

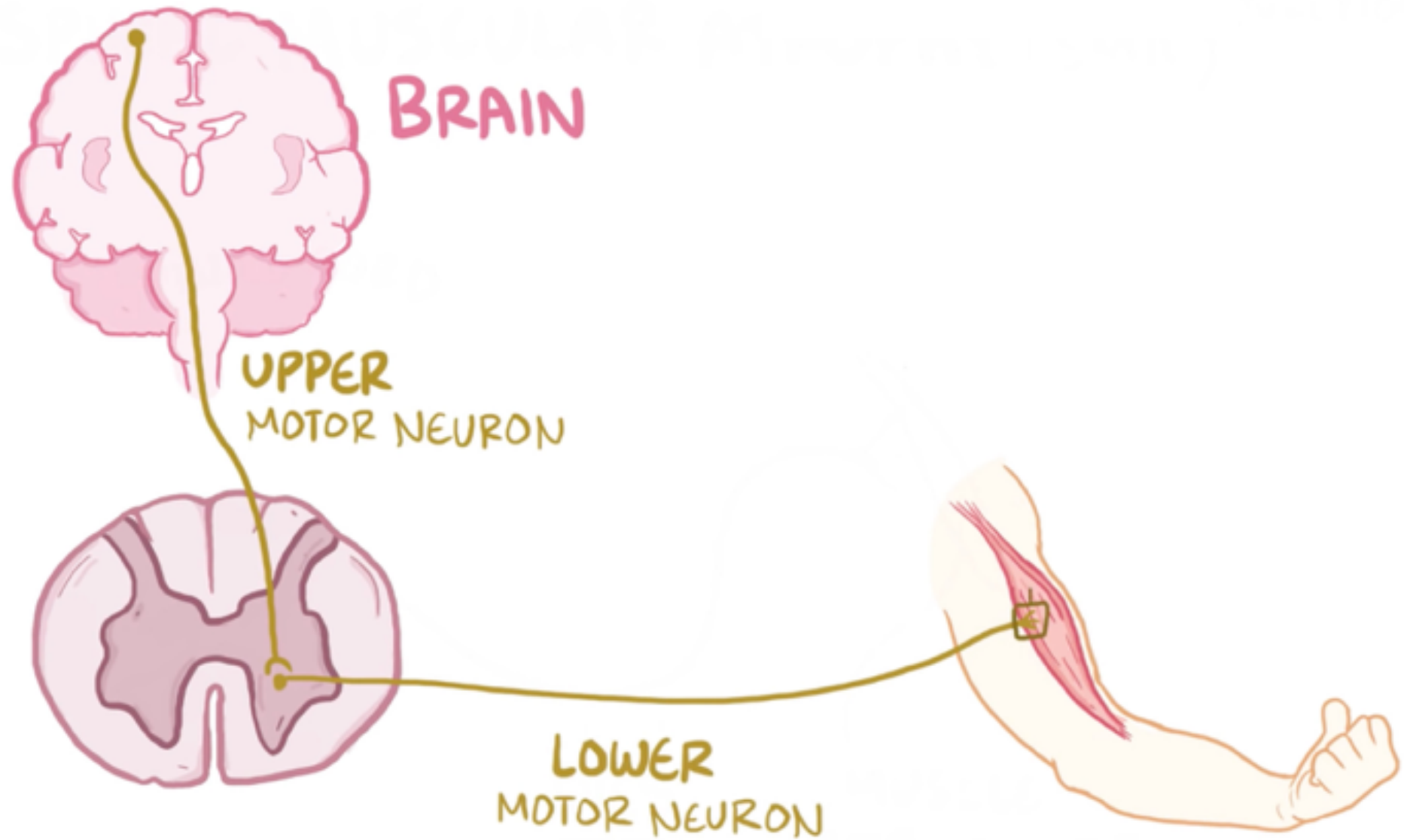


Spinal muskelatrofi:

