ONKOLIS
Testikkelkreft
29. april, 2022

Torgrim Tandstad
Overlege Kreftklinikken
Fagansvarlig testikkelkreft og prostatakreft
St. Olavs Hospital
Førsteamanuensis, NTNU
Leder SWENOTECA
Medlem EAU Guidelines testikkelkreft

SWENOTECA
Swedish Norwegian Testicular Cancer Group
ST. OLAVS HOSPITAL
TRONDHEIM UNIVERSITY HOSPITAL
NTNU

Testikkelkreft

Epidemiologi, patologi og behandling

Contents lists available at ScienceDirect

Social Science & Medicine

journal homepage: www.elsevier.com/locate/socscimed

Stability and change in disease prestige: A comparative analysis of three surveys spanning a quarter of a century

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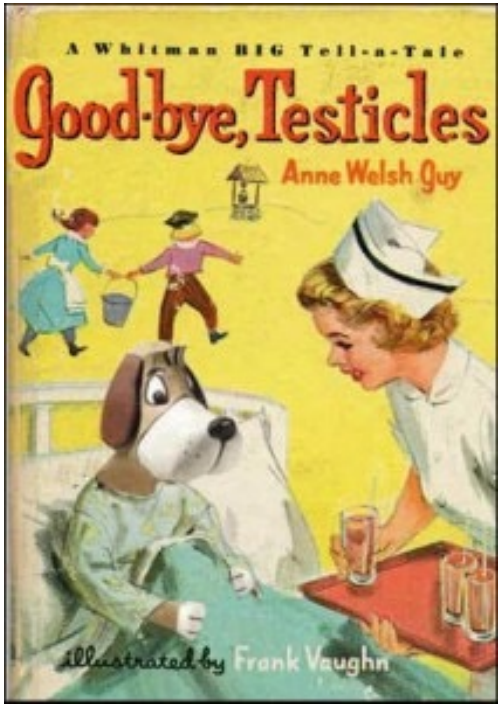
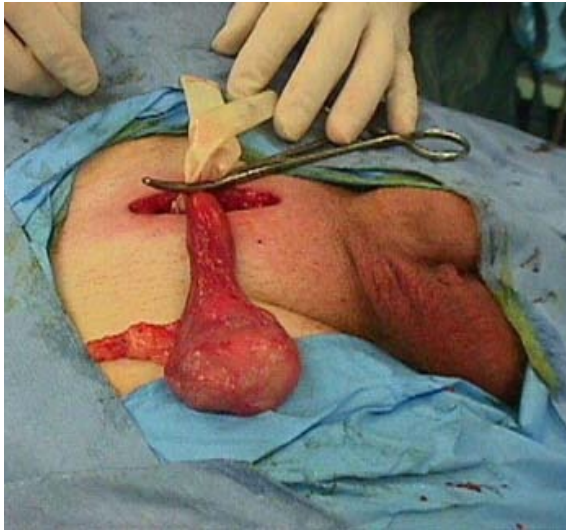
Table 2
Disease prestige. Rank and mean scores (SDs) in 1990, 2002 and 2014 samples, sorted after the 2014 sample.

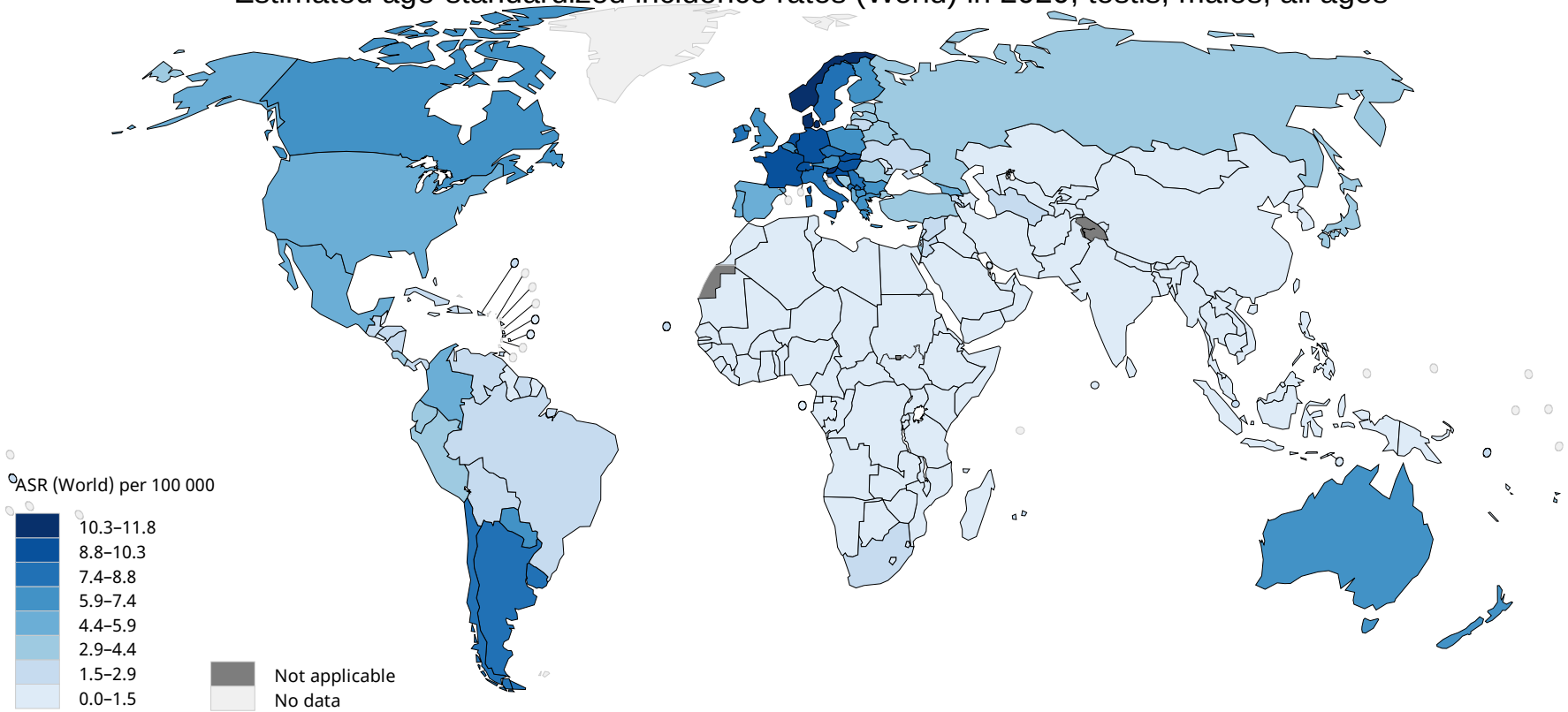
Samples		1990		2002		2014
N		98		241		291
Leukaemia	2	6.8 (1.5)	1	6.9 (1.4)	1	6.9 (1.5)
Brain tumour	3	6.6 (1.6)	3	6.6 (1.7)	2	6.7 (1.7)
Myocardial infarction	1	7.1 (1.2)	1	6.9 (1.4)	2	6.7 (1.6)
Testicle cancer	5	6.3 (1.6)	5	6.5 (1.5)	4	6.6 (1.6)
Spleen rupture	5	6.3 (1.7)	3	6.6 (1.5)	5	6.4 (1.5)
Pulmonary embolism	7	6.2 (1.5)	6	6.3 (1.5)	5	6.4 (1.5)
Colon cancer	11	5.6 (1.5)	11	5.7 (1.4)	7	6.1 (1.5)
Extra-uterine pregnancy	8	6.1 (1.8)	7	6.1 (1.6)	8	6.0 (1.7)
Ovarian cancer	13	5.5 (1.5)	11	5.7 (1.5)	9	5.9 (1.5)
Thyroid cancer	9	6.0 (1.5)	9	5.9 (1.5)	9	5.9 (1.6)
Angina pectoris	4	6.4 (1.3)	8	6.0 (1.4)	11	5.8 (1.5)
Pancreatic cancer	16	5.3 (1.9)	18	5.2 (1.7)	12	5.7 (1.7)
Appendicitis	16	5.3 (2.1)	14	5.5 (1.7)	13	5.6 (1.7)
Bechterew's disease	23	4.9 (1.6)	23	4.9 (1.5)	26	4.8 (1.4)
Femoral neck fracture	27	4.1 (1.5)	25	4.6 (1.5)	27	4.7 (1.5)
Arthritis	25	4.6 (1.6)	27	4.4 (1.3)	28	4.6 (1.3)
Inguinal hernia	28	3.9 (1.8)	28	4.2 (1.5)	29	4.2 (1.5)
Psoriasis	31	3.7 (1.4)	30	3.8 (1.2)	30	3.9 (1.3)
Cerebral palsy	32	3.6 (1.6)	31	3.6 (1.4)	30	3.9 (1.5)
Schizophrenia	34	3.2 (1.8)	34	3.2 (1.4)	32	3.5 (1.6)
AIDS	29	3.8 (2.8)	32	3.5 (2.1)	33	3.4 (1.9)
Anorexia	29	3.8 (2.0)	32	3.5 (1.5)	33	3.4 (1.5)
Depressive neurosis	35	2.9 (1.2)	35	3.1 (1.3)	35	3.2 (1.3)
Hepatocirrhosis	37	2.8 (1.4)	35	3.1 (1.5)	35	3.2 (1.6)
Anxiety neurosis	35	2.9 (1.2)	37	2.8 (1.4)	37	2.9 (1.4)
Fibromyalgia	38	2.4 (1.3)	38	2.3 (1.2)	38	2.4 (1.3)

Primær kirurgisk behandling





Estimated age-standardized incidence rates (World) in 2020, testis, males, all ages



Data source: GLOBOCAN 2020
Graph production: IARC (http://gco.iarc.fr/today)
World Health Organization

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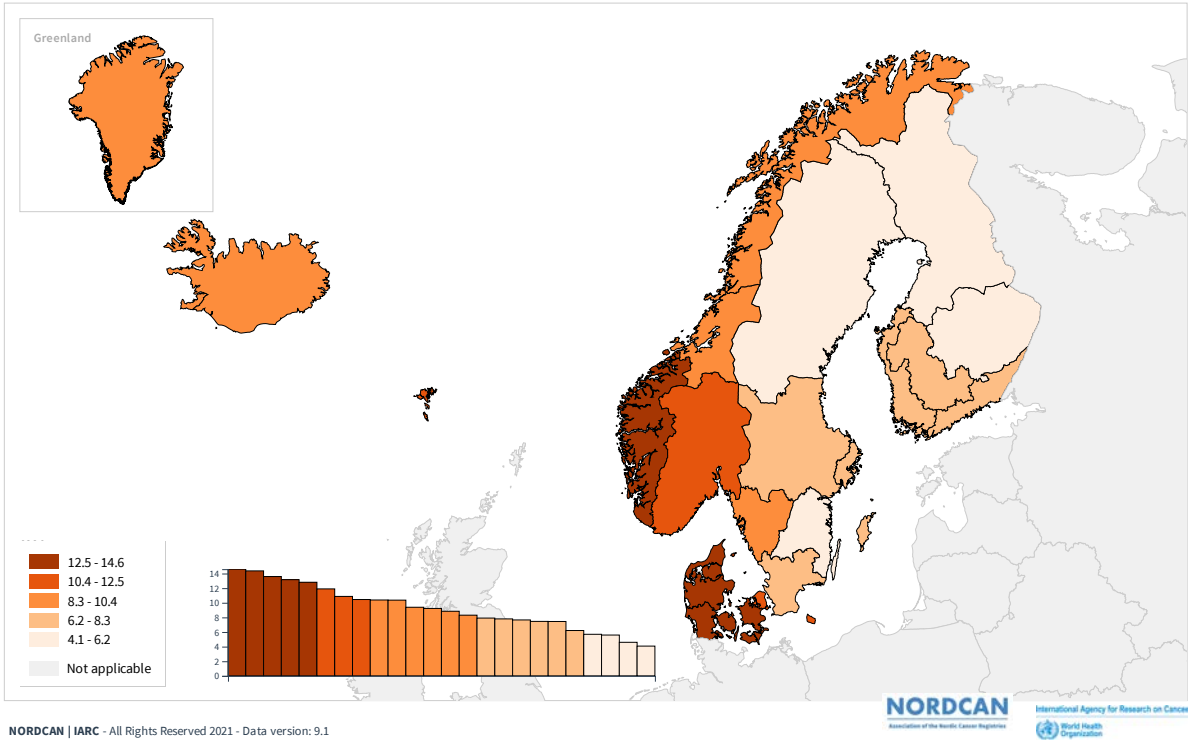
Testikkelkreft Norge

- 300 pasienter årlig
- Høy insidens
- 1 % av norske menn vil utvikle testikkelkreft



