SMOKING AND HEALTH

SMOKING IS THE MAIN SINGLE PREVENTABLE FACTOR,
ALL FORMS OF TOBACCO ARE ADDICTIVE AND LETHAL
TYPES OF TOBACCO PRODUCTS

- CIGARETTES, PIPES, CIGARS
- BIDIS, KRETEKS, STICS
- WATER PIPES, e-CIGARETTES
- SMOKELESS: SNUFS (MOIST, DRY), CHEWING TOBACCO
USING TOBACCO HAS:

- IMMEDIATE EFFECTS
- MID-TERM EFFECTS
- LONG-TERM EFFECTS
- ON HUMAN HEALTH
* IMMEDIATE EFFECTS

- ACTIVATION OF BRAIN RECEPTORS
- CARDIOVASCULAR CHANGES
- HYPOXEMIA
- IRRITATION
NICOTINE IN BRAIN

- NICOTINE REACHES THE BRAIN WITHIN 10-20 SECONDS AFTER THE PUFF,
- WITHIN 20-30 MINUTES AFTER TRANSDERMAL TRANSPORT
- NICOTINE OCCUPIES THE SPECIFIC CHOLINERGIC RECEPTORS AND INDUCES THEIR ACTIVATION
ACETYLCOLINE RECEPTORS - nAChRs

- TWO UNITS: ALPHA, BETA
- SEVERAL SUBUNITES
- PRESENT ON NEURAL CELLS (both central and peripheral), and
- ON TISSUE CELLS
- SOME SUBUNITES ARE NICOTINE SPECIFIC (activated by nicotine)
RELEASE OF NEUROTRANSMITTERS:

- DOPAMINE
- SEROTONINE
- ACETYLCHOLINE
- EPINEPFRINE, NOREPINEPHRINE,
- BETA-ENDORPHINE
- ACTH, ADRENALINE
EFFECTS OF NICOTINE

- WELL BEING (DOPAMINE)
- COPING THE STRESS (ACTH)
- BETTER SHORT-TERM PERFORMANCE (ACETYLCHOLINE, ADRENALINE)
TWO FACES OF TOBACCO COMPANIES

• „NICOTINE IS THE ADDICTING AGENT IN CIGARETTES“
  Private statement, Brown & Williamson official in 1983

• „I BELIEVE THAT NICOTINE IS NOT ADDICTIVE“
  Sworn testimony before the US Congress;
  CEOs of the seven leading tobacco companies in 1994
WHAT IS TRUE?

- ALL FORMS OF TOBACCO CAN DEVELOP AN ADDICTION
- THE DRUG IS NICOTINE
- ITS PATHWAYS AND POWERTY IS SIMILAR AS THOSE OF HEROINE and COCCAINE

US. Surgeon General Report, 1988
OFFICIAL STATUS

- Dg. F 17:
  PSYCHOLOGICAL AND BEHAVIORAL DISORDERS CAUSED BY TOBACCO USE

International statistic classification of diseases, 10th revision, 1991
SMOKING ADDICTION

• 80 – 85% OF CURRENT SMOKERS WILL BE DEPENDENT, SIMILARLY LIKE CURRENT USERS OF HEROINE OR COCCAIN

• ABOUT ONE THIRD OF OCCASSIONAL SMOKERS WILL BE DEPENDENT
SMOKING IS A DISEASE

• Dependence on smoking is not a lack of willing or „bad habit“ but
• Chronical, progressive and relapsing disease
• Both pharmacological and behavioral addiction
ALTERED DOPAMINERGIC SYSTEM

- PREMATURAL ACTIVATION OF FETAL RECEPTORS
- DECREASED AMOUNT OF NEURAL CELLS IN THE BRAIN
- SUDDEN INFANT DEATH SYNDROME
- IMPAIED NEURO-PSYCHOLOGICAL DEVELOPMENT
- BEHAVIORAL and COGNITIVE PROBLEMS
ALTERED SEROTONERGIC SYSTEM

• MAJOR PSYCHIATRIC DISORDERS (SCHIZOPHRENIA, DEPRESSION)
• 2-3 times HIGHER FREQUENCY OF SUICIDES
• SMOKING CAUSES DEPRESSION
• DEPRESSION CAUSES SMOKING
CARDIOVASCULAR CHANGES

