

Konsekvenser av røyking hos kreftpasienter

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SFK

Sørlandet sykehus

Kristiansand

Røyking og sykdom, 1900-2000

- Dr Angel Roffo (1882-1947): første legen som publiserte om karsinogenitet av tobakk



- 1950: British Medical Journal: Doll og Hill, case-control study: 'Smoking is an important cause of lung cancer'

BRITISH MEDICAL JOURNAL

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SMOKING AND CARCINOMA OF THE LUNG

PRELIMINARY REPORT

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In England and Wales the phenomenal increase in the number of deaths attributed to cancer of the lung provides one of the most striking changes in the pattern of mortality recorded by the Registrar-General. For example, in the quarter of a century between 1922 and 1947 the annual number of deaths recorded increased from 612 to 9,287, or roughly fifteenfold. This remarkable increase is, of course, out of all proportion to the increase of population—both in total and, particularly, in its older age groups. Stocks (1947), using standardized death rates to allow for these population changes, shows the following trend: rate per 100,000 in 1901-20, males 1.1, females 0.7; rate per 100,000 in 1936-9, males 10.6, females 2.5. The rise seems to have been particularly rapid since the end of the first world war: between 1921-30 and 1940-4 the death rate of men at ages 45 and over increased sixfold and of women of the same ages approximately threefold. This increase is still continuing. It has occurred, too, in Switzerland, Denmark, the U.S.A., Canada, and Australia, and has been reported from Turkey and Japan.

Many writers have studied these changes, considering whether they denote a real increase in the incidence of the disease or are due merely to improved standards of diagnosis. Some believe that the latter factor can be regarded as wholly, or at least mainly, responsible—for example, Willis (1948), Clemmesen and Busk (1947), and Steiner (1944). On the other hand, Kewenaw and Kewenaw (1947) and Stocks (1947) have given good reasons for believing that the rise is at least partly real. The latter, for instance, has pointed out that "the increase of certified respiratory cancer mortality during the past 20 years has been as rapid in country districts as in the cities with the best diagnostic facilities, a fact which does not support the view that such increase merely reflects improved diagnosis of cases previously certified as bronchitis or other respiratory affections." He also draws attention to differences in mortality between some of the large cities of England and Wales, differences which it is difficult to explain in terms of diagnostic standards.

The large and continued increase in the recorded deaths even within the last five years, both in the national figures and in those from teaching hospitals, also makes it hard to believe that improved diagnosis is entirely responsible. In short, there is sufficient reason to reject that factor as the whole explanation, although no one would deny that it may well have been contributory. As a corollary, it is right and proper to seek for other causes.

Possible Causes of the Increase

Two main causes have from time to time been put forward: (1) a general atmospheric pollution from the exhaust fumes of cars, from the surface dust of tarred roads, and from gas-works, industrial plants, and coal fires; and (2) the smoking of tobacco. Some characteristics of the former have certainly become more prevalent in the last 20 years, and there is also no doubt that the smoking of cigarettes has greatly increased. Such associated changes in time can, however, be no more than suggestive, and until recently there has been singularly little more direct evidence. That evidence, based upon clinical experience and records, relates mainly to the use of tobacco. For instance, in Germany, Müller (1939) found that only 3 out of 86 male patients with cancer of the lung were non-smokers, while 56 were heavy smokers, and, in contrast, among 86 "healthy men of the same age groups" there were 14 non-smokers and only 31 heavy smokers. Similarly, in America, Schrek and his co-workers (1950) reported that 14.6% of 42 male patients with cancer of the lung were non-smokers, against 23.9% of 522 male patients admitted with cancer of sites other than the upper respiratory and digestive tracts. In this country, Thelwall Jones (1949—personal communication) found 8 non-smokers in 82 patients with proved carcinoma of the lung, compared with 11 in a corresponding group of patients with diseases other than cancer; this difference is slight, but it is more striking that there were 28 heavy smokers in the cancer group, against 14 in the comparative group.

Clearly none of these small-scale inquiries can be accepted as conclusive, but they all point in the same direction. Their evidence has now been borne out by the results of a large-scale inquiry undertaken in the U.S.A. by Wynder and Graham (1950).