- *Diagnose og bakgrunn*

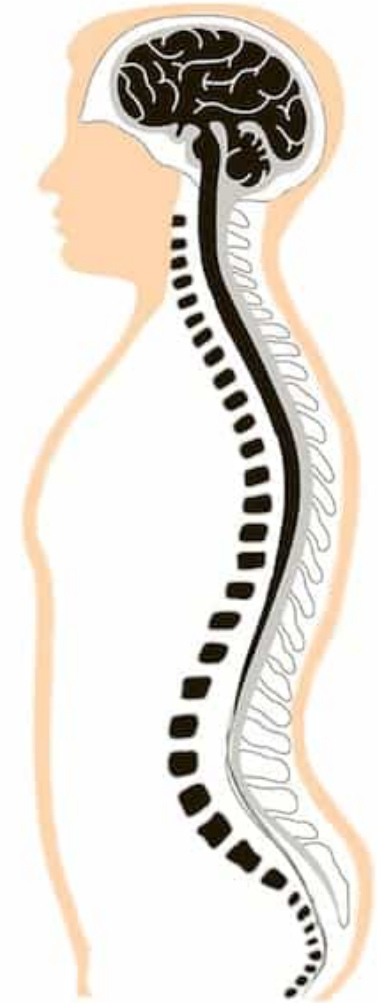
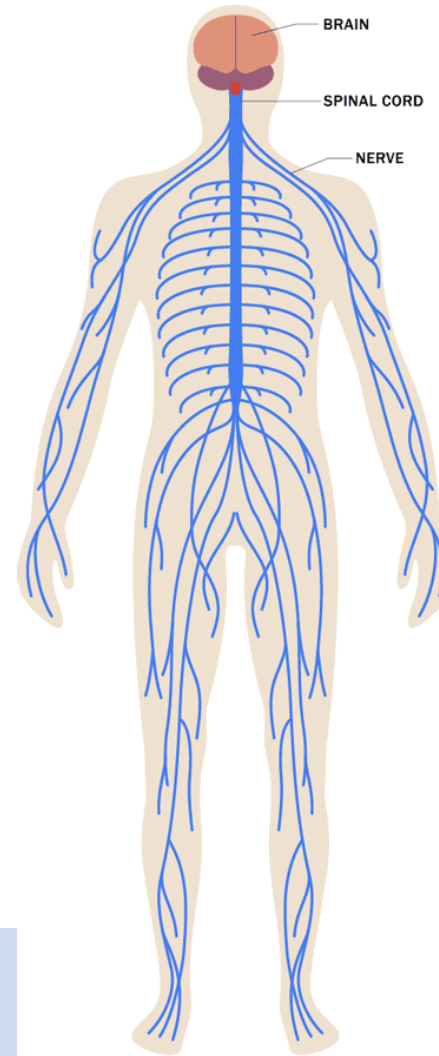
Sean Wallace PhD, og Magnhild Rasmussen PhD

Barneavdeling for nevrofag, OUS



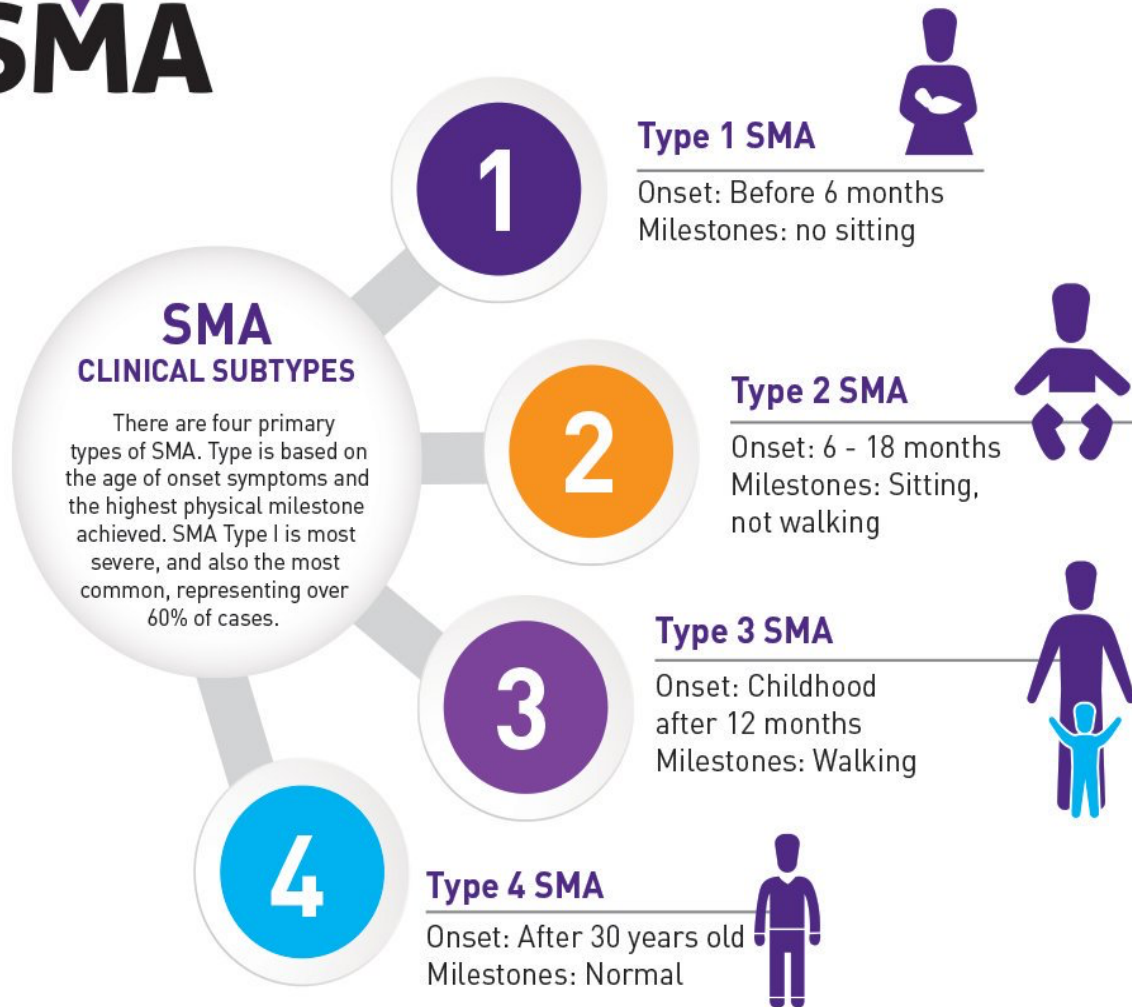
Spinal Muskelatrofi

- Spinal ryggmarg
- Muskelatrofi muskelsvin
- Diagnose genetisk
- Klassifikasjon klinisk