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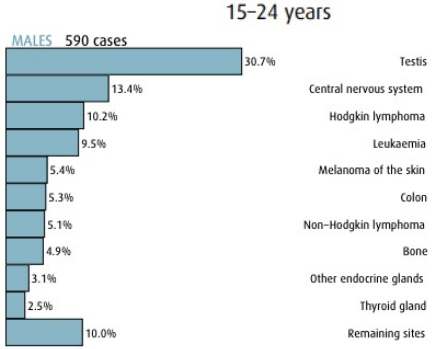
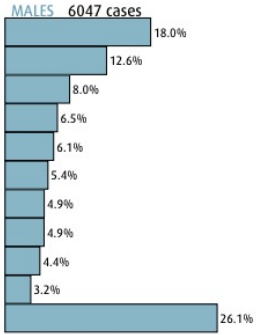
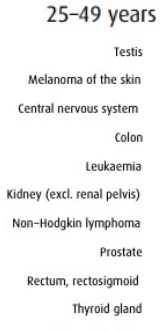
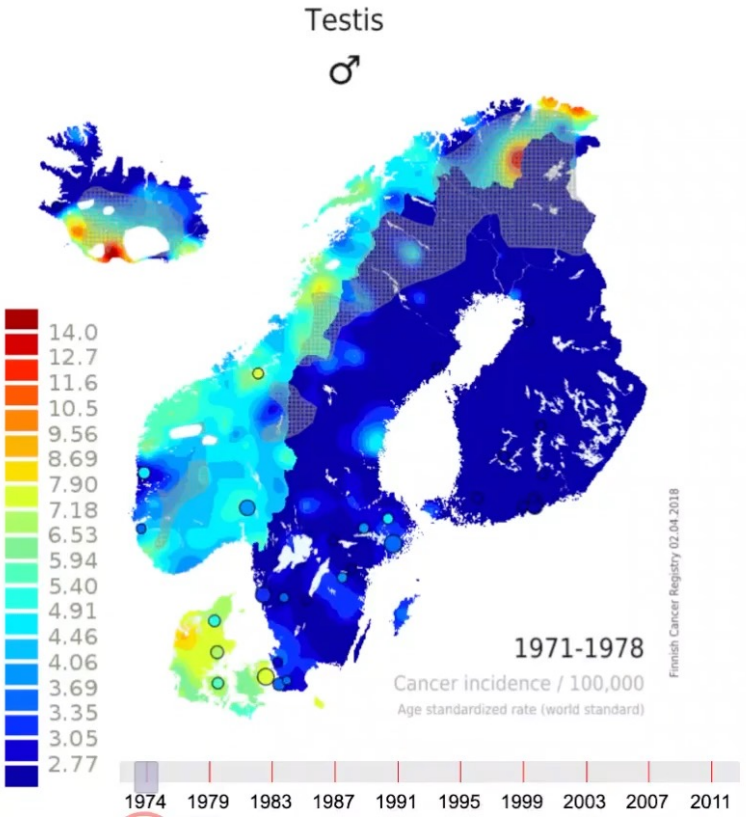
Gradvis økende forekomst

- Økende insidens i de fleste vestlige land
- Prevalensen øker drastisk









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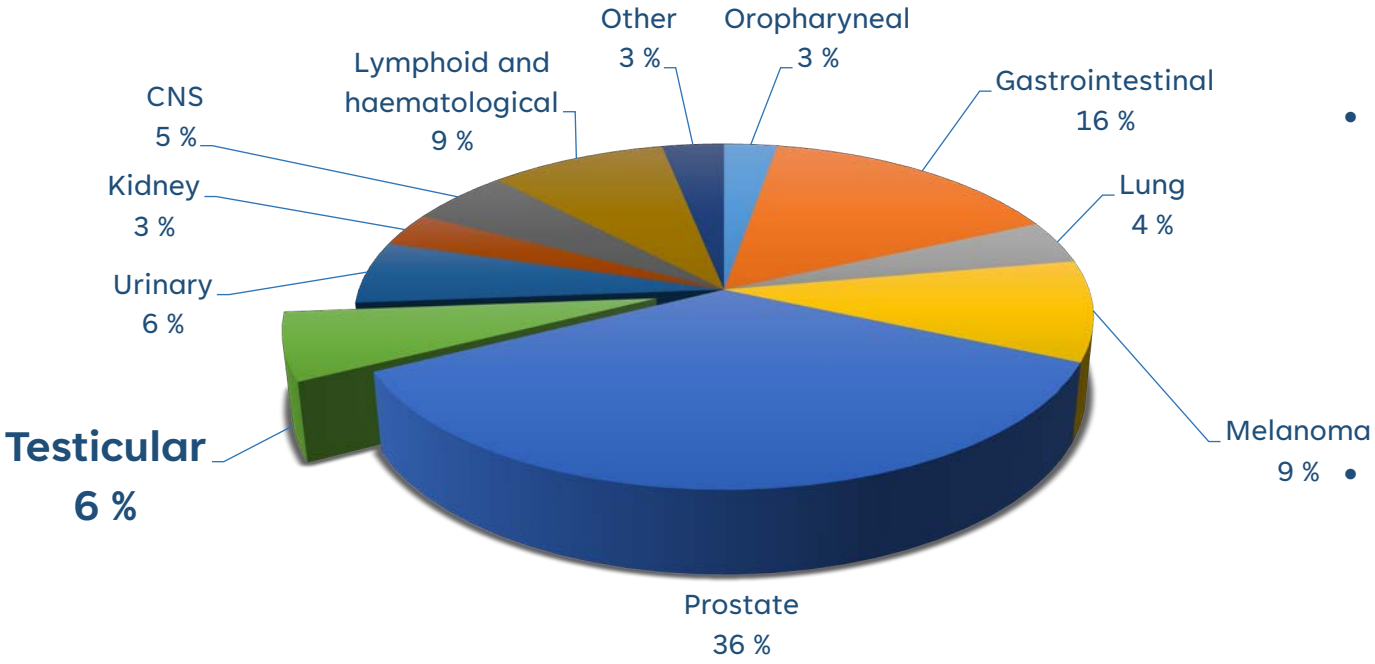
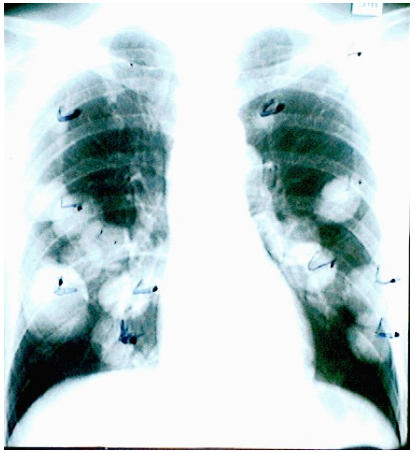
Prevalens

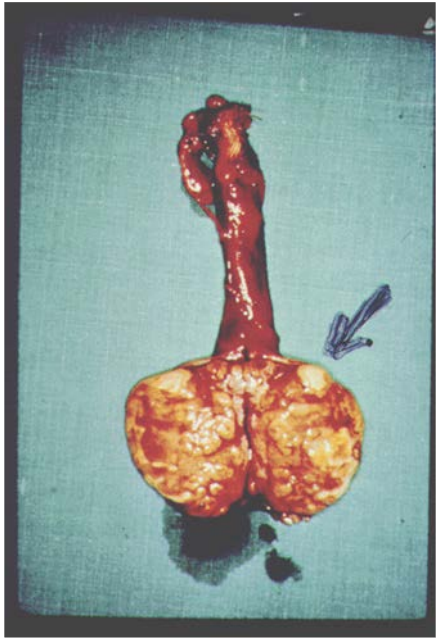


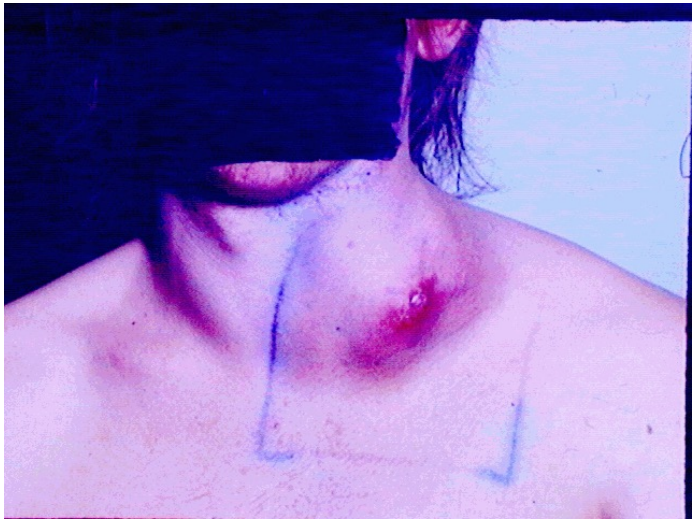
- Relativt sjelden sykdom, men lav median alder, god prognose og økt frekvens har medført at prevalensen har økt kraftig
- Over 60% av testikkelkreftoverlevere fikk diagnosen for mer enn 10 år siden

Fra unge menns tragedie til modellsykdom

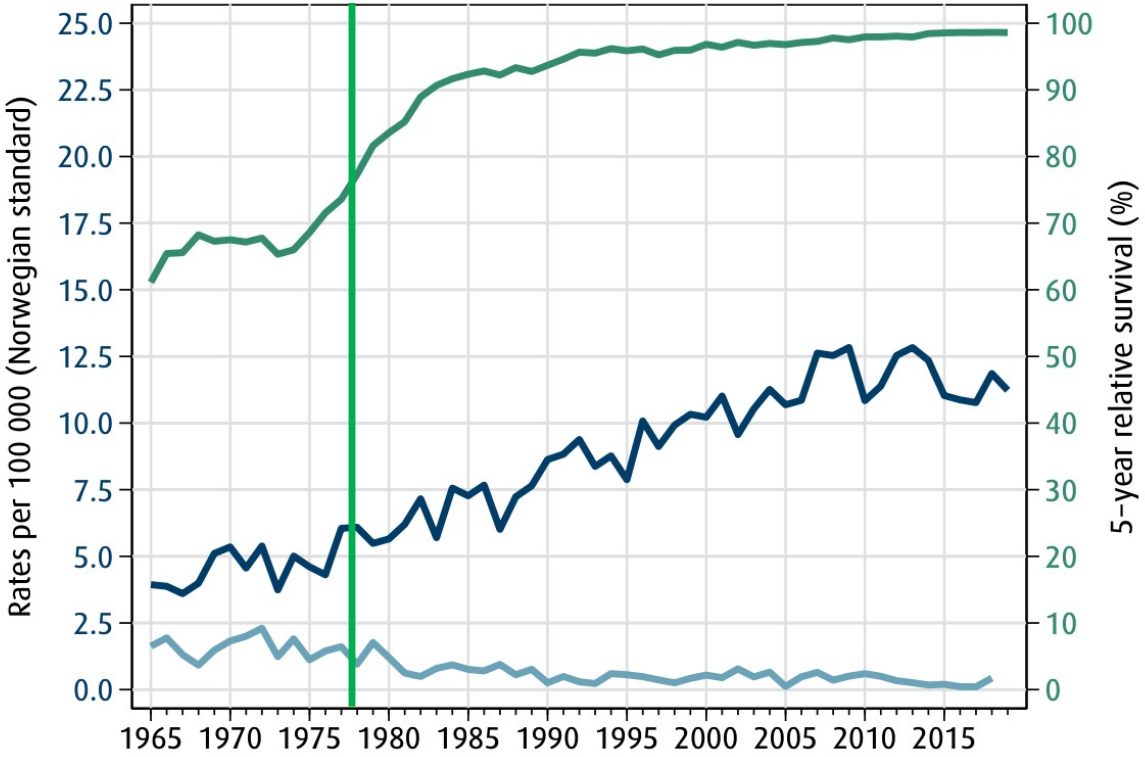
- I 1960 årene var testikkelkreft hyppigste dødsårsak av enkeltsykdommer i Norge





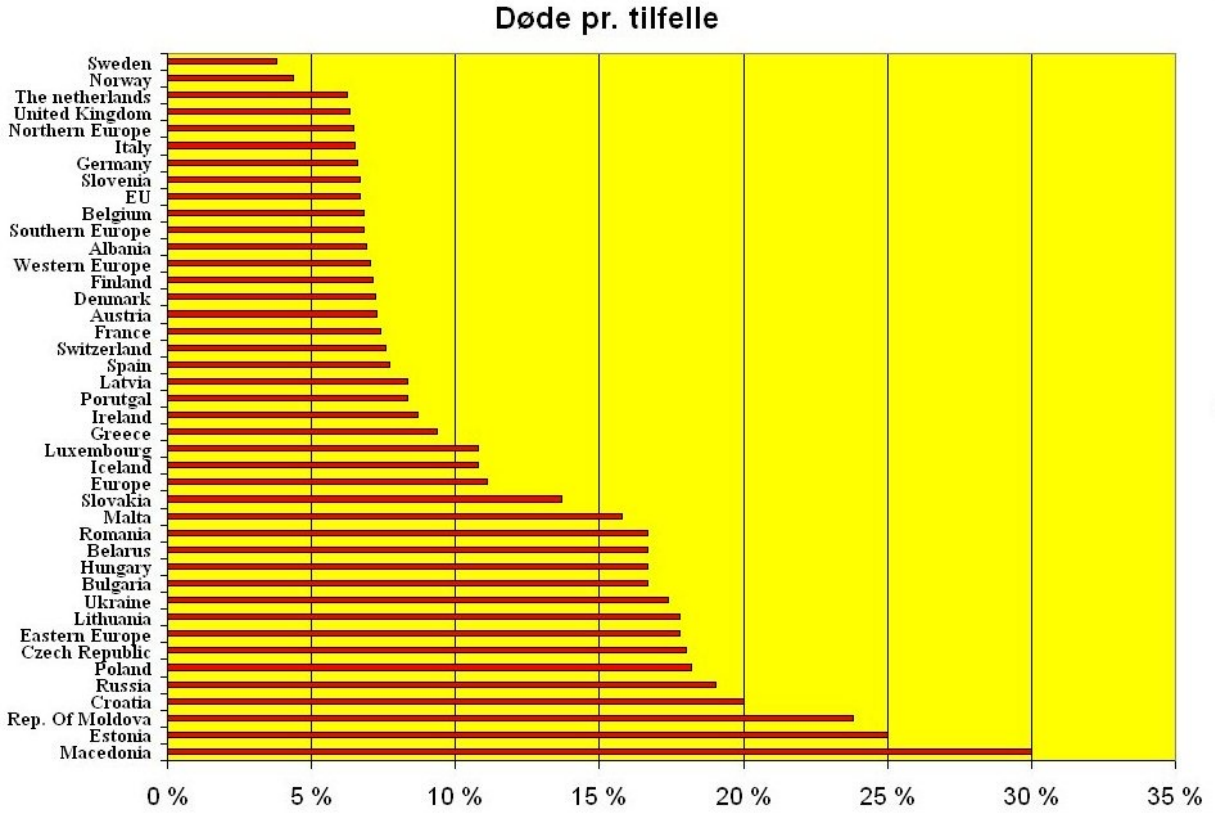


Best prognose av alle kreftformer



Incidens og mortalitet, testikkelkreft

Etter Bray et al, Eur J Cancer 38 (2002) 99 - 166



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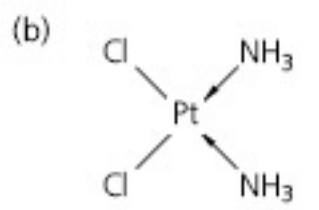
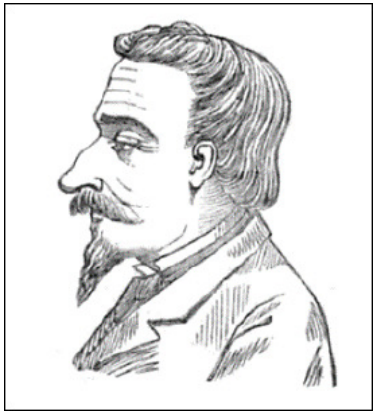
Cisplatin Episode 1 - Tyskland