Wynder and Graham found that of 665 men with epidermoid, undifferentiated, or histologically unclassified types of bronchial carcinoma only 1.3% were "non-smokers"—that is, had averaged less than one cigarette a day for the last 20 years—whereas 51.2% of them had smoked more than 20 cigarettes a day over the same

Røyking og sykdom, 1900-2000

- 1964: Surgeon General Report 'Smoking and health':

Røyking er kausal relatert til lungekreft

- 1979: ny Surgeon General Report:
Smoking is far more dangerous than was supposed in 1964



He's one of the best-
known in town. While his
duty may say fifteen hours
a day, he's actually on a bit
24 hours a day.
The doctor is a doctor,
a diplomat, and a friendly
sympathetic human being
all in one, not to mention how
long and hard his schedule.

According to a recent Nationwide survey:

MORE DOCTORS SMOKE CAMELS THAN ANY OTHER CIGARETTE

DOCTOR survey branch of analysis—11,191
in all—was given in this nationwide study
of cigarette preferences. Those leading research
organizations made the survey. The gist of the query
was: What cigarette do you smoke, Doctor?

The brand named most was Camel.
The rich, full flavor and cool milky of Camel's
super blend of choice tobacco seem to have
been agreed to the smoking tastes of doctors as to
millions of other smokers. If you are a Camel
smoker, this preference finding doesn't tell hardly
anything new. If you're not a Camel, try Camel now.



Your "T-Zone" Will Tell You...

If you smoke...
If you throat...
Don't your
growing ground
for any cigarette
but if Camels
don't suit you
"T-Zone" to a "T."



CAMELS Castler Tobacco



20,679* Physicians
say "LUCKIES
are less irritating"

"It's toasted"

Your Throat Protection against irritation against cough

Røyking og sykdom, 1900-2000

- 1980: Passiv røyking er kausal relatert til lungekreft
- 1984: Nicotine tyggegummi for avvenning kom på markedet



Røyking og sykdom, 1900-2000

- 2000: Udiskutabel bevis for kausal sammenheng mellom røyking og kreft, samt mange andre ikke-maligne sykdommer

Røyking og kreft

- Røyking er kausal relatert til følgende kreftsykdommer:

Blære

Bryst

Cervix uteri

Colon

Lever

Leukemi

Lunge

Nyre

Ovarium

Pankreas

Rectum

Ventrikkel

Øre, nese, hals

Øsofagus

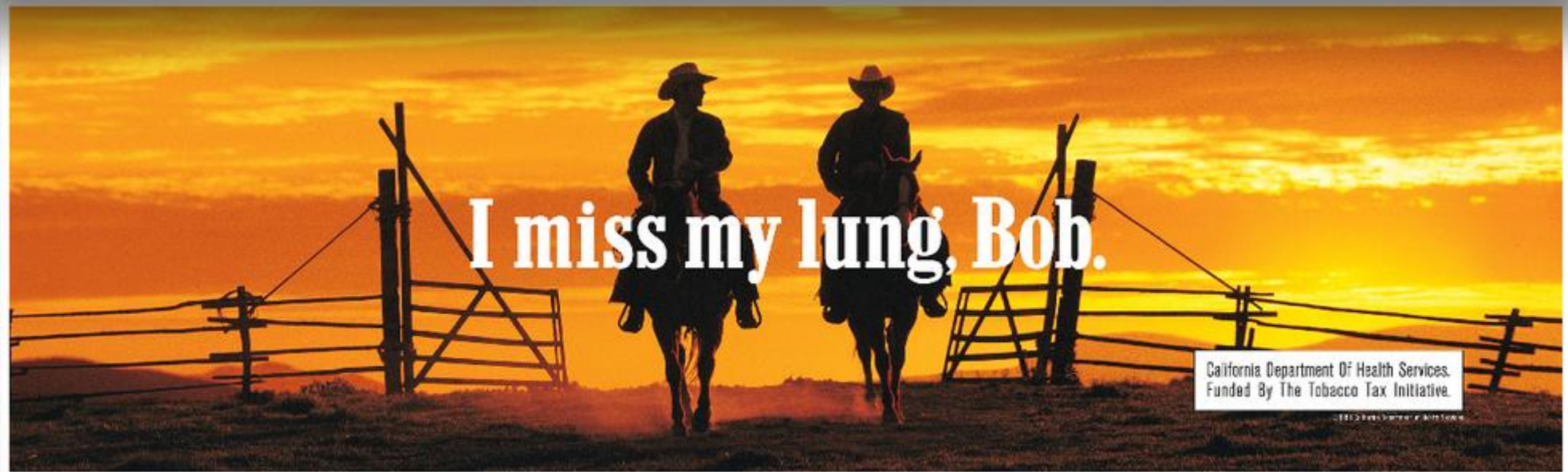
~ 30% av alle kreftdødsfall er en følge av røyking

