loss. Permanent loss becomes more likely with increased total radiation scalp dose but there is individual variation. Efforts to keep to a minimum the areas of scalp receiving a high radiation dose will be worthwhile.

Late effects of Wilms' tumor treatment: can appropriate life style minimize the consequences? M:14

Radvansky, Jiri[1]; Radvanska, Jitka[2]; Slaby, Krystof[3]; Sulc, Jan[4]; Safarova, Marcela[5]
[1]Motol University Hospital - 2nd Medical Faculty - Charles University Prague, Department of Sports Medicine, Prague, Czech Republic; [2]Motol University Hospital, Department of Paediatric hematology/oncology, Prague, Czech Republic; [3]Motol University Hospital, Department of Sports Medicine, Prague, Czech Republic; [4]Motol University Hospital, Department of Paediatrics, Prague, Czech Republic; [5]Motol University Hospital, Department of Rehabilitation, Prague, Czech Republic

Background: Nephroblastoma in children has got excellent outcome and low incidence of fatal late complications. Despite this fact minor abnormities can in these patients bring additional risk for future life. Aim of our study is to find the incidence and severity of functional impairment in cardiopulmonary, renal and metabolic system on a major cohort of nephroblastoma survivors.

Methods: We screened 274 survivors out of a total of 315 patients who were treated for Wilms' tumor at our hospital between 1980 and 2004. They were treated by vincristine and actinomycine D and in advanced stages also by anthracyclines and radiotherapy. We have examined up to now 64 patients, including abdominal ultrasonography, ECHO, renal function test, exercise test and screening by physiotherapist. As the evaluation of scoliosis and functional posture impairment is difficult for measurement, we tested also pulmonary function as a possible impairment by posture problems. The median survival time of the subgroup is 14.2 years (range: 6.6-26.3). Solitary kidney has 97% of cohort.

Results: (mean±SD): Glomerular filtration rate 1.57±0.84 ml/s*1.73m2, urinary protein excretion median 140.5 mg/m2*24h (range 42-3004). Pulmonary function: Vital capacity 102%±15, total lung capacity 103%±12 of reference values, functional residual capacity/total lung capacity 110%±9 (mild sign of lung hyperinflation). 3% of patients is currently treated for hypertension, 40% has exaggerated blood pressure reaction to dynamic exercise. No patient with impaired systolic heart function and/or major diastolic dysfunction was found. Low exercise capacity (maximal oxygen consumption) was found in 23%. Dyslipaemia was found in 22%. At least 60% have risk of developing civilization diseases from family history.

Conclusion: Despite excellent outcome, substantial part of survivors has minor functional impairments, low exercise capacity and metabolic impairment, at least partly preventable by adequate lifestyle modification.

Supported by grant NR 8796-3 of the Int. Grant Agency of the Czech Ministry of Health

Treatment-induced ototoxicity in pediatric medulloblastoma patients

M:15

Lafay-Cousin, Lucie[1]; Mabbott, Don[1]; Druker, Susan[2]; Bartels, Ute[1]; Huang, Annie[1]; Forte, Vito[3]; Bouffet, Eric[1]

[1]Hospital for Sick Children, Pediatric Brain Tumor program, Toronto, Canada; [2]Hospital for Sick Children, Audiology, Toronto, Canada; [3]Hospital for Sick Children, ENT, Toronto, Canada

Purpose: To report on the kinetic of cisplatinum(CDDP) induced ototoxicity and to correlate the need for hearing assistance in pediatric medulloblastoma patients.

Patients and Method: Clinical records of 37 children(older than 3 yrs) with medulloblastoma were reviewed. Results of serial pre-chemotherapy audiograms and during follow-up as well as use of hearing aids were recorded.

Results: 24 patients were treated according to average risk(AR) protocol including reduced dose of CSI and intended CDDP cumulative dose of 600mg/m2 in 8 cycles. 13 high risk(HR) patients were intended to received conventional CSI and 3 cycles of CDDP(cumulative dose of 270 mg/m2) High frequencies hearing loss (greater than 55db) occured very early on therapy in up to 54% of the AR patients after 2 cycles and 90% after 4cycles. In HR patients high frequencies HL raised from 53.8% to 100% between cycle 1 to 3. 21% of the AR patients had HL (greater than 55db) between 2000 and 4000Hz frequencies after 5 cycle of CDDP. After completion of chemotherapy, 15.8% of AR patients and 25% of the HR patients had HL greater than 25db below 2000Hz. 45.9% of the patients(17/37) required 50% CDDP dose reduction at a median of 4 cycles (2-8) The median cumulative dose of CDDP administred was 412.5 mg/m2, (intended cumulative dose of 600mg/ m2) in AR patients and 270mg/m2 in HR patients(intended cumulative dose of 270mg/ m2). CDDP was discontinued in 6/37 patients. 6/37 required either hearing aids. Interestingly 5/6 developed moderate HL(median=50db) between 2000 and 4000Hz early on therapy(cycle 3)

Discussion/Conclusion: High frequencies HL occured early on therapy. AR patients showed greater HL between 2000-4000Hz frequencies compare to HR patients. In AR patients, ototoxicity led to early dose adjustement (cycle 4) and limited the delivered dose by 2/3 of the intended dose in AR patients. Early HL below 4000 Hz might predicte further need for hearing support. Correlation between hearing loss and academic achievement are under investigation

Index of Authors

** Presenting author*

Map of Lundagård