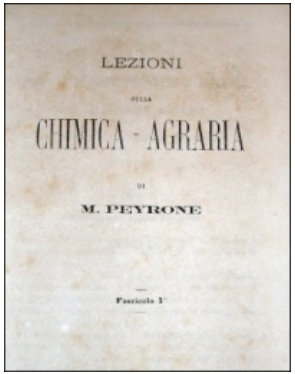
- 1844, University of Gießen
  - Peyrone´s yellow salt, i.e. *cis-diamminedichloroplatinum (II)*



Peyrone's chloride,
$[PtCl_2(NH_3)_2]$



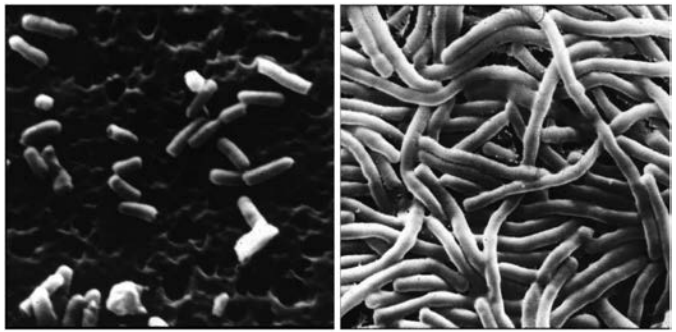
Michele Peyrone
1813-1883

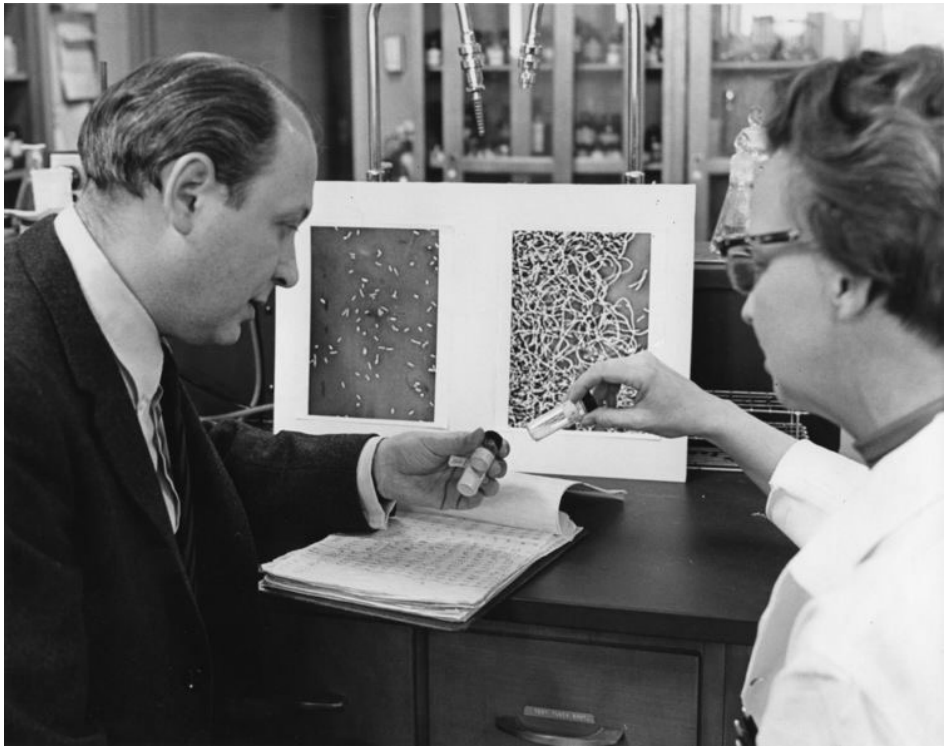


"I am determined to pursue this subject with all my energies, without having regard for the difficulties to be encountered at every step in such expensive and delicate a research"

Cisplatin Episode 2 - USA

- 1965, Michigan State University
- Tilfeldig funn:
  - I en petriskål med e. coli der man hadde et elektrisk felt, så delte ikke e.coli seg, men dannet lange filamentøse tråder



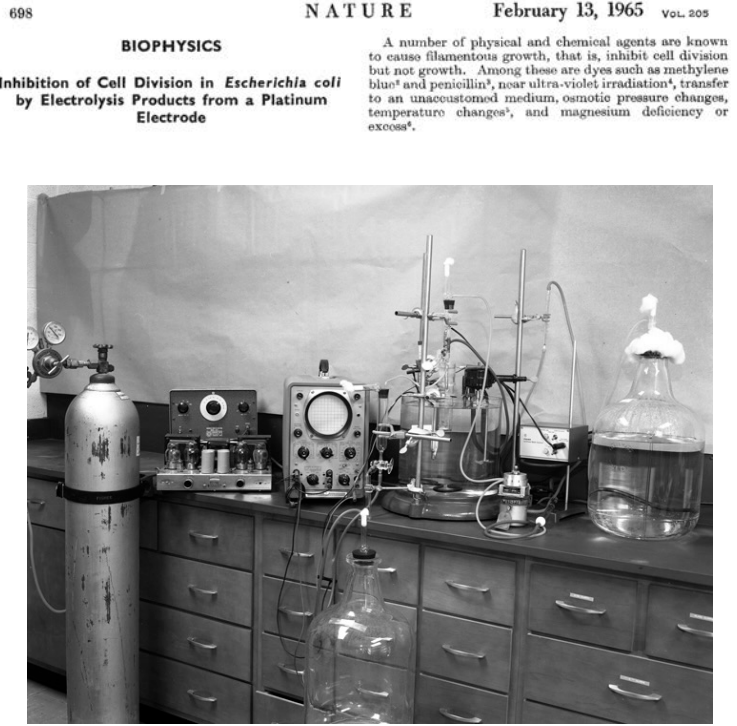


Barnett Rosenberg 1924-2009

Cisplatin Episode 2 - USA

- Mange variabler i eksperimentet, tett samarbeid om å indentifisere hva som hadde skjedd

- Hypotesen var til slutt at elektrodene som var laget av platinum, dannet $(NH_4)_2PtCl_6$ som gav det observerte resultatet, senere ble det observert at dette stoffet reagerte i elektrisk felt og man fikk identifisert $Pt(NH_3)_2Cl_2$ (Peyrone´s yellow salt) som det mest potente forbindelsen til å hemme celledeling



698 NATURE February 13, 1965 Vol. 205

BIOPHYSICS

Inhibition of Cell Division in *Escherichia coli* by Electrolysis Products from a Platinum Electrode

A number of physical and chemical agents are known to cause filamentous growth, that is, inhibit cell division but not growth. Among these are dyes such as methylene blue[1] and penicillin[2], near ultra-violet irradiation[4], transfer to an unaccustomed medium, osmotic pressure changes, temperature changes[3], and magnesium deficiency or excess[5].

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Cisplatin Episode 2 - USA

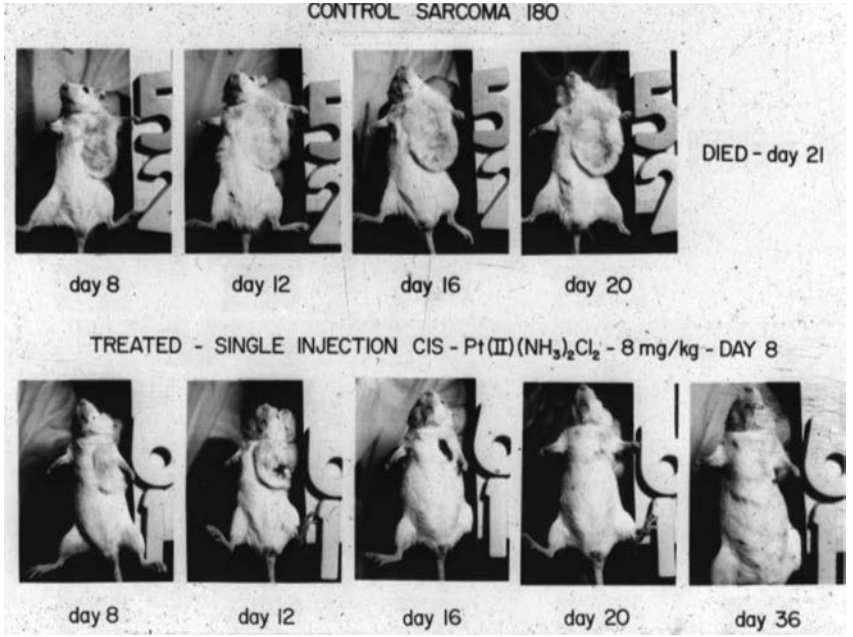
- Dyreforsøk publisert 1970
- Menneskestudier i regi av NCI 1972
- 1972-1974: Cisplatin var for toksisk i monoterapi (kvalme, nyreskade, hørselskade, nevropati) og fase I studier var mislykket, men noen CR hos pasienter med testikkelkreft

[CANCER RESEARCH 30, 1799–1802, June 1970]

The Successful Regression of Large Solid Sarcoma 180 Tumors by Platinum Compounds[1]

Barnett Rosenberg and Loretta VanCamp

Biophysics Department, Michigan State University, East Lansing, Michigan 48823



Cisplatin Episode 3 - USA

- 1974, Indiana University
- Fase II studie: Cisplatin, vinblastine, bleomycin
- 50 pasienter, 32 kurert (65%)

Cis-Diamminedichloroplatinum, Vinblastine, and Bleomycin Combination Chemotherapy in Disseminated Testicular Cancer

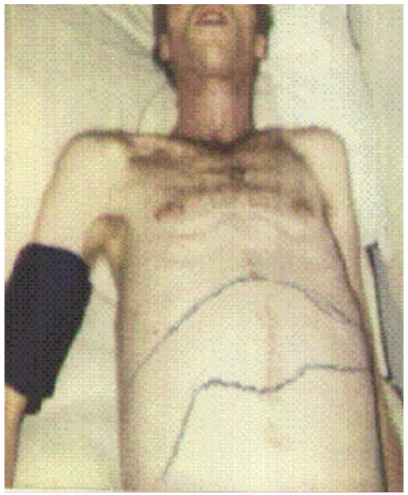
LAWRENCE H. EINHORN, M.D., F.A.C.P.; and JOHN DONOHUE, M.D.; Indianapolis, Indiana

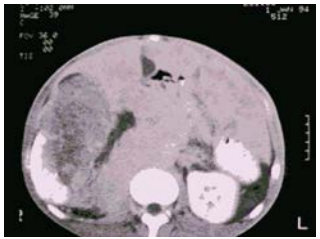
(Reprinted with permission from Ann Intern Med, 87: 293–298, 1997)

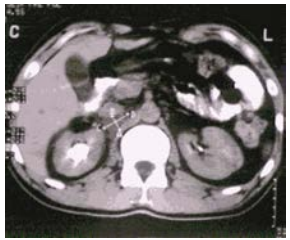
Lawrence Einhorn 1942-

Cisplatin Episode 4 - Norge

- Cisplatin-sommeren 1978
  - 36 menn med metastatisk cancer testis ventet på behandling
  - Olbjørn Klepp snek cisplatin gjennom tollen på Fornebu 16. mai 1978, første pasienter behandlet 18. mai
  - 90% av pasientene responderte
- Etablering SWENOTECA 1981







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SWENOTECA

- Swedish Norwegian Testicular Cancer Group
- Etablert i 1981
- Utarbeider retningslinjer for testikkelkreft
- Tett samarbeid mellom onkologer og urologer
- www.swenoteca.org

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BEP: Internasjonal gullstandard kjemoterapi

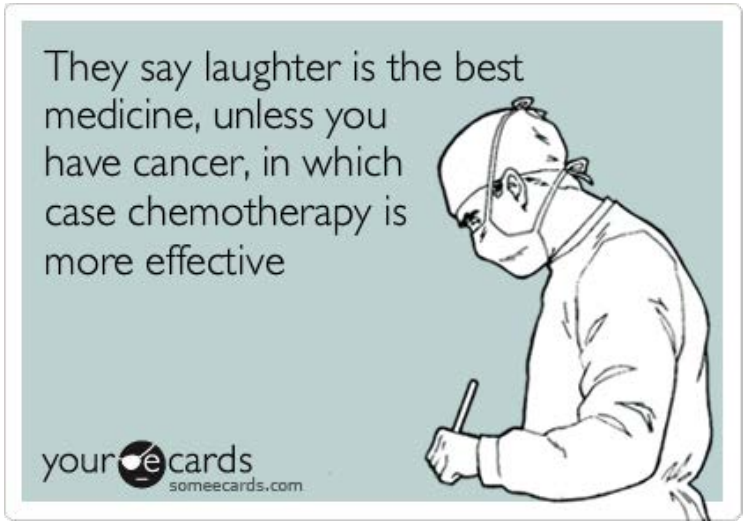
- Cisplatin 20 mg/m^2 Dag 1 – 5
- Etoposid 100 mg/m^2 Dag 1 – 5
- Bleomycin 30 000IE Dag 1, 5, 15
- Gis hver 3. uke