Spinal Muskelatrofi

<i>International SMA consortium:</i>			
TYPE	DEBUT	MOTORIKK	LIFE EXP.
SMA 1 - alvorlig	< 6 mnd.	Sitter aldri	< 2 år
SMA 2 - intermediær	6 – 18 mnd.	Sitter; Går aldri	50% 20 – 30 år
SMA 3 - mild	> 18 mnd.	Går	Normal



SMA - 1 in 11,000 live births

1 in 40 to 67 adults is a carrier.

SMA I occurs in 5.83 per 100,000 live births,
or 60% of all SMA cases

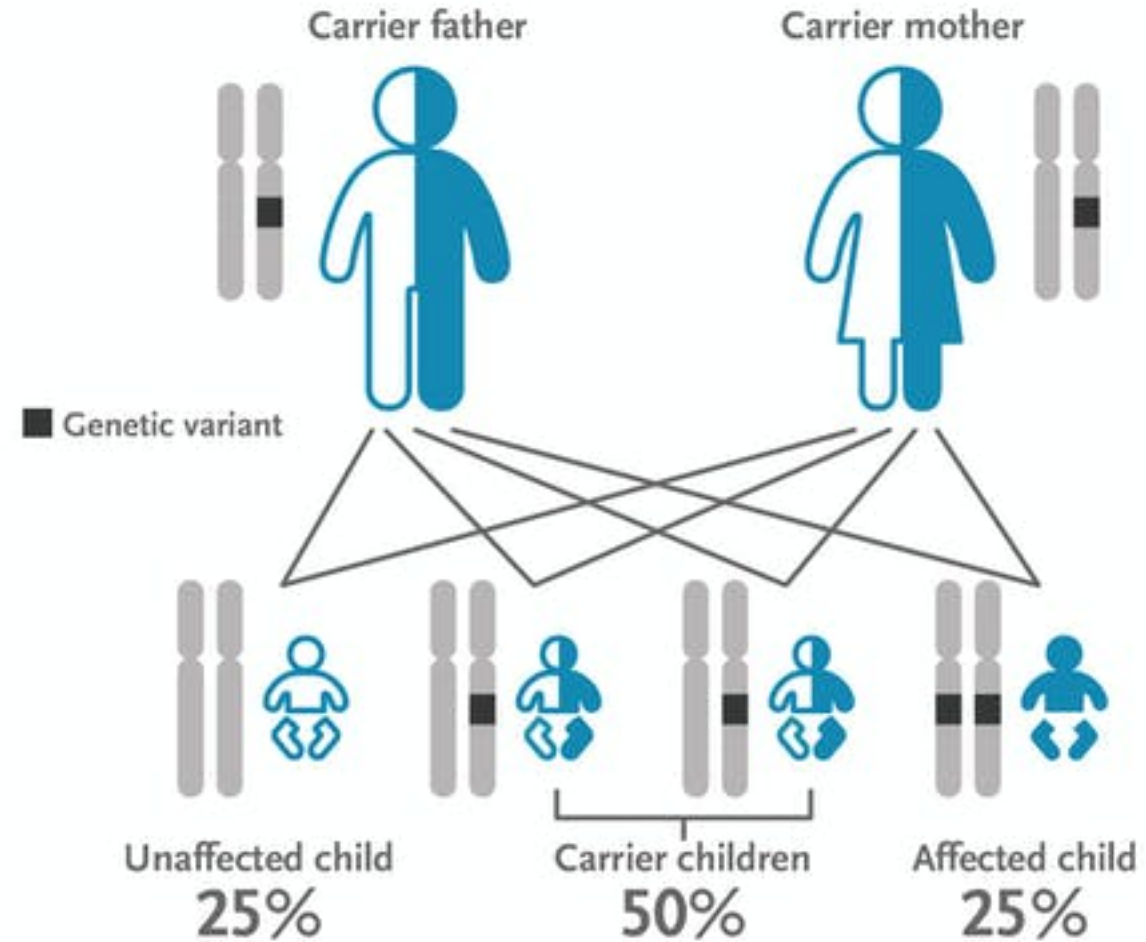
SMA II occurs in 2.66 per 100,000 live births,
or 27% of all SMA cases