- VASOCONSTRICTION: SKIN, CORONARY, BRAIN, ABDOMINAL, VERTEBRAL, PLACENTAL ARTERIES
- HIGHER BLOOD PRESSURE
- HIGHER HEART RATE
- HIGHER HEART VOLUME/MIN
- DECREASED SKIN TEMPERATURE
MECHANISMS OF ACTION

- ACTIVATION OF SYMPATHIC NERVOUS SYSTEM
- RELEASE OF SUPRARENAL HORMONES (ADRENALINE, NORADRENALINE)
- BY QUICK ADMINISTRATION OF NICOTINE
HYPOXEMIA

- DECREASED AMOUNT OF BLOOD DUE TO VASOCONSTRICTION (caused by nicotine)
- DECREASED AMOUNT OF OXYGEN IN BLOOD (caused by carbon monoxide – COHb)
- DECREASED BLOOD-TISSUE TRANSPORT OF OXYGEN (caused by hydrogen cyanide HCN)
IN PREGNANCY

- LOCAL PLACENTAL NECROSIS (caused by cadmium Cd)
- POWERFULL AFFINITY OF FETAL HEMOGLOBIN TO CARBON MONOXIDE ENHANCES COHb LEVELS BY 25% (fetal x maternal blood)
CONSEQUENCES OF HYPOXEMIA and HYPONUTRITION

- FETAL GROWTH RETARDATION = FETAL TOBACCO SYNDROME
- ALTERATION OF FETAL LUNG DEVELOPMENT
- RISK OF PRE-TERM BIRTH
- RISK OF INTRAUTERINE DEATH
HYPOXEMIA IN ADULTS

- HEART ATTACK (IM)
- CEREBROVASCULAR ATTACK (STROKE)
- WRINKLING, PREMATURE AGEING
- IMPAIRED WOUND HEALING
- LEG AND HAND PAIN, GANGRENE – PERIPHERAL VASCULAR DISEASE
IRRITATION

- EYES: excessive tearing, blinking, stinging
- NOSE: bad smell, stinging, phlegm
- NASOPHARYNX: cough, cold in the chest
- STRESS DUE TO DYSCOMFORT
* SHORT/MILD-TERM EFFECTS

- IMPAIRED IMMUNITY
- HORMONAL DYSBALANCE
- IMPAIRED BLOOD LIPIDS
- IMPAIRED HEMOCOAGULATION
- CHRONIC INFLAMMATION
IMMUNE SYSTEM

• IMPAIRED RESISTANCE TO INFECTION
• CONTRIBUTION TO ALLERGIES
• INFANTS AND CHILDREN ARE THE MOST VULNERABLE POPULATION
• IMPAIRED RESISTANCE TO CANCER (Natural Killers)
MALE REPRODUCTION

- IMPOTENCE
- IMPAIRED SPERMIOGENESIS: deformity, loss of motility, reduced number, aneuploid sperm cells
- FETAL MALFORMATIONS
- INFERTILITY
FEMALE REPRODUCTION

- PAINFUL MENSTRUATION
- EARLIER MENOPAUSE
- INFERTILITY
- ECTOPIC PREGNANCY
- PLACENTA PRAEVIA
- PREMATURE BIRTH
- SPONTANEOUS ABORTION
OTHERS

• HORMONAL DYSBALANCE CONTRIBUTES TO
• DIABETES MELLITUS and COMPLICATIONS
• OSTEOPOROSIS and
• HIP FRACTURES
BLOOD LIPIDS

- INCREASED LEVELS OF
  - TOTAL CHOLESTEROL
  - LDL – CHOLESTEROL
  - VLDL – CHOLESTEROL

- DECREASED LEVELS OF
  - HDL- CHOLESTEROL
HEMOCOAGULATION

• ENHANCED ACTIVITY OF THROMBOCYTES and

• FACTOR VIII =>

• ARTERIAL/CORONARY THROMBOSIS
SMOKING IS RESPONSIBLE

- FOR 25% OF ISCHEMIC HEART D.
- FOR 25% OF VASCULAR DISEASES (stroke, Burger d., aneurysma, macular degeneration, cataracts)
- FOR EARLIER ATHEROSCLEROSIS
- FOR 75% OF CHRONIC OBSTRUCTIVE PULMONAL DISEASE (chr. Bronchitis, emphysema)
SMOKING CONTRIBUTES TO