BEP

- Aldri dosereduser
- Hold intervaller
- Alltid bleomycin til tross for nøytropeni

BEP

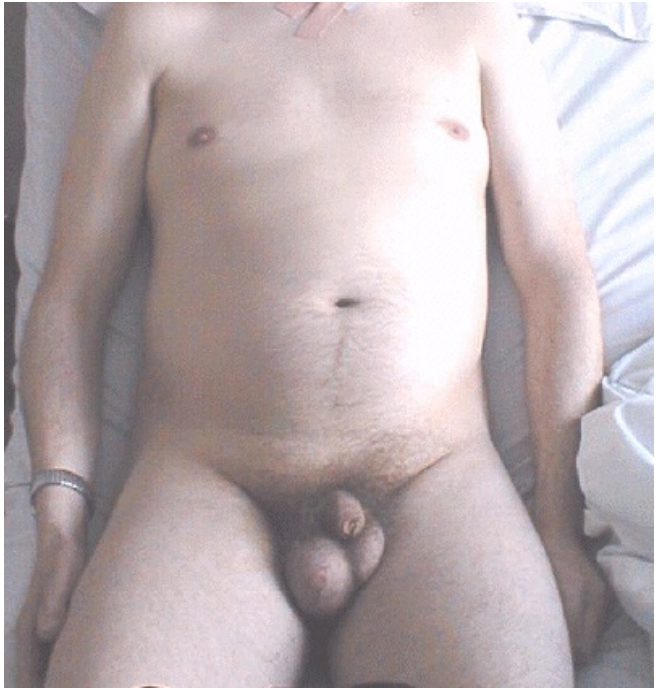
- Høyemetogen
- Nefrotoksisk
- Ototoksisk
- Nevrotoksisk
- Myelotoksisk
- Pneumonitt



Utredning av pasienter med testikkelkreft

VED DIAGNOSETIDSPUNKT (før orkiektomi):

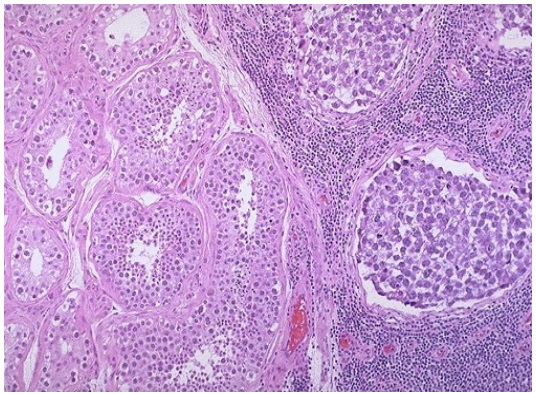
- Ultralyd begge testikler
- CT thorax/abd/bekken (metastaser?)
- Tumormarkører AFP, hCG og LD
- Hormonanalyser (testosteron, FSH, LH, SHBG)



Histologi

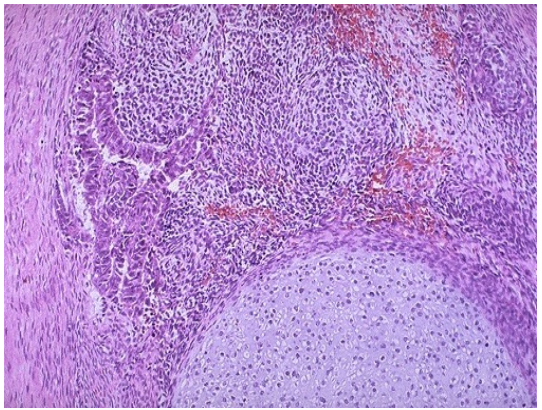
- Seminom

- Nonseminom (alle andre som ikke består av rent seminom)
  - Embryonalt karsinom
  - Plommesekktumor
  - Choriocarsinom
  - Teratom
  - Seminom



Rent seminom

Nonseminom (embryonalt karsinom og teratom)



Seminom vs. Nonseminom

Seminom:

- Medianalder 35-37 år
- Senere spredning
- Oftest lymfogen spredning
- Ekstremt stråleføIsom
- Responderer godt på kjemoterapi
- Produserer ikke AFP (NB: noen har habituelt forhøyet AFP)
- ⇧hCG 20 - 40%

Nonseminom

- Medianalder 25-29
- Tidlig spredning
- I tillegg til lymfogen spredning, ofte hematogen spredning
- Mindre stråleføIsom
- Responderer godt på kjemoterapi
- ⇧AFP og/eller hCG hos >70%

Cryopreservering av sæd

- Tilbys pasienten før orkiektomi om mulig
- Redusert fertilitet hyppig ved testiscancer
- Spesielt viktig ved kontralateral atrofisk testikkel
- Pasienten skal tilbys testikkelprotese

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Tumormarkører

- hCG

  Halveringstid ≤ 3 døgn

- AFP

  Halveringstid ≤ 7 døgn

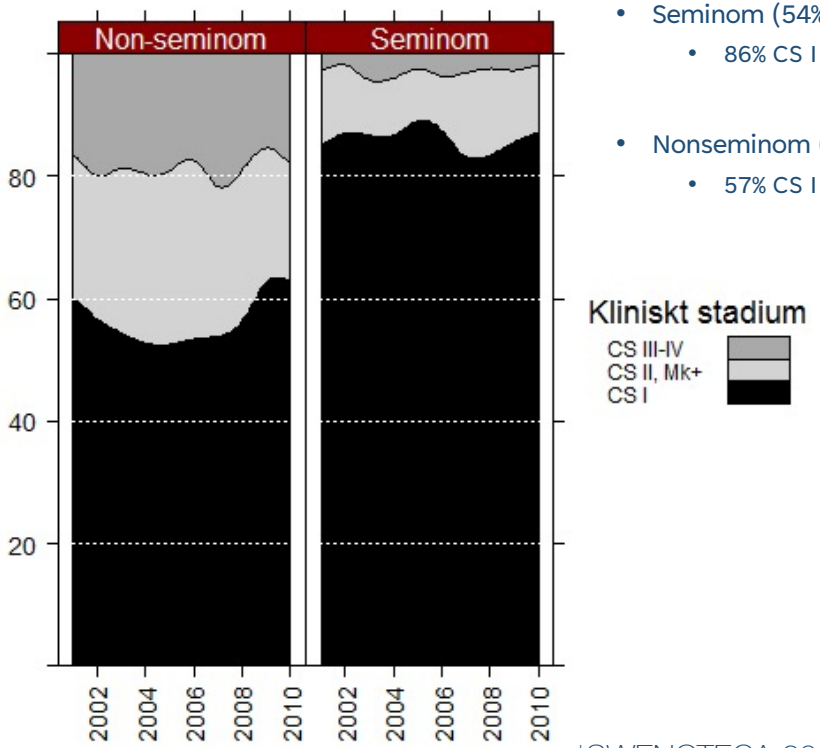
- Skal følges til normalisering etter orkiektomi, og

  under eventuell kjemoterapi (metastatisk sykdom)

Stadieinndeling, SWENOTECA / RMH

- CS I:
  - Ingen kliniske/radiologiske tegn til metastaser
- CS Mk+:
  - Forhøyde serum tumormarkører (AFP og/eller hCG) som eneste tegn til metastaser
- CS II:
  - Spredning til lymfeknuter under diafragma
- CS III
  - Spredning til lymfeknuter over diafragma
- CS IV
  - Ekstralymfatiske metastaser

  - A: Lymfeknuter i buken < 2 cm
  - B: Lymfeknuter i buken 2-5 cm
  - C: Lymfeknuter i buken > 5–10 cm
  - D: Lymfeknuter i buken > 10 cm



- Seminom (54%)
  - 86% CS I
- Nonseminom (46 %)
  - 57% CS I

*SWENOTECA 2001-2010

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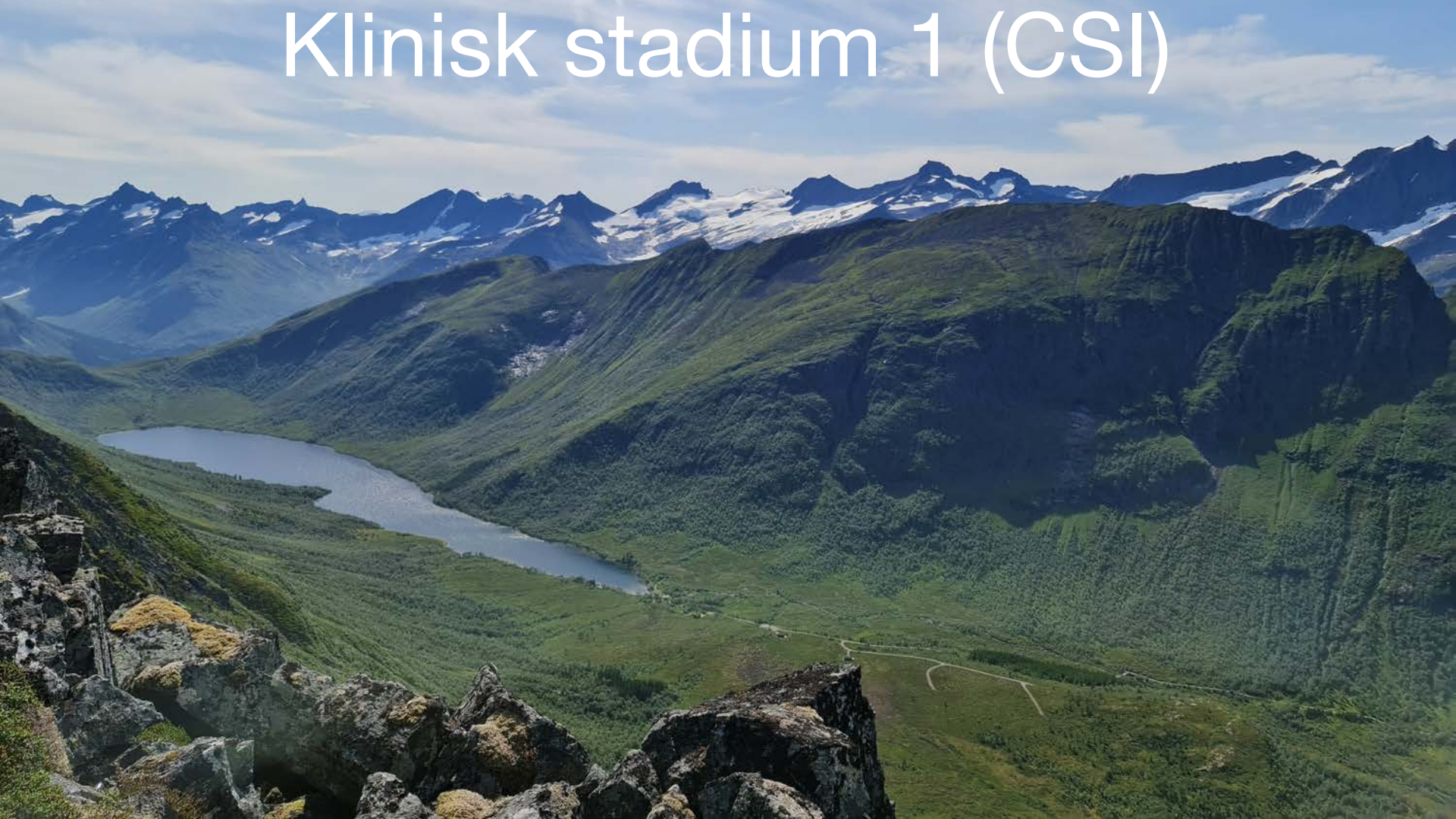
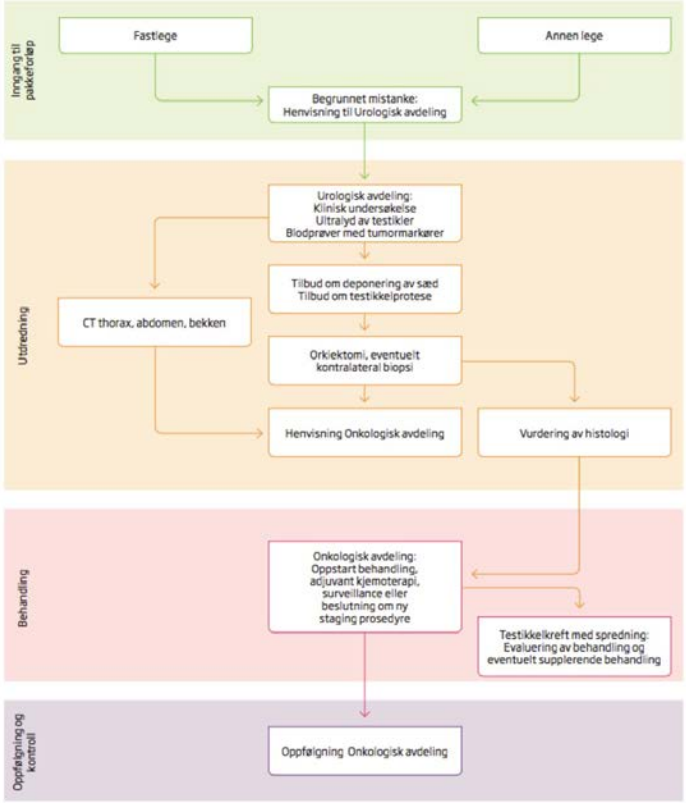
Klinisk stadium 1 (CSI)



Henvisningsrutiner urolog-onkolog CS I

- Henvises direkte til kreftavdeling, ikke vent på histologisk svar!
- Organiser kontroller av tumormarkører ved utreise
- Nonseminom: Blir kalt inn til endelig staging 6-8 uker etter orkiektomi
- Seminom: Blir kalt inn elektivt forløpende
- Info-skriv om testikkelkreft blir sendt til pasientens