A photograph of two men in cowboy hats and western attire sitting on horses in a grassy field under a clear blue sky. The man on the left is wearing a denim jacket over a red shirt, and the man on the right is wearing a dark jacket over a blue shirt. They are both looking towards the right.

Bob, I've got emphysema.

WARNING: Cigarette Advertising Makes
Smoking Look Cool And Cowboys Look Stupid.

© 2007 California Department of Health Services

A photograph showing the silhouettes of two cowboys on horses riding away from the viewer across a field. The sky is a vibrant orange and yellow from a low sun, creating a strong backlight effect. A wooden fence is visible in the foreground.

I miss my lung, Bob.

California Department Of Health Services.
Funded By The Tobacco Tax Initiative.

© 2007 California Department of Health Services

Sammensetningen av tobakksrøyk

- Røyk inneholder ca 7000 forskjellige stoffer og nikotin er stoffet som skaper avhengighet
- 60 stoffer er per i dag bekreftet karsinogene
- Stoffene entrer blodet i lungene og påfører dermed også skade utenfor luftveiene

Sammensetningen av tobakksrøyk

- Filtersigaretter og light sigaretter førte absolutt ikke til helsegevinst:

Nikotin behovet var der, og røykere begynte både å røyke flere sigaretter daglig og å inhalere dypere

> Enda flere tilfeller av lungekreft



Kreft og røyking

■ 2014: Surgeon General Report:

Kreftpasienter som røyker har:

- Større dødelighet og kreftspesifikk dødelighet
- Større risiko for tumorresidiv og sekundærkreft
- Større behandlingsrelatert akutt- og sentoksisitet
- Lavere effekt av medikamentell- og strålebehandling

Høyere dødelighet og kreftspesifikk dødelighet hos røykere

Død

RR

■ Lungekreft- og ØNH kreftpas

1,5 – 2,5

■ Prostatakreft pas

2,5 – 5

Kreftdød

RR

■ Lungekreft- og ØNH kreftpas

1,5 – 2,5

■ Prostatakreft pas

3

Mer sekundærkreft og residiver hos røykere

Sekundærkreft

RR

■ Lungekreft pas

17 - 32

■ Prostatakreft pas

2 – 3,5

■ Brystkreft pas

2 - 9

Tumorresidiv

RR

■ ØNH pas

1,4

■ Prostatakreft pas

2

Større behandlingsrelatert toksisitet

	RR
■ Prostatakraft pas (tarmtoks)	2,7 – 9
■ Brystkreft pas	2
■ Gyn kreft pas	2,3

prostataca strålebeh	aldri- / ex-røykere	røykere
tarmkramper	2%	18%
urge	20%	53%
diare	9%	24%
kontinensproblemer	5%	23%

Hva med eks-røykere?

- Risikoen for død og komplikasjoner hos pasienter som *sluttet med å røyke før start av onkologisk behandling* er fremdeles noe høyere enn hos aldri røykere
- Men risikoen er signifikant lavere enn hos røykere: å slutte gir 30-50% risikoreduksjon

Bonus: Quality of Life og Performance

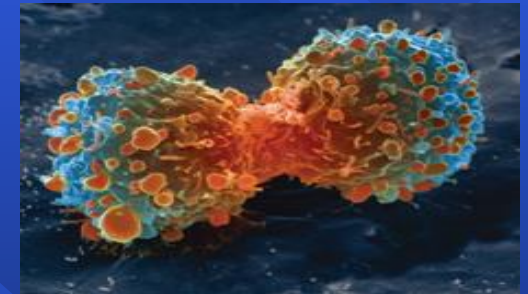
- Signifikant høyere overall Quality of Life etter røykeslutt
- Signifikant høyere Performance status etter røykeslutt
- Dette gjelder også for palliative pasienter!