SMA III occurs in 1.20 per 100,000 live births,
or 12% of all SMA cases



Genetikk

Autosomal recessive





Werdnig
description
1891



1893
Hoffmann
description

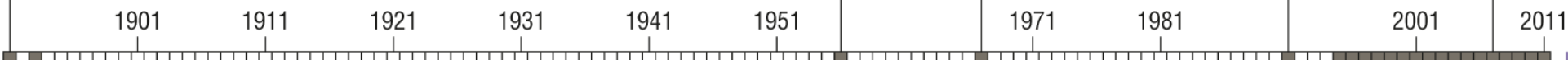


Kugelberg/
Welander
description
1956

3 Groups
outlined
1967

3 Type
classification
1991

Standard
of care
document
2007



1995 1996 1997 1998 1999 2000 2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011

**Discovery
of *SMN*
gene**

Molecular genetics of
SMN/SMN2 gene



↑ *SMN* by RNA-based therapy

Preclinical use of RNA-based therapy

↑ *SMN* by small molecules
Preclinical use of small molecules

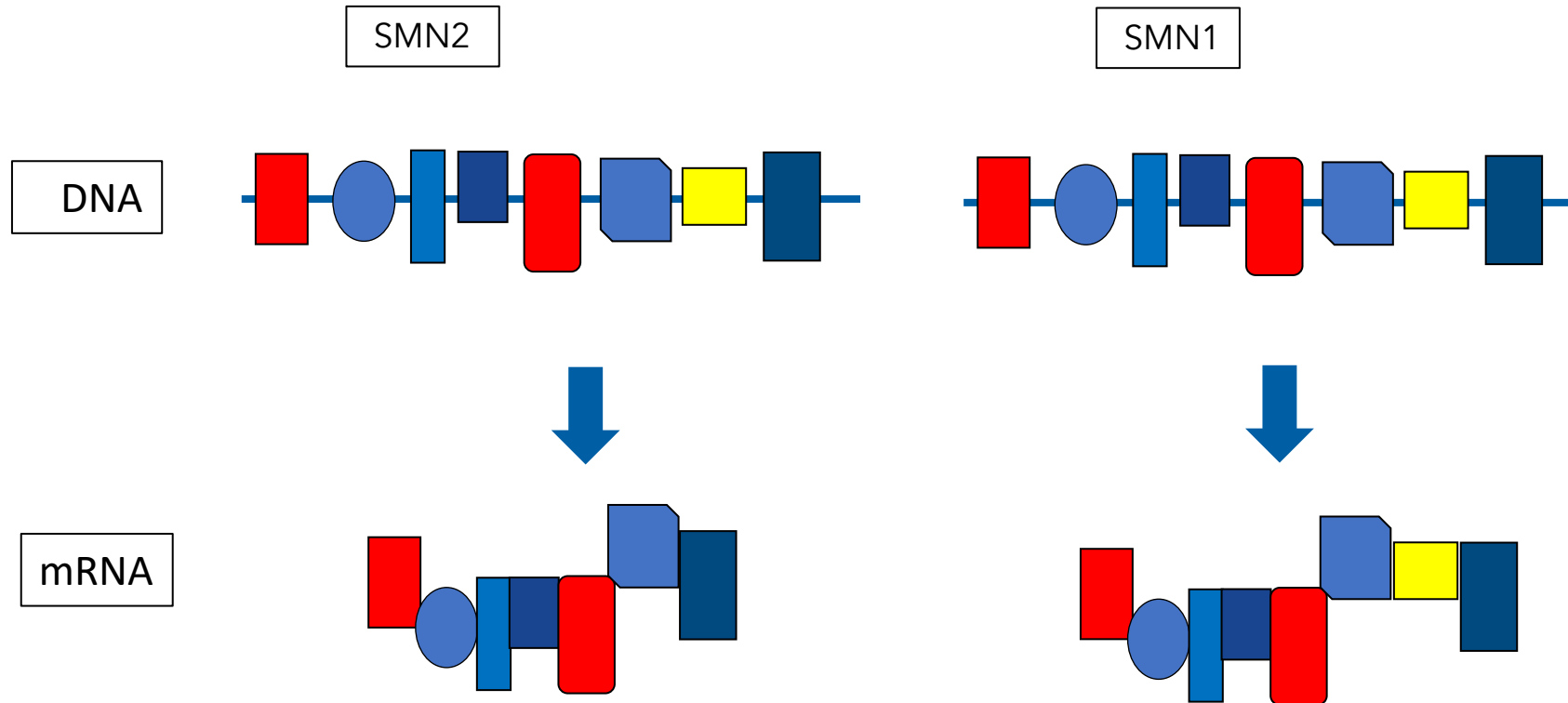
Clinical trials using small molecules

↑ *SMN* by gene therapy
Preclinical use of gene therapy

**Motor
neuron
survival**



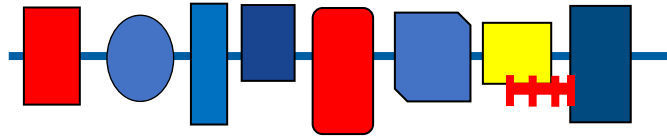
Genetik: Kromosom 5p13