  (kan også finnes på www.swenoteca.org)
- Samtykke SWENOTECA



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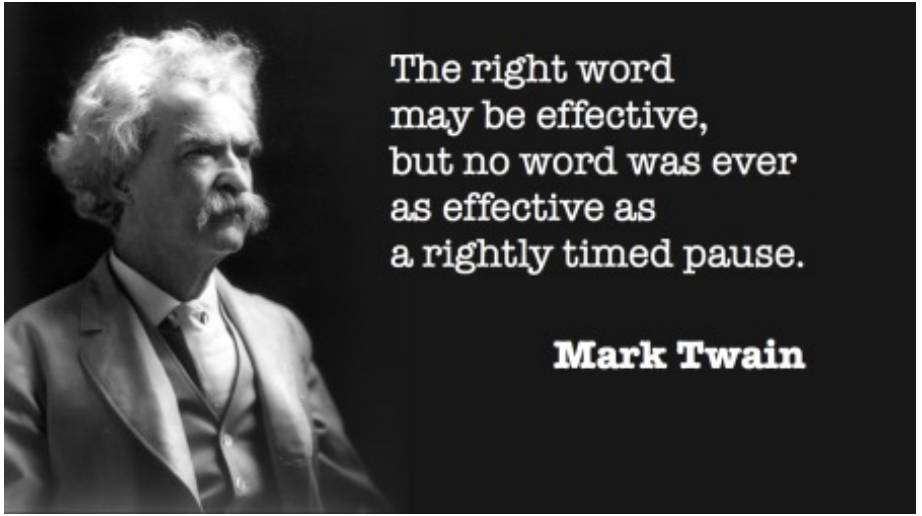
Utredning av pasienter med testikkelkreft CS I
Endelig staging 6-8 uker etter orkiektomi (nonseminom)

- Klinisk us.
- CT thorax/abdomen/bekken
- Tumormarkører/hormonanalyser
- Evt. regranskning av histologi



Seminom CS I

- Risikofaktorer
  - Stromal innvekst i rete testis
  - Tumor > 4 cm

- Risiko for recidiv
  - 5-8 % ved 0 risikofaktorer
  - 20 % ved 1-2 risikofaktorer

Seminom CS I terapimuligheter

- Strålebehandling
  - Adjuvant RT mot paraaortale ± iliacale lymfeknuter
- Adjuvant kjemoterapi
  - 1 kur karboplatin reduserer tilbakefall av sykdom med ca 60-70 %, dvs fra 15 % til 5-6 %
- Surveillance
  - Kun tette kontroller i 10 år, 15 % tilbakefall

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Management of Seminomatous Testicular Cancer: A Binational Prospective Population-Based Study From the Swedish Norwegian Testicular Cancer Study Group (SWENOTECA)

Torgrim Tandstad, Rune Smaaland, Arne Solberg, Roy M. Bremnes, Carl W. Langberg, Anna Laurell, Ulrika K. Stierner, Olof Ståhl, Eva K. Cavallin-Ståhl, Olbjørn H. Klepp, Olav Dahl, and Gabriella Cohn-Cedermark

From St. Olavs University Hospital, Trondheim; Stavanger University Hospi

ABSTRACT

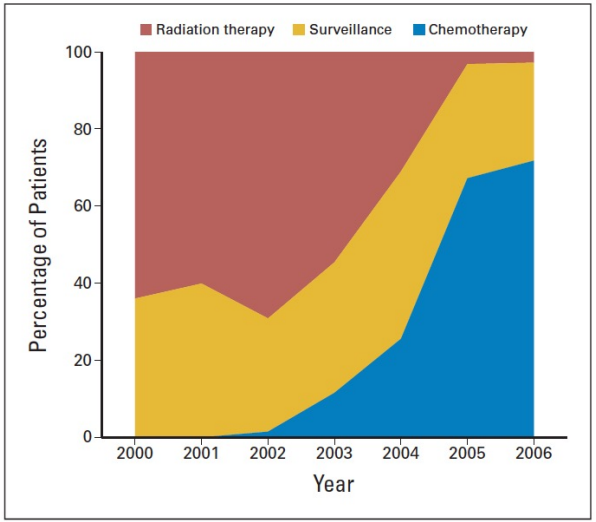


Fig 1. Development in the treatment of clinical stage 1 seminoma, 2000 to 2006.

SWENOTECA Swedish Norwegian Testicular Cancer Group · ST. OLAVS HOSPITAL TRONDHEIM UNIVERSITY HOSPITAL · NTNU

Seminom CS I terapimuligheter

- Alle modaliteter gir samme overlevelse på kort sikt 98-99 %
- Ulike bivirkninger
- Ulike seneffekter

Seminom CS I Strålebehandling

- Strålebehandling: Øker risiko for annen dødelig kreft senere i livet
- Ikke lenger standard behandling

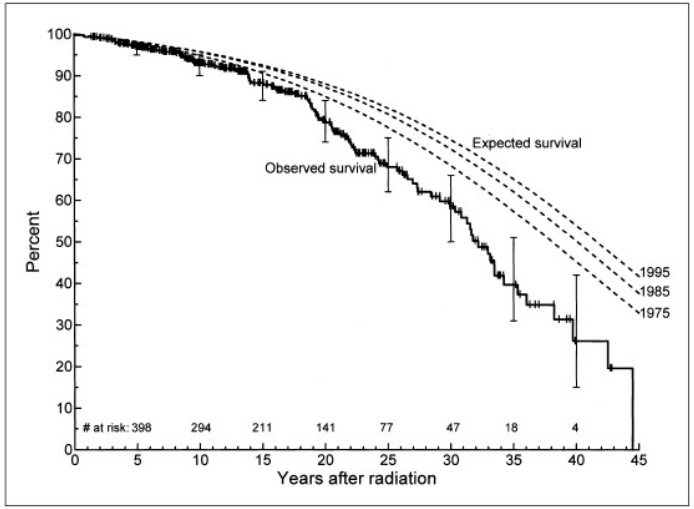


Fig 1. Survival of all 453 patients. Vertical bars are 95% CIs. The number of men at risk is shown above the abscissa. The individually age- and race-adjusted expected survival curves from life-tables for the male US population in 1975, 1985, and 1995 are also shown. These survival curves give the age- and race-adjusted expected survival rates for individuals subjected to the force of mortality in the US male population for that year.

Seminom CS I Adjuvant Karboplatin

- 88 % ingen nytte av behandling
- 12 % slipper tilbakefall (3 kurer kjemoterapi, 98 % overlevelse)

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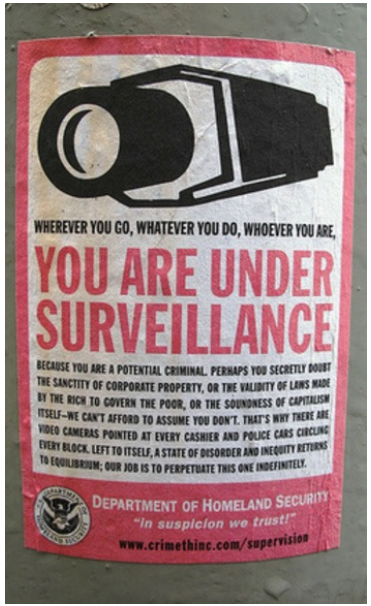
Seminom CS I Surveillance

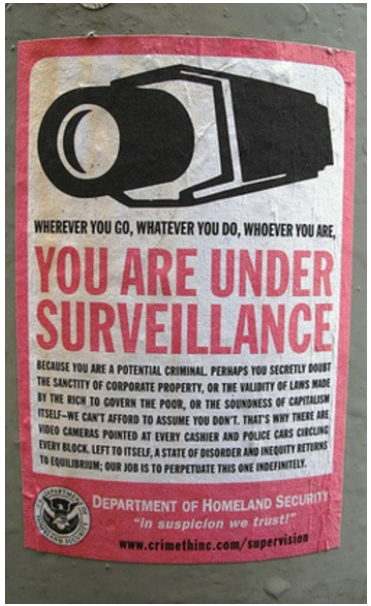
- 85 % kurert av orkiektomi alene
- 15 % får tilbakefall (3 kurer kjemoterapi, 98 % overlevelse)



Seminom CS I anbefalinger

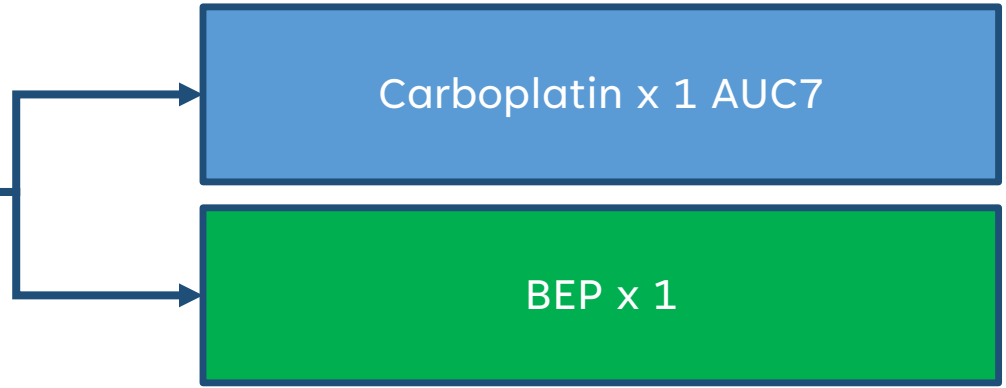
Samvalg: Diskusjon med pasienten etter muntlig/skriftlig informasjon

- Ingen risikofaktorer:
  - Surveillance
- 1-2 risikofaktorer:
  - Surveillance eller en kur adjuvant karboplatin
- Stråleterapi kan vurderes i individuelle tilfeller, men er ikke anbefalt som noen standard behandling



SWENOTECA ABC-study

High-risk CS1 Seminoma
Stromal invasion rete testis
and/or >4cm
1:1 randomization



Primary endpoint:
Relapse rate
Secondary endpoints:
Short-term toxicity
Long-term toxicity
Health related quality of life Overall survival
Health economy analysis

Status:
Inclusion pr. April 27, 2022 285/348
Protocol: www.swenoteca.org
PI: T. Tandstad

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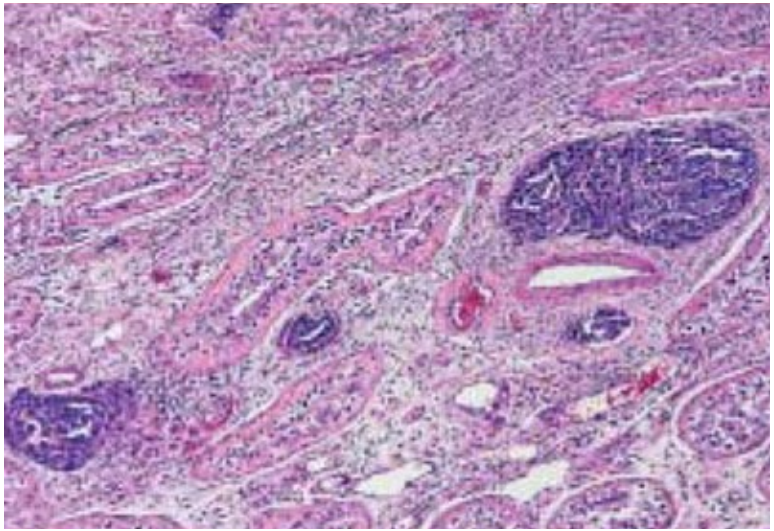
Nonseminom CS I

- Risiko for tilbakefall ved surveillence:
  - LVI+: 50% (30 % av pasienter)
  - LVI-: 15% (70 % av pasienter)

- 90 % av tilbakefall kommer de første to år etter orkiektomi

- Ca 2/3 av alle residiv kommer retroperitonealt

LVI+: Tumorceller i kar



Nonseminom CS I terapimuligheter

- RPLND
  - Unilateralt
- Adjuvant kjemoterapi
  - 1 kur BEP, reduserer risiko for tilbakefall med 90-95 %
- Surveillance
  - Kun tette kontroller i 5 år, 25 % tilbakefall (15 % hos VASC– og 50 % hos VASC+)

Nonseminom CS I terapimuligheter

- 75 % er kurert ved orkiektomi alene
- 25 % vil få tilbakefall (3 kurer BEP ± (kirurgi)
  - Kun 15 % med LVI-
  - Hele 50 % med LVI+

Nonseminom CS I Adjuvant BEP

- Reduserer risiko for tilbakefall med 90-95 %
- Kun 15 % av pasienter med LVI- har nytte av behandlingen
- 50 % av pasienter med LVI+ har nytte av behandlingen

Annals of Oncology

original articles

Annals of Oncology 25: 2167–2172, 2014
doi:10.1093/annonc/mdu375
Published online 11 August 2014

One course of adjuvant BEP in clinical stage I nonseminoma mature and expanded results from the SWENOTECA group

T. Tandstad[1*], O. Ståhl[2], U. Håkansson[3], O. Dahl[4,5], H. S. Haugnes[6,7], O. H. Klepp[8], C. W. Langberg[9], A. Laurell[10], J. Oldenburg[9], A. Solberg[1], K. Söderström[11], E. Cavallin-Ståhl[2], U. Stierner[12], R. Wahlquist[13], N. Wall[14] & G. Cohn-Cedermark[15,16] on behalf of SWENOTECA

VOLUME 27 · NUMBER 13 · MAY 1 2009

JOURNAL OF CLINICAL ONCOLOGY

ORIGINAL REPORT

Risk-Adapted Treatment in Clinical Stage I Nonseminomatous Germ Cell Testicular Cancer: The SWENOTECA Management Program

Torgrim Tandstad, Olav Dahl, Gabriella Cohn-Cedermark, Eva Cavallin-Stahl, Ulrika Stierner, Arne Solberg, Carl Langberg, Roy M. Bremnes, Anna Laurell, Hans Wijkström, and Olbjørn Klepp

From the Department of Oncology, St Olavs University Hospital, Trondheim;

A B S T R A C T

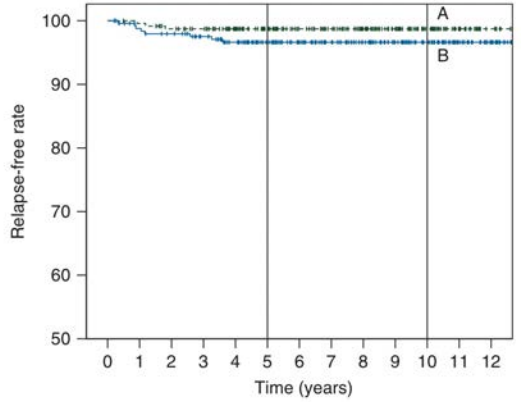


Figure 1. Kaplan–Meier curves for relapse-free rates by risk group; (A) patients without lymphovascular invasion; (B) patients with lymphovascular invasion.