Røyking hos kreftpasienter

Patofysiologien bak

1. Mer aggressiv deling

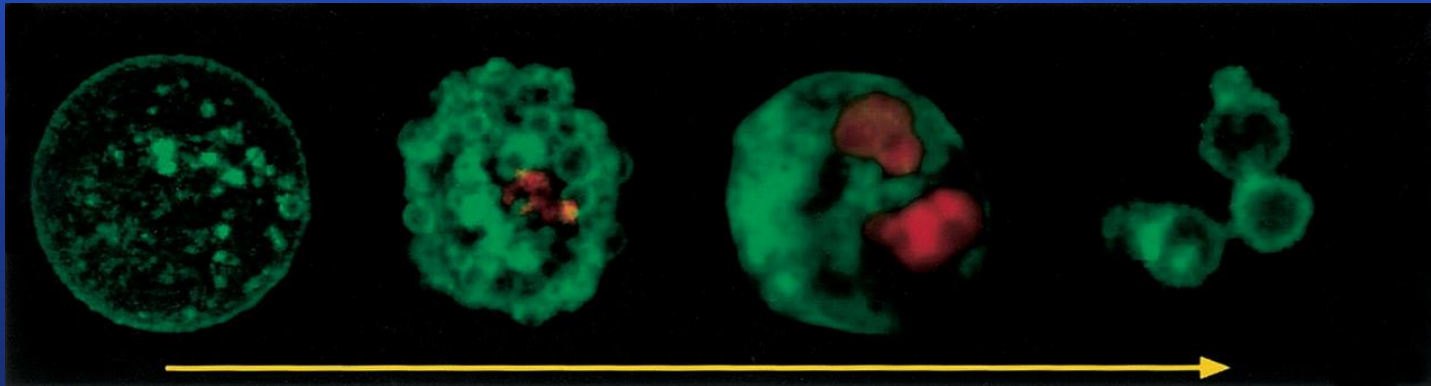
- Mange forskjellige cellulære reseptor pathways som er involvert i celledeling, f.eks. EGFR pathway, blir påvirket av tobakksrøyk



- Resultatet er at cancercellene endrer seg til en mer malign og raskere delende fenotype

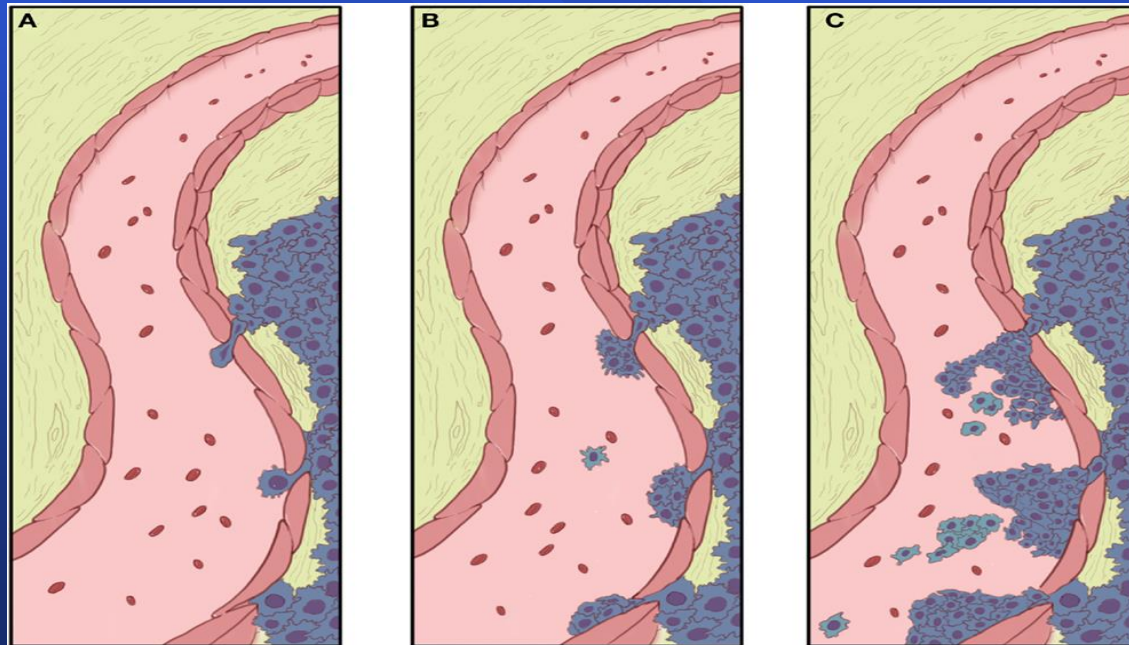
2. Mindre apoptosis

- Eksponering til tobakksrøyk fører til færre apoptoser og dermed til utvikling av en pro-survival fenotype