- STOMACH AND DUODENAL ULCERS
- TEETH LOOSE
- GUM DISEASES – GINGIVITIS, PERIODONTITIS
- PROGRESSION OF PRESBYACUSIS
- PSORIASIS and other skin diseases
- TREMOR
* LONG-TERM EFFECTS

• TOBACCO SMOKE CONTAINS OVER 5,000 CHEMICALS,

• 67 OF WHICH ARE KNOWN OR SUSPECTED HUMAN CARCINOGENS
CARCINOGENS IN SMOKE

- POLYCYCLIC AROMATIC H. (benzo/a/pyrene)
- HEAVY METALS (Cd, As)
- RADIOACTIVE POLONIUM 210
- INDUSTRIAL CARCINOGENS: beta-naphthylamine, 4-aminobiphenyle, benzene, formaldehyde
TOBACCO SPECIFIC NITROSAMINES

- NNK: 4-(methyl)nitrosamino)-1-(3-pyridyl)-1-butanone
- NNAL
- NNN
- And many others
SMOKING IS RESPONSIBLE

• FOR 90-95% OF ALL LUNG CA
• FOR 40-60% OF HEAD/NECK CA
• FOR 40-60% OF KIDNEY/BLADDER CA
• FOR 30% OF CERVICAL CA
• FOR 30% OF GASTRIC/PANCREATIC CA
• FOR COLON, LIVER, BREAST CA
PATHWAYS:

• GENOTOXICITY => INITIATION OF CARCINOGENESIS

• METABOLIC ACTIVATION – microsomal enzymes P 450 – HEREDITARY DETERMINATION

• EPIGENETIC EFFECTS => MODULATE CELLULAR FUNCTIONS => TUMOR PROMOTION and PROGRESSION
GENOTOXIC CARCINOGENESIS:

- INITIATION of DNA MUTAGENIC CHANGES
- REPLICATION
- PROMOTION
- PROGRESSION
- METASTASES
ROLE of nACh RECEPTORS:

- THEIR OVEREXPRESSION INDUCED BY SMOKING =>
- RELEASE of NEUROTRANSMITTERS, SIGNALISING PATHWAYS and GROWTH FACTORS =>
- MOLECULAR PATHWAYS ARE PROBABLY THE MOST IMPORTANT
CONSEQUENCES:
PROMOTION

- CELL´S PROLIFERATION
- ANTIAPOPTOSIS
- PROTEIN SYNTHESIS
- MITOCHONDRIA DYSFUNCTION
- INCREASING of REPLICATIVE LIFESPAN
CONSEQUENCES: PROGRESSION

- ANGIOGENESIS
- INVASION
- METASTASIS
EPIGENETIC CARCINOGENIC ACTIVITIES

- MEDIATED THROUGH nAChR WERE FOUND FOR:
  - NICOTINE
  - NNK
  - POLYCYCLIC AROMATIC HYDROCARBONS
nACh RECEPTORS:

- CELL – TYPE – SPECIFIC
- MODIFIED BY VARIOUS ENVIRONMENTAL FACTORS
- UNDERSTANDING of MOLECULAR MECHANISMS => FUTURE DEVELOPMENT IN CANCER DIAGNOSES/THERAPIES
SMOKING KILLS

- HALF OF ALL LIFETIME USERS
- HALF OF THEM WILL DIE BETWEEN 30-69 YEARS OF AGE
- IN THE 20th CENTURY,
  100 MILLION PEOPLE DIED FROM TOBACCO USE
SMOKING KILLS

IN 2000
- 4.8 MIL ANNUAL PREMATURE DEATH
- 3.8 MILLION MEN
- 1.0 MILLION WOMEN

BY 2020 TOBACCO WILL KILL ABOUT
- 10 MILLION