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Nonseminom CS I anbefalinger

Pas deltar i beslutningen etter muntlig/skriftlig informasjon

- LVI+: 1 kur adjuvant BEP
- LVI- : Surveillance, men mulighet for 1 kur adjuvant BEP etter pasientens ønske

Metastatisk sykdom

Henvisningsrutiner urolog-onkolog

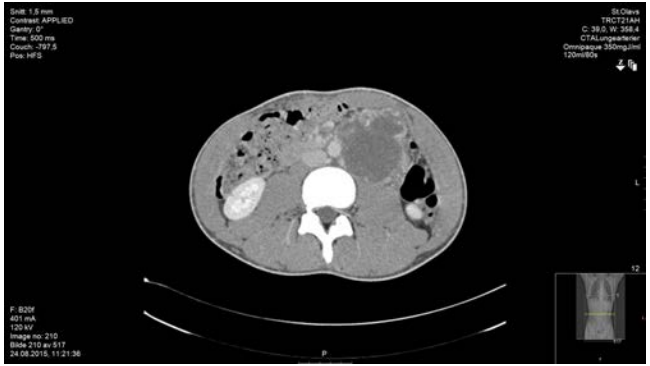
- Ved metastaser skal pasienten utredes og behandles snarest ved Universitetssykehus (Oslo, Bergen, Trondheim, Tromsø)
- Henvis pasienten direkte, enten ved intern henvising eller kontakt (telefon, fax). Ikke avvent til epikrise!
- Utbredt metastasering, klinisk sikker testikkelkreft og patologiske verdier av hCG eller AFP og kritisk syk pasient:
  - Start av kjemoterapi høyeste prioritet ofte uten forutgående orkiektomi

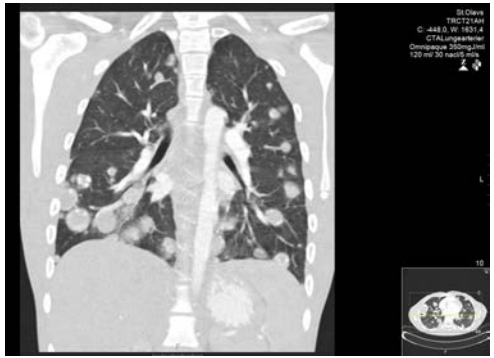
Metastatisk sykdom

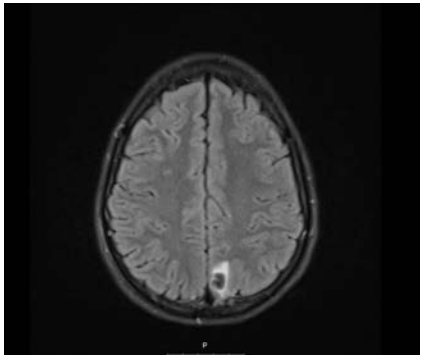
Metastaser på diagnosetidspunkt:

- 15 % ved seminom
- 45 % ved non seminom

- Helbredelse oppnås hos >90%
- Prognose er avhengig av stadium og tumormarkører







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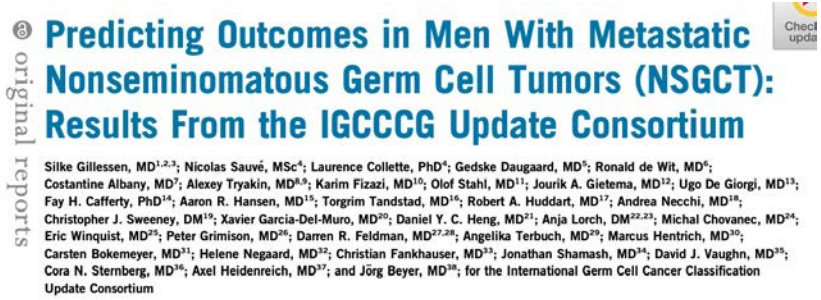
Prognostiske grupper

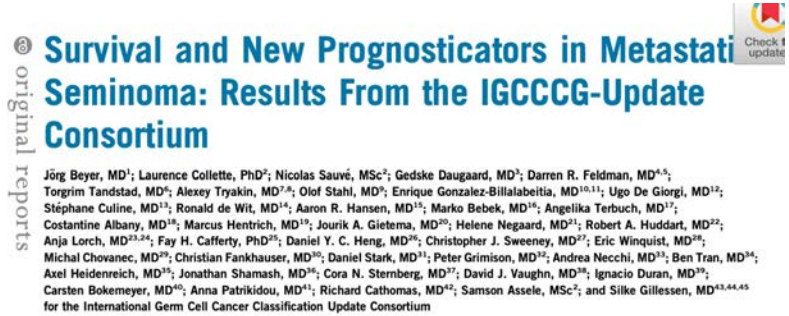
- Tar hensyn til:
  - Primært utgangspunkt (gonadal / ekstragonadal)
  - Histologisk type (seminom / nonseminom)
  - Lokalisering av evt. ekstragonadal primærtumor
  - Lokalisering av viscerale metastaser (kun lunge-metastaser versus andre ikke-nodale metastaser)
  - Serum-verdi av AFP, hCG, LDH



original reports

Predicting Outcomes in Men With Metastatic Nonseminomatous Germ Cell Tumors (NSGCT): Results From the IGCCCG Update Consortium

Silke Gillessen, MD[1,2,3]; Nicolas Sauvé, MSc[4]; Laurence Collette, PhD[4]; Gedske Daugaard, MD[5]; Ronald de Wit, MD[6]; Costantine Albany, MD[7]; Alexey Tryakin, MD[8,9]; Karim Fizazi, MD[10]; Olof Stahl, MD[11]; Jourik A. Gietema, MD[12]; Ugo De Giorgi, MD[13]; Fay H. Cafferty, PhD[14]; Aaron R. Hansen, MD[15]; Torgrim Tandstad, MD[16]; Robert A. Huddart, MD[17]; Andrea Necchi, MD[18]; Christopher J. Sweeney, DM[19]; Xavier Garcia-Del-Muro, MD[20]; Daniel Y. C. Heng, MD[21]; Anja Lorch, DM[22,23]; Michal Chovanec, MD[24]; Eric Winquist, MD[25]; Peter Grimison, MD[26]; Darren R. Feldman, MD[27,28]; Angelika Terbuch, MD[29]; Marcus Hentrich, MD[30]; Carsten Bokemeyer, MD[31]; Helene Negaard, MD[32]; Christian Fankhauser, MD[33]; Jonathan Shamash, MD[34]; David J. Vaughn, MD[35]; Cora N. Sternberg, MD[36]; Axel Heidenreich, MD[37]; and Jörg Beyer, MD[38]; for the International Germ Cell Cancer Classification Update Consortium



original reports

Survival and New Prognosticators in Metastati Seminoma: Results From the IGCCCG-Update Consortium

Jörg Beyer, MD[1]; Laurence Collette, PhD[2]; Nicolas Sauvé, MSc[2]; Gedske Daugaard, MD[3]; Darren R. Feldman, MD[4,5]; Torgrim Tandstad, MD[6]; Alexey Tryakin, MD[7,8]; Olof Stahl, MD[9]; Enrique Gonzalez-Billalabeitia, MD[10,11]; Ugo De Giorgi, MD[12]; Stéphane Culine, MD[13]; Ronald de Wit, MD[14]; Aaron R. Hansen, MD[15]; Marko Bebek, MD[16]; Angelika Terbuch, MD[17]; Costantine Albany, MD[18]; Marcus Hentrich, MD[19]; Jourik A. Gietema, MD[20]; Helene Negaard, MD[21]; Robert A. Huddart, MD[22]; Anja Lorch, MD[23,24]; Fay H. Cafferty, PhD[25]; Daniel Y. C. Heng, MD[26]; Christopher J. Sweeney, MD[27]; Eric Winquist, MD[28]; Michal Chovanec, MD[29]; Christian Fankhauser, MD[30]; Daniel Stark, MD[31]; Peter Grimison, MD[32]; Andrea Necchi, MD[33]; Ben Tran, MD[34]; Axel Heidenreich, MD[35]; Jonathan Shamash, MD[36]; Cora N. Sternberg, MD[37]; David J. Vaughn, MD[38]; Ignacio Duran, MD[39]; Carsten Bokemeyer, MD[40]; Anna Patrikidou, MD[41]; Richard Cathomas, MD[42]; Samson Assele, MSc[2]; and Silke Gillessen, MD[43,44,45] for the International Germ Cell Cancer Classification Update Consortium

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Overlevelse Prognostiske Grupper

- Seminom
  - God prognosegruppe: 95%
  - Intermediær: 88%
- Nonseminom
  - God prognosegruppe: 96%
  - Intermediær: 90%
  - Dårlig: 67%

I. Prognostic risk group classification according to IGCCCG

Nonseminoma	Seminoma
Good prognosis	
Primary site: Testis or retroperitoneum **and** No non-pulmonary visceral metastases (for example liver, bone, brain) **and all** good markers ß-hCG < 5000 IU/L (1000 µg/L) **and** AFP < 1000 µg/L **and** LDH < 1.5 x ULN	Any primary site **and** No non-pulmonary visceral metastases (for example liver, bone, brain) **and** any ß-hCG, any LDH and normal AFP *LDH > 2.5 x ULN may imply a worse prognosis within the good prognosis group*
Intermediate prognosis	
Primary site: Testis or retroperitoneum **and** No non-pulmonary visceral metastases (for example liver, bone, brain) **and any** intermediate markers ß-hCG ≥ 5000 IU/L and ≤ 50000 IU/L **or** AFP ≥ 1000 and ≤ 10000 µg/L **or** LDH ≥ 1.5 x ULN ≤ 10 x ULN	Non-pulmonary visceral metastases (for example liver, bone, brain)
Poor prognosis	
Mediastinal primary **or** Non-pulmonary visceral metastases (for example liver, bone, brain) **or any** poor markers ß-hCG > 50000 IU/L) **or** AFP > 10000 µg/L **or** LDH > 10 x ULN	No seminoma with poor prognosis

Formål med dagens behandling: Bevare kurasjon, minske bivirkninger

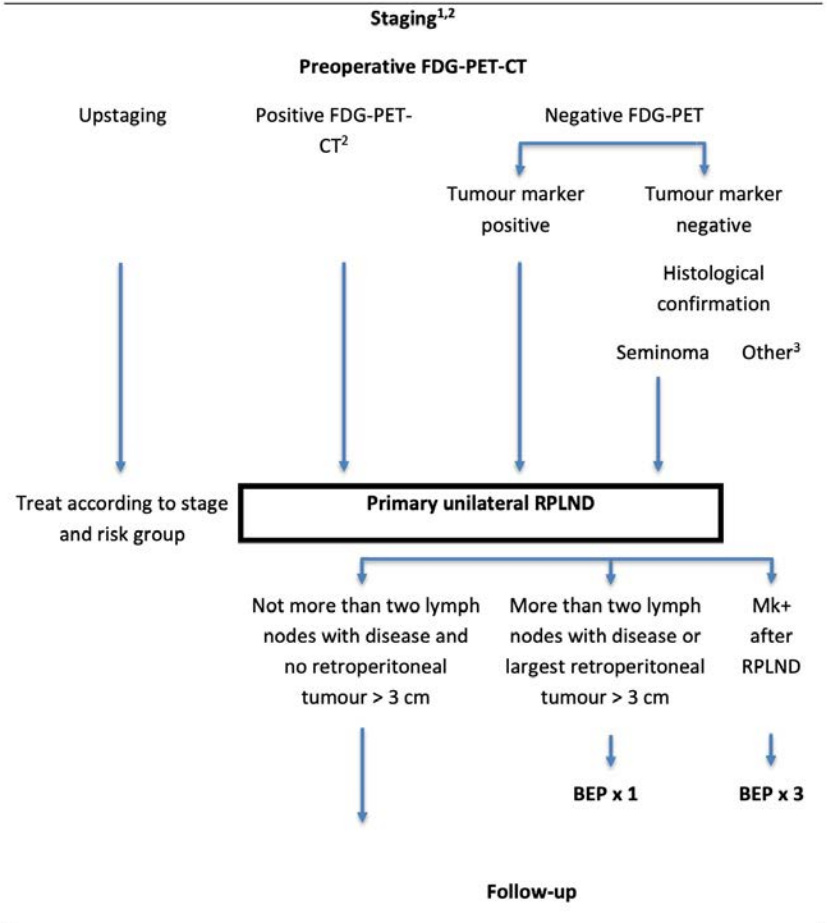
- Mindre strålebehandling
- Mindre cellegift
- Færre tilbakefall
- Bedre livskvalitet