3. Mer invasjon / spredning

- Kreftceller som er langvarig utsatt for røyk endrer karakter til en celletype som vokser mer invaderende og gir raskere fjernspredning



4. Immunmodulasjon

- Flere immunsystem-relaterte pathways blir berørt av tobakksrøyk >

Immuunsystemet blir mindre effektiv

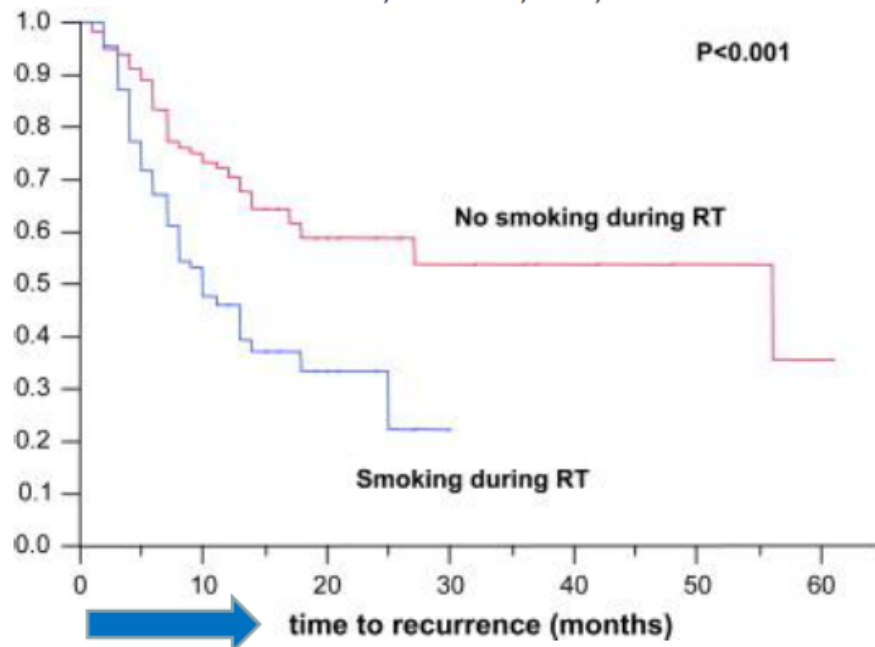
- Dette er gunstig for tumorcellene og ugunstig for friskt vev

5. Enzyminduksjon

- Tobakksrøyk induserer enzymer som spiller en rolle i nedbryting av forskjellige kjemoterapeutika
- Økt enzymaktivitet gir raskere nedbryting av medikamentet
- Raskere nedbryting kan gi dårligere medikament virkning

6. Dårligere effekt av strålebehandling

Rades D, Effect of Smoking During Radiotherapy
in Patients Irradiated for NSCLC
Int J Rad Onc, 2008, 71;4:1134–1142



Lokal kontroll, 181 pts	1 år	2 år
Røykere mens RT	46%	34%
Ikke røykere mens RT	71%	58%

Residiv: RR 1,74

Konsekvenser for onkologisk behandling

- Dårligere effekt av strålebehandling og større toksisitet
- Sterk antydning til dårligere effekt av flere typer cellegift og moderne kreftmedisiner (f.eks. tyrosin kinase hemmere!)
- Økt risiko for post-operative komplikasjoner

Evidensbasert onkologisk behandling

1. Vi skal informere våre pasienter om dette
2. Et røykeslutt program bør sannsynligvis bli et integrert del av det onkologiske behandlingstilbudet
3. En norsk studie er nå i gang

Anbefalt artikkel

Lancet Oncology, November 2014

Graham Warren

The biological and clinical effects of smoking by patients with cancer and strategies to implement evidence-based tobacco cessation support