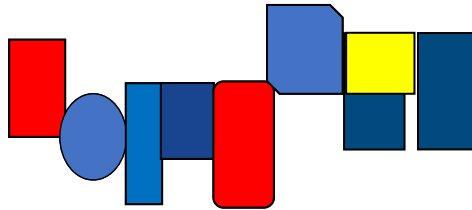
Genetik: Kromosom 5p13

Centromeric copy – SMN2

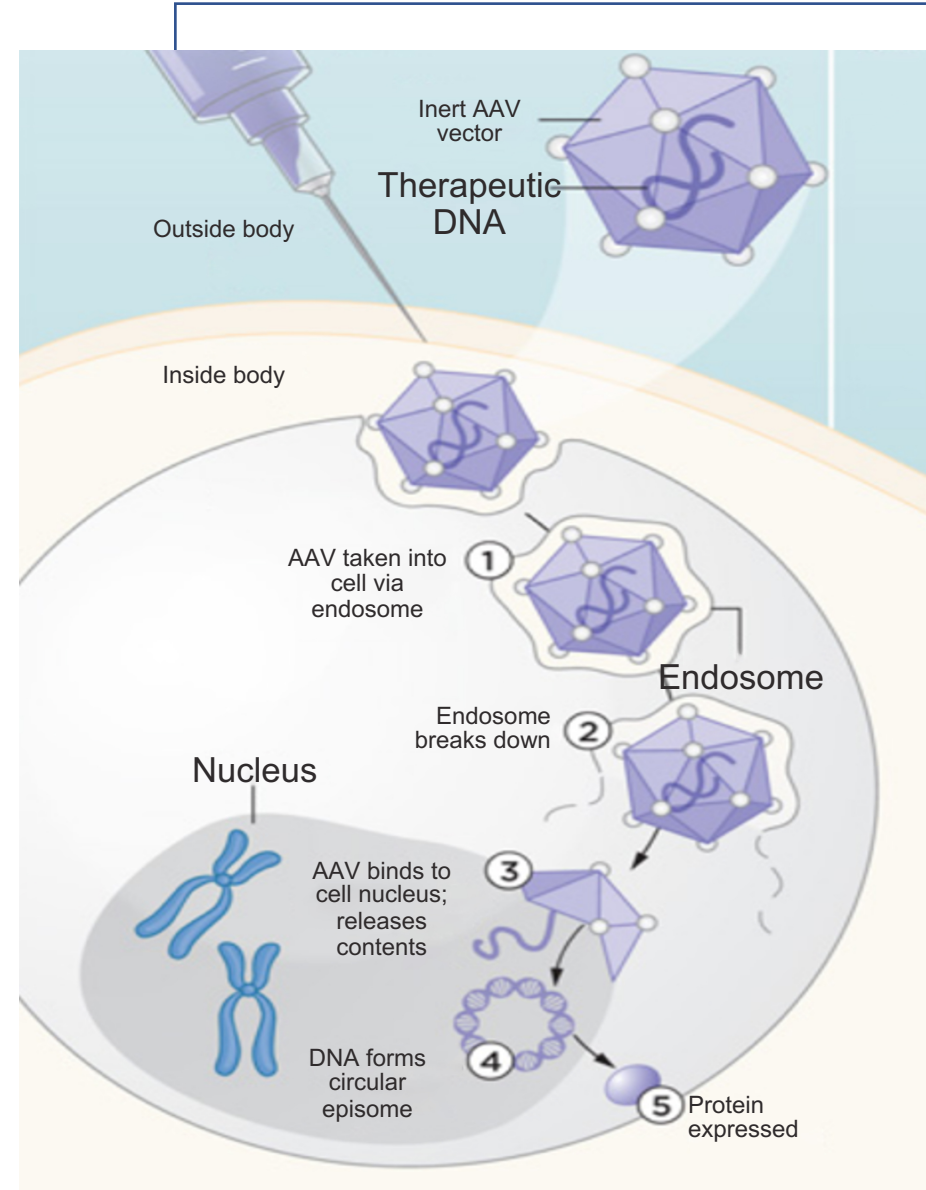
DNA



RNA



Genterapi



Progredierende sykdom

Milestones - milepæler



Milestones - milepæler



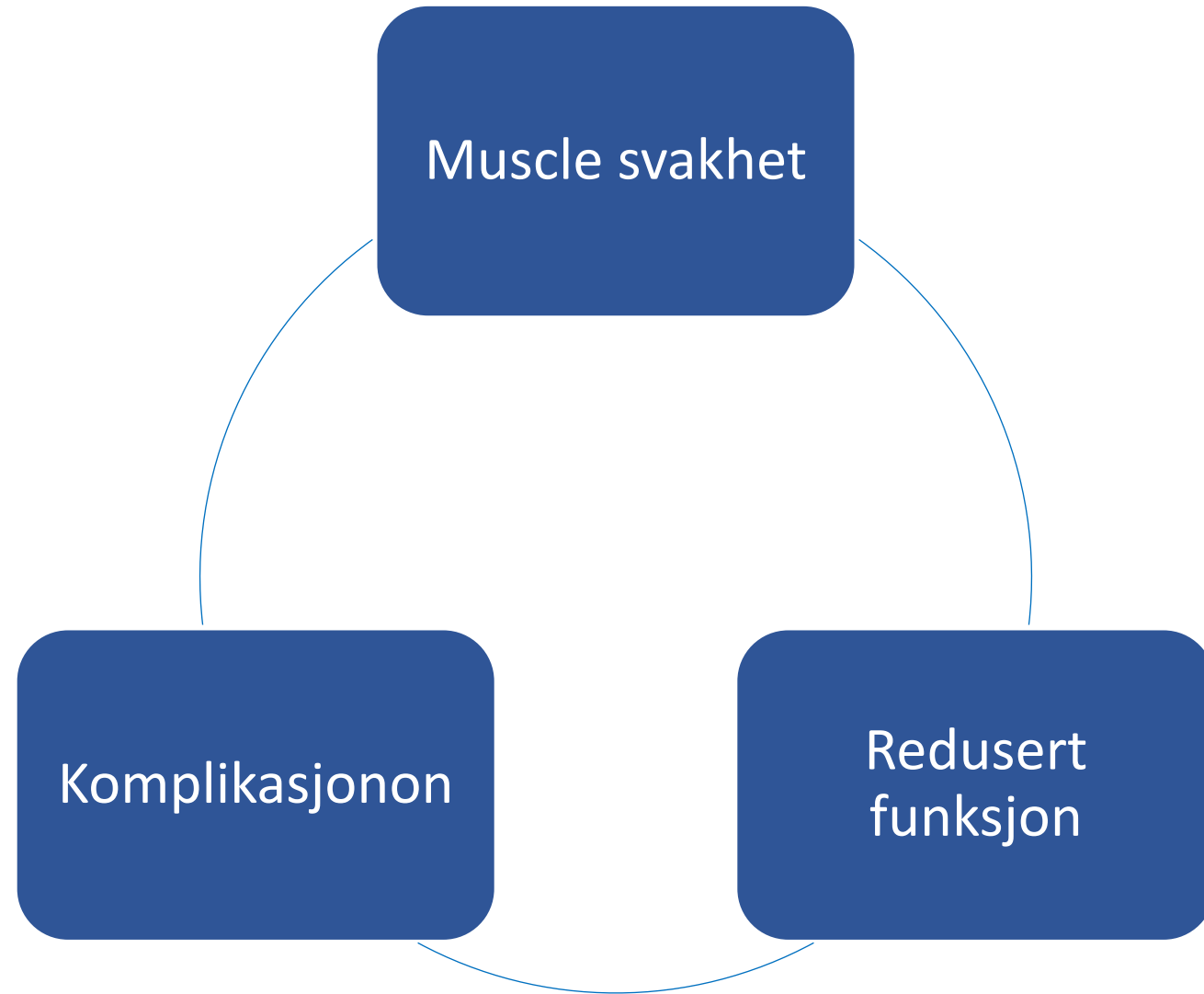
CHOP Intend

MEASURE: MOTOR FUNCTION INFANTS AND CHILDREN WITH SMA (≈4 months to >4 years of age)

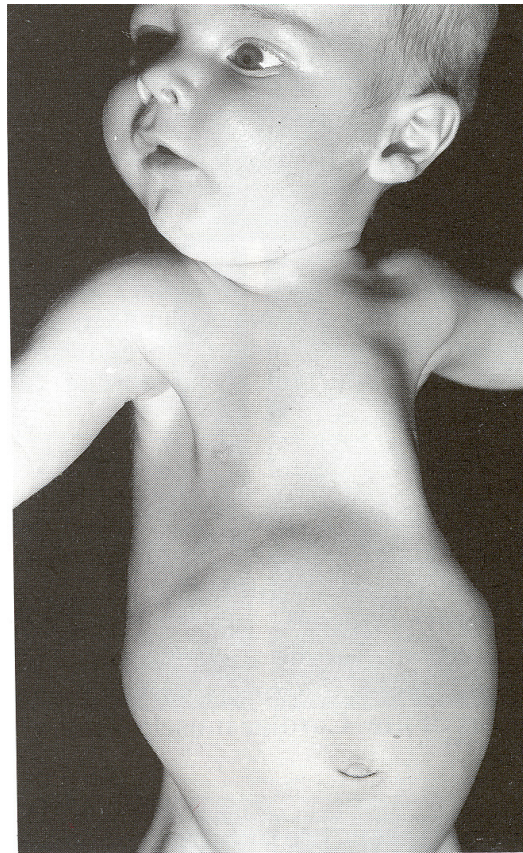
The Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND) may be used to evaluate the motor skills of infants with SMA^{10,11}:

- CHOP INTEND was developed by evaluating infants (n=26) with Type I SMA, mean age 11.5 months (1.4-37.9 months), and has been shown to be valid for the assessment of children ranging in age from 3.8 months to over 4 years who have an infant's repertoire of motor skills
- Includes 16 items used to assess motor skills. Each item is graded on a scale of 0-4¹²:
0=No response
4=Complete response
- Total score ranges from 0-64

1	Spontaneous movement (upper extremity)
2	Spontaneous movement (lower extremity)
3	Hand grip
4	Head in midline with visual stimulation
5	Hip adductors
6	Rolling: elicited from legs
7	Rolling: elicited from arms
8	Shoulder and elbow flexion and horizontal abduction
9	Shoulder flexion & elbow flexion
10	Knee extension
11	Hip flexion and foot dorsiflexion
12	Head control
13	Elbow flexion
14	Neck flexion
15	Head/Neck extension
16	Spinal incurvation



Spinal muscular atrophy, type I



From: V.Dubowitz: Muscle Disorders in Childhood



SMA CLINICAL SUBTYPES

There are four primary types of SMA. Type is based on the age of onset symptoms and the highest physical milestone achieved. SMA Type I is most severe, and also the most common, representing over 60% of cases.