Behandling god prognose metastatisk sykdom

BEP x 3

- Nonseminom: RPLND ved restforandringer (over 1 cm, uansett plan) etter fullført kjemoterapi
- Seminom: PET av restforandringer etter fullført kjemoterapi over 3 cm (ved positive PET, videre utredning og evt kirurgi)

III. Flowchart RPLND Clinical Stage IIA-IIB (≤ 3 cm) Seminoma

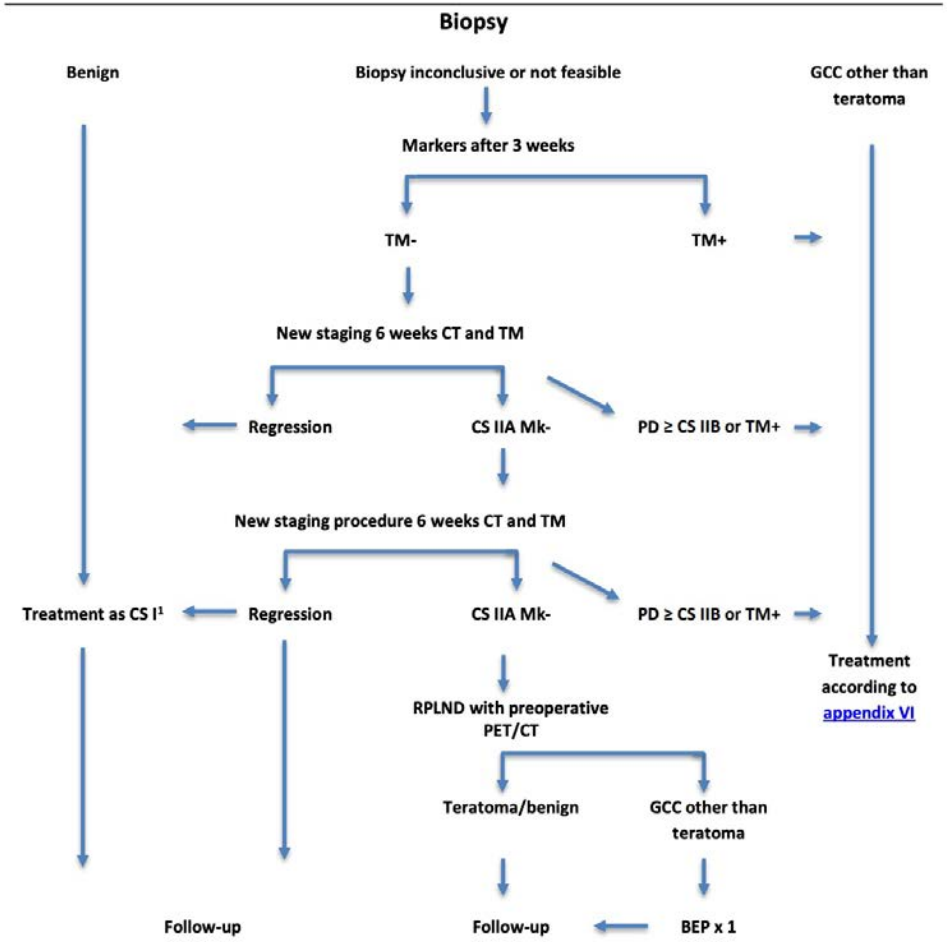


[1]To properly stage patients in CS IIA, see 5.7.1
[2]Not more than two lymph nodes or disease outside unilateral RPLND template
[3]Surveillance if benign, treat according to stage and risk group if nonseminoma

Unntak 1

Metastatisk seminom:
1-2 lymfeknutemetastaser
max størrelse 3 cm

VI. Flowchart Nonseminoma CS IIA Mk- at Diagnosis/Staging



Unntak 2

Metastatisk nonseminom CSIIA

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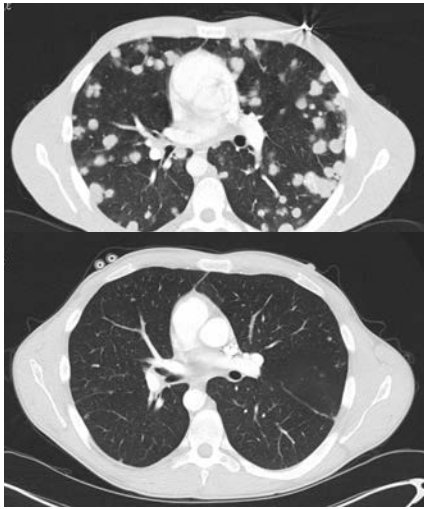
Behandling intermediær og dårlig prognose metastatisk sykdom

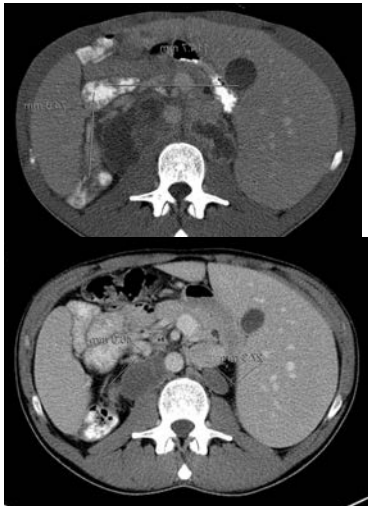
BEP x 4

- Nonseminom: RPLND ved restforandringer (over 1 cm, uansett plan) etter fullført kjemoterapi
- Seminom: PET av restforandringer etter fullført kjemoterapi over 3 cm (ved positive PET, videre utredning og evt kirurgi)

Evaluering under behandling

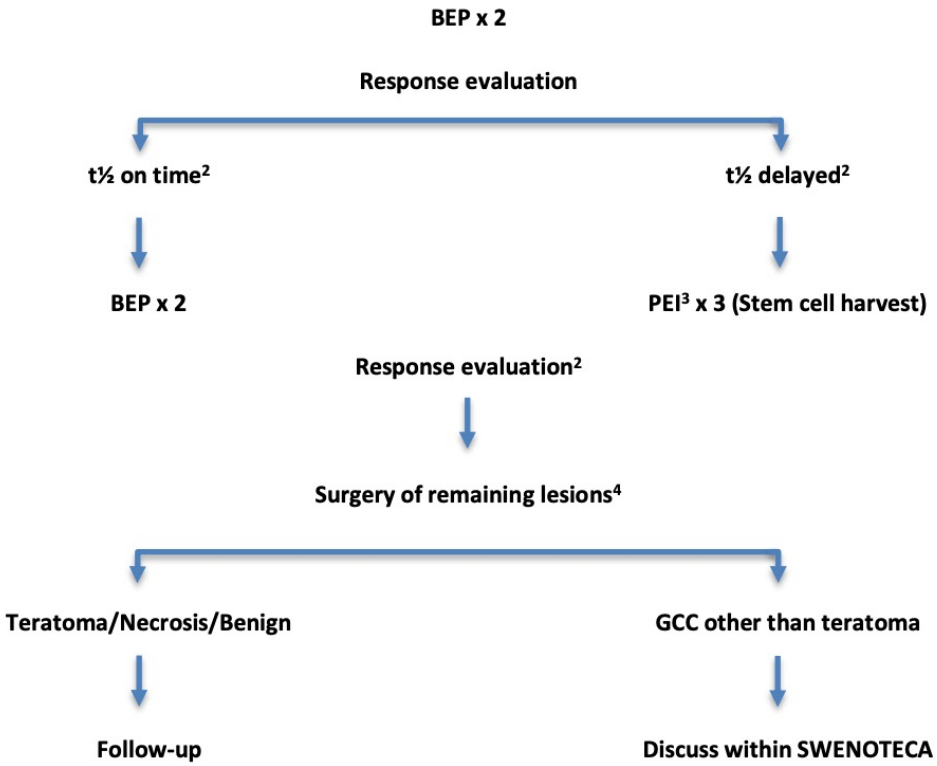
- CT thorax/abdomen/bekken
- Tumormarkører bør falle i henhold til halveringstid (AFP 7 døgn, hCG 3 døgn)





- Om tumormarkørene faller for sent blir behandlingen intensifisert

Flowchart Metastatic Nonseminoma Intermediate and Poor Prognosis, excluding Non-pulmonary Visceral Metastasis or Primary Mediastinal Tumour [1]



Eksempel på intensivering

Metastasekirurgi etter kjemoterapi

- **Non-seminom**

  RPLND ved restglandler > 1 cm.

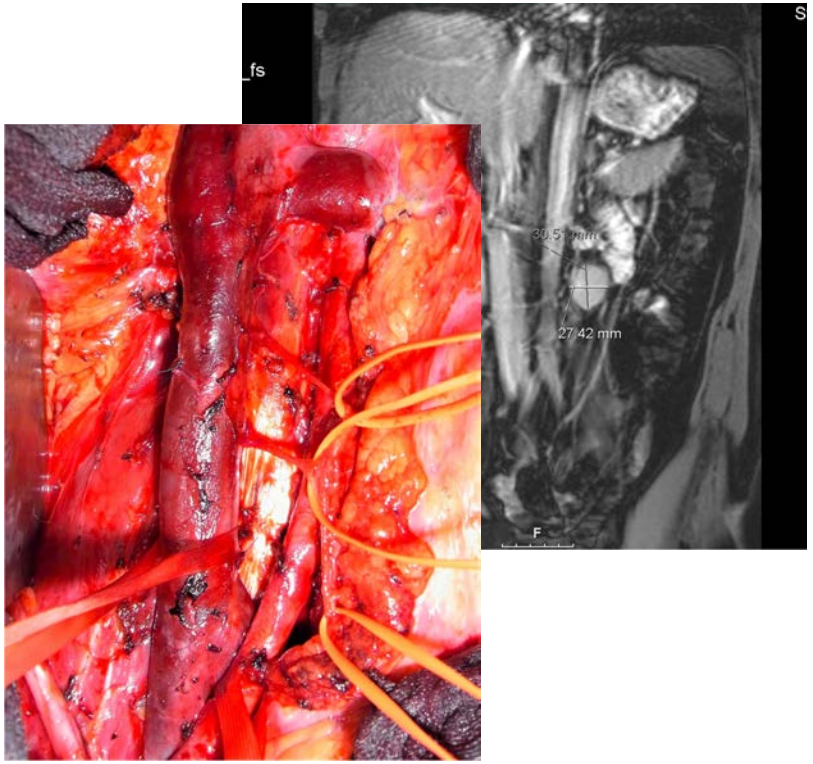
  1/3 av pasientene har vitalt tumorvev,

  1/3 har teratom, som må fjernes radikalt

  1/3 har kun nekrose/fibrose

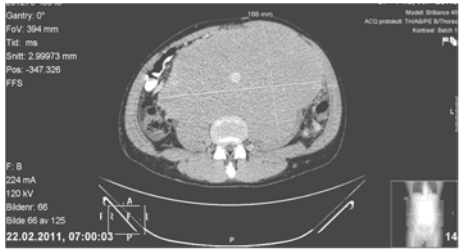
  Kirurgi ved øvrige restforandringer

  (lunge, lever, hjerne...)



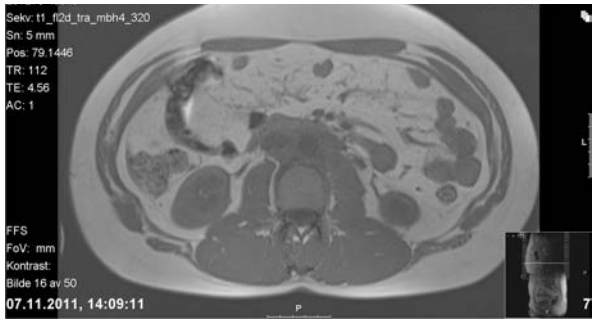
Etterkontroll ved testikkelkreft

- Ved tilbakefall er det alltid kurativ behandlingsintensjon



Etterkontroller spesielt viktig der man har "valgt bort" adjuvant behandling

- I Norge sentralisert til regional onkologisk avdeling



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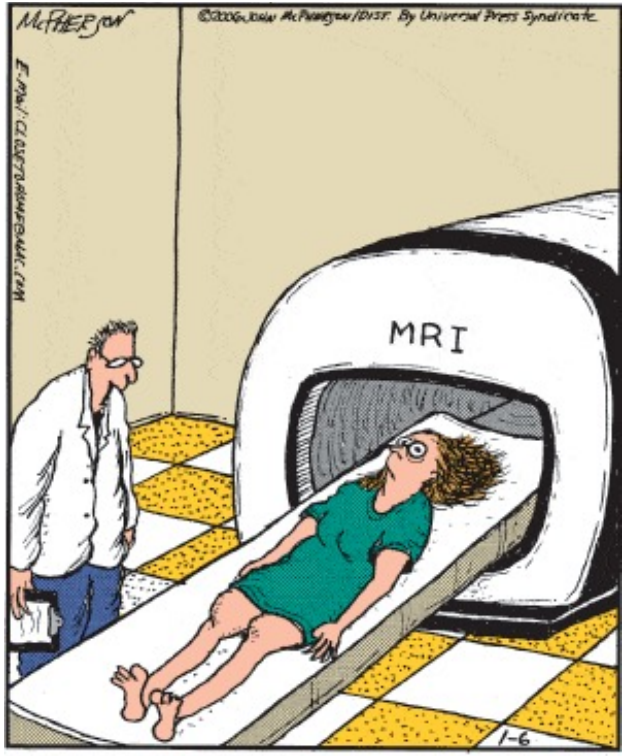
Etterkontroll ved testikkelkreft, prinsipper

- Regelmessige kontroller

  Se swenoteca.org

- Innhold
  - Klinisk status (obs gjenværende testis)
  - MR abd/bekken
  - Tumormarkører
  - (Rtg thorax)



"OK, Mrs. Dunn. We'll slide you in there, scan your brain, and see if we can find out why you've been having these spells of claustrophobia."

XV. Follow-up schedule for nonseminoma stage I, surveillance

Name: _____Civic registration number: _____
Orchiectomy, date: _____Side: right / left LVI: yes/no
Date definitive staging: _____
Recurrence date: _____fill out new form and switch FU

TUMOR MARKERS SHOULDBE CHECKED EVERY 2 MONTHS YEAR 1 FOR PATIENTS WITH LVI+ MANAGED BY SURVEILLANCE

Control type **B**: Patient contact, AFP, β-hCG, LDH, S-creatinine, **MRI of the retroperitoneum/** (abdominopelvic CT).
Control type **C**: Like B with addition of clinical examination, testosterone, SHBG, LH, FSH.
Control type **TM**: Tumour markers, AFP, β-hCG and LDH *(List the patient for a telephone appointment).*

Scrotal ultrasound when clinically indicated. Metabolic screening (lipids, fasting glucose, HbA1c), and blood pressure at 1- and 5-year visit. Inform Swedish patients at 1- and 5- year visit that a quality of life questionnaire will be sent out from RCC Syd, Sweden.

Months from end of treatment:

	TM	B	TM	C	Follow-up year 1
0	3	6	9	12	
	TM	B	TM	B	Follow-up year 2
12	15	18	21	24	
		TM		C	Follow-up year 3
24		30		36	
		TM		B	Follow-up year 4
36		42		48	
		TM		C	Follow-up year 5
48		54		60	

Postpubertal teratoma: No TM check-up month 3, 9, 15, 21

Etterkontroller eksempel

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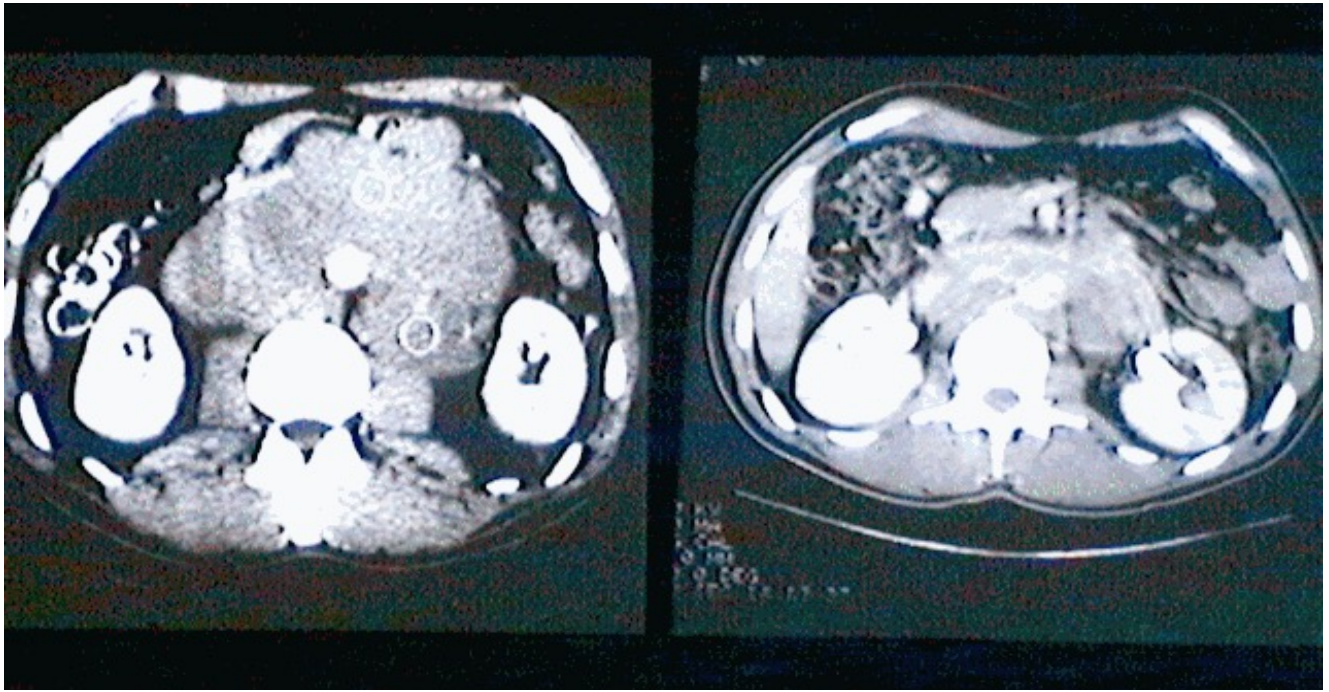
Seminom-metastaser før og etter en abdominal CT…

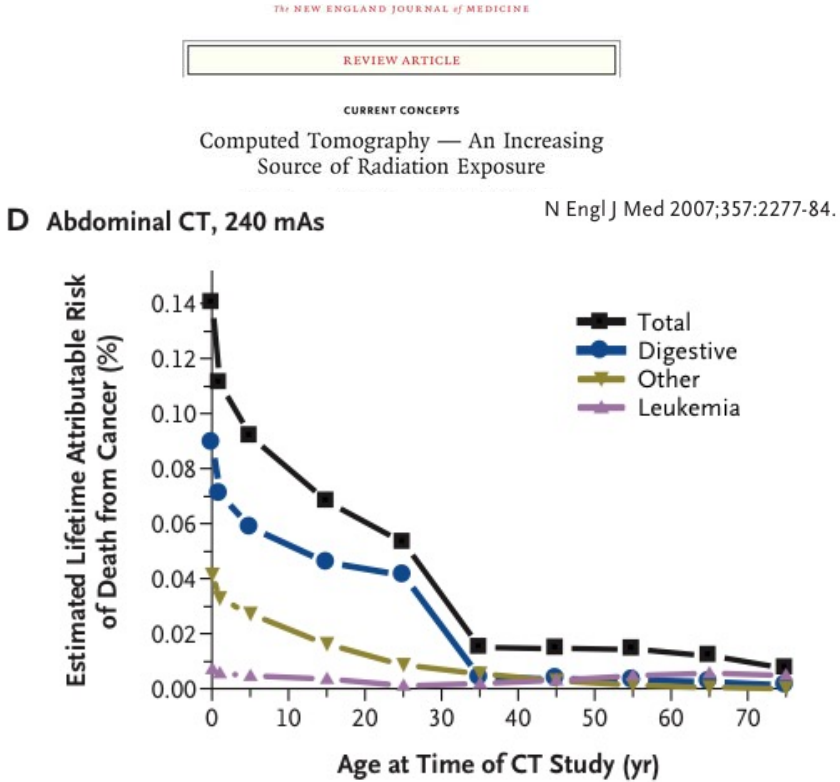


After treatment – During follow-up

- Secondary cancer from medical imaging?
  - CT abdomen 10 mSv
  - CT abdomen /pelvis 14 mSv
  - CT whole body 20-25 mSv

- Abdominal imaging during follow-up
  - SWENOTECA CSI nonseminom:
    - 1998: 14 CT abdomen/pelvis
    - 2012: 6 MRI abdomen/pelvis
- MRI
  - No ionizing radiation

- Whole body PET-CT
  - Up to 32 mSv[1], i.e.0.032 Gy
    - Bladder 80 mSv



Background radiation: 2.4 mSv

[1]Huang et al. Radiology 2009

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Etterkontroll ved testikkelkreft

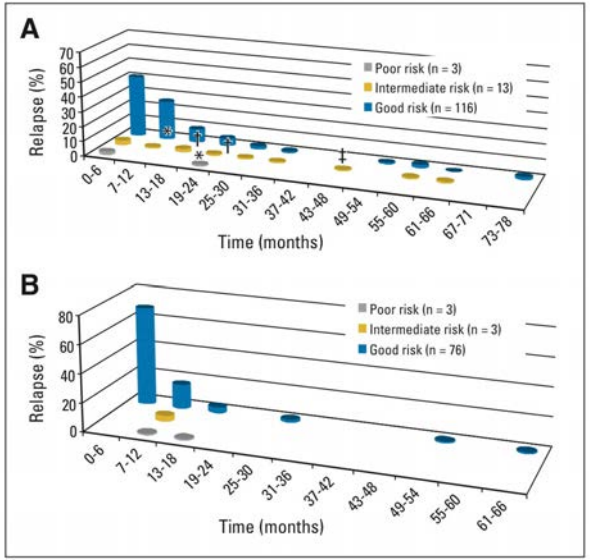
- De fleste tilbakefall kommer innen 18 måneder
- Oftere sene residiv ved seminom
- 60 - 70% av residivene først retroperitonealt
- Ved nonseminom 60 - 70% forhøyet AFP/hCG v. residiv

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Patterns of Relapse in Patients With Clinical Stage I Testicular Cancer Managed With Active Surveillance

Peter C. Black and Alan I. So, University of British Columbia, The Vancouver

Christian Kollmannsberger, Torgrim Tandstad, Philippe L. Bedard, Gabriella Cohn-Cedermark, Peter W. Chung, Michael A. Jewett, Tom Powles, Padraig R. Warde, Siamak Daneshmand, Andrew Protheroe, Scott Tyldesley, Peter C. Black, Kim Chi, Alan I. So, Malcom J. Moore, and Craig R. Nichols



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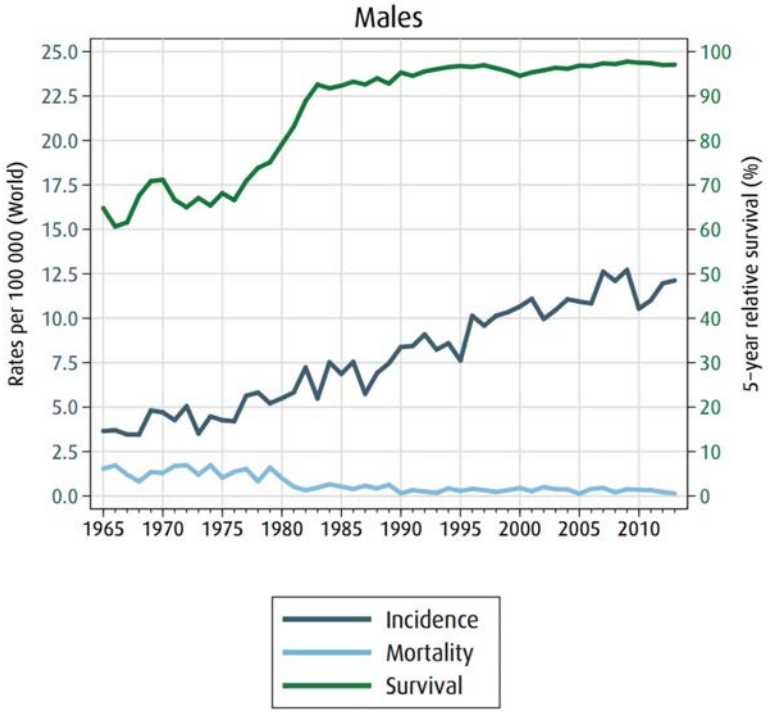
Why is long-term toxicity important in testicular cancer survivors (TCS)?

Very high cure rate

- CS I
  - 5 years OS: >98%[1,2]
- Metastatic
  - Nonseminoma: 5 years OS: >90%[3]
  - Seminoma: 5 years OS: >96%[2]

Long life-expectancy following treatment (40-70 years)



[1]Tandstad et al. JCO 2009; [2]Tandstad et al. JCO 2011; [3]Olofsson et al. JCO 2011

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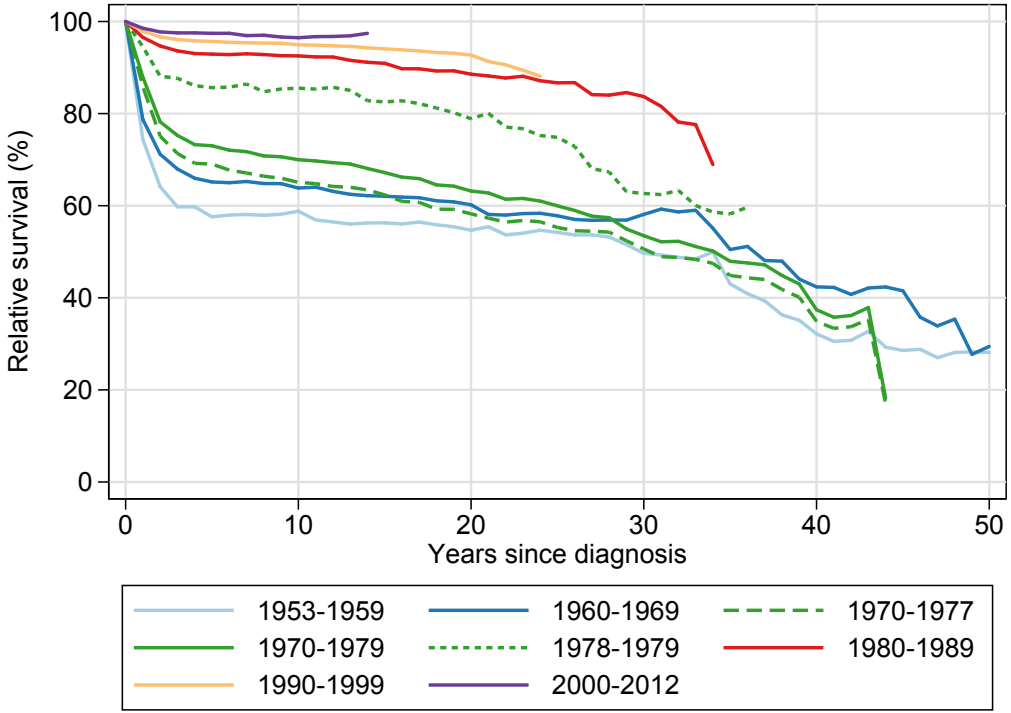
The Past - Consequences



- Relative survival of TCS (graph should be flat if survival was comparable with general population)
- Late effects affecting mortality does not show until 20+ of follow-up

Kvammen & Tandstad et al. (in press)

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