1

Type 1 SMA

Onset: Before 6 months
Milestones: no sitting



2

Type 2 SMA

Onset: 6 - 18 months
Milestones: Sitting, not walking



3

Type 3 SMA

Onset: Childhood after 12 months
Milestones: Walking



4

Type 4 SMA

Onset: After 30 years old
Milestones: Normal



SMA

www.cureSMA.org • [#CureSMA](https://twitter.com/CureSMA)

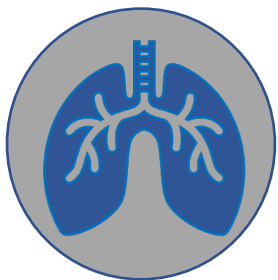
Komplikasjoner



Redusert mobilitet
Redusert ledd beveglighet
Redusert funksjon
Obstipasjon
Smerte



Redusert mimikk
Forsinket språk
Svelgevansker
Aspirasjon
Refluks

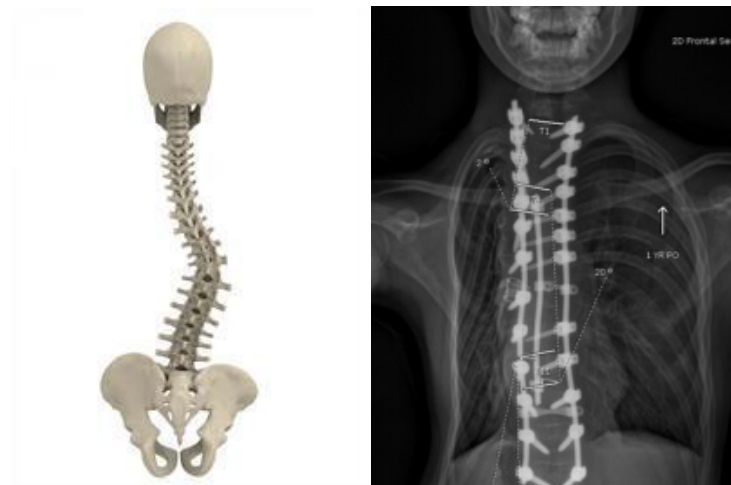


Hypoventilering
Redusert hostekraft
Kronisk Resp. svikt
Slimproblematikk
infeksjoner
Brystkasse forandringer
Energi behov



Ledd kontrakturer
Hofte dysplasi
Skoliose
Osteoporose

Komplikasjoner



Nyfødt screening..?

The NEW ENGLAND JOURNAL of MEDICINE

EDITORIAL



The Dilemma of Two Innovative Therapies for Spinal Muscular Atrophy

Ans T. van der Ploeg, M.D., Ph.D.

Two innovative therapies for SMA may now bring some hope —
but what do they mean for patients and their families?

Beslutningsforum Norge - Nye metoder

Tilgjengelig dokumentasjon viser at effekten av nusinersen (Spinraza) er størst hos de yngste barna og de barna som starter behandlingen tidlig i sykdomsforløpet. Nusinersen (Spinraza) kan nyttes til behandling av barn med SMA ... forutsetninger:

CHOP Intend

MEASURE: MOTOR FUNCTION INFANTS AND CHILDREN WITH SMA (≈4 months to >4 years of age)

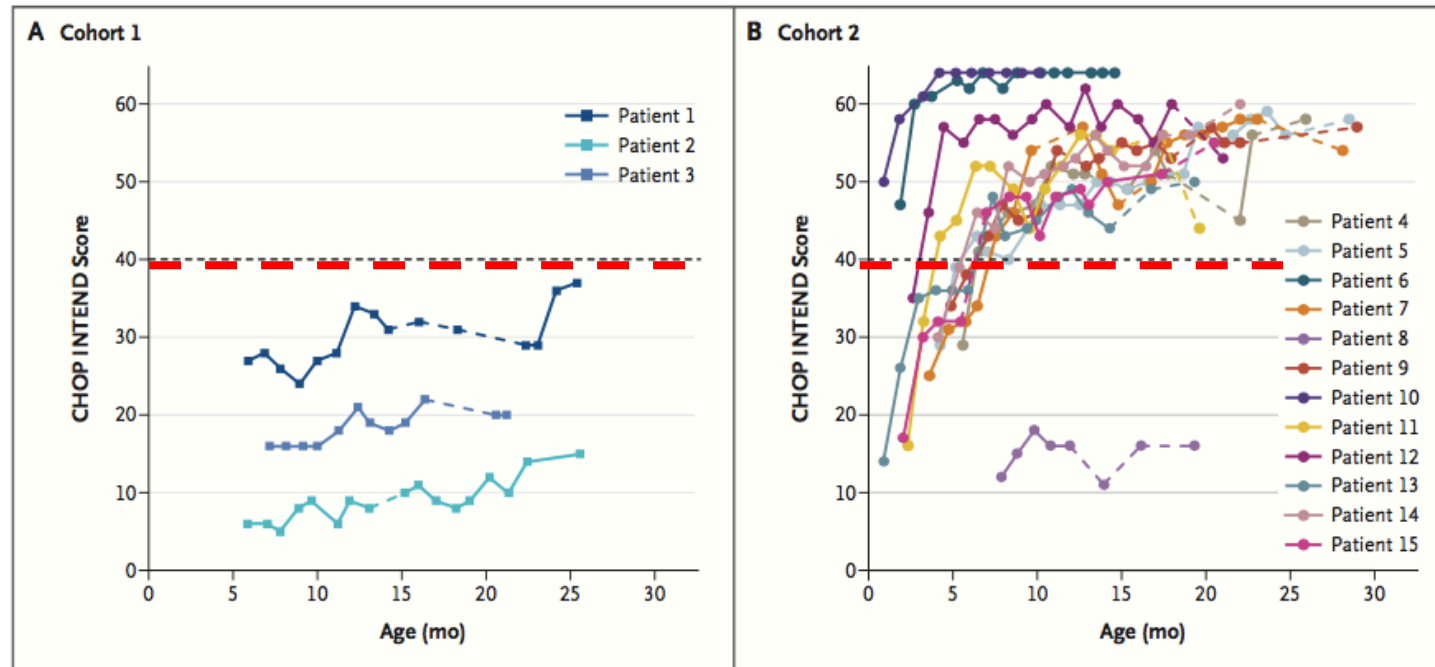
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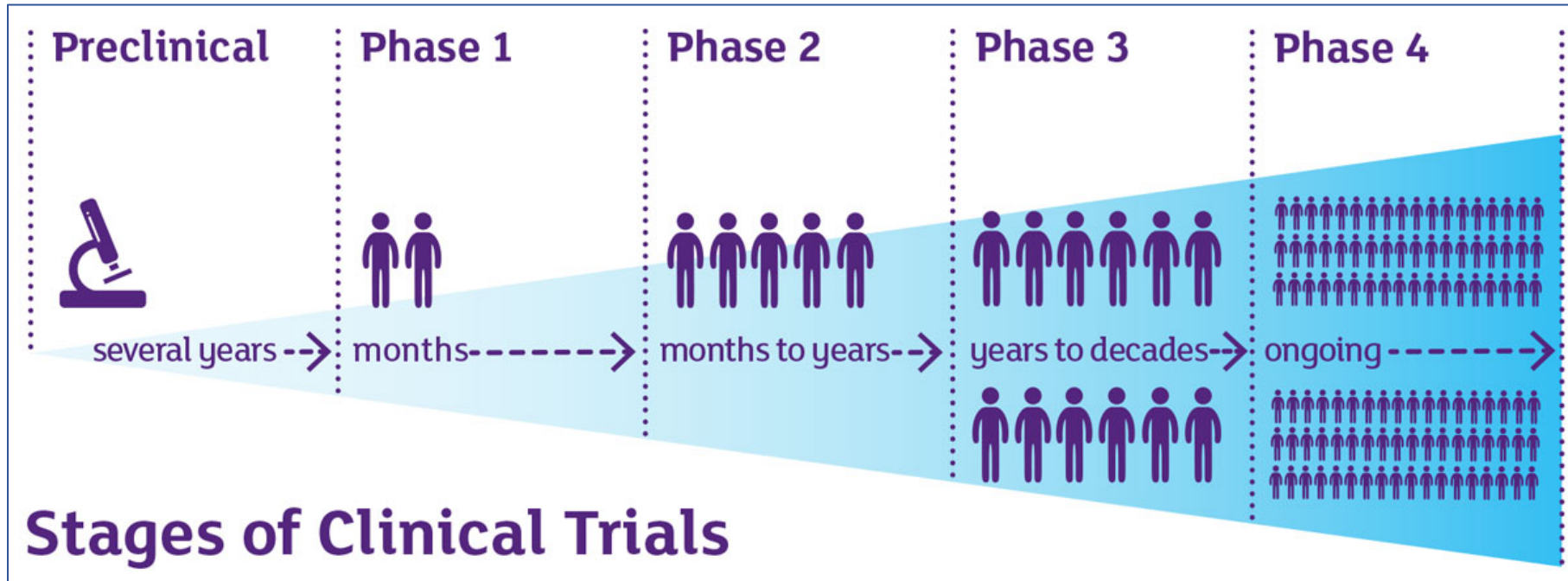
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Motor Function after Gene Therapy - CHOP intend



Resultater i Norge



Diagnosis

- “Floppy Baby”
- Ring til genetisk labratorium
- Har vi samme mening om oppstart av behandling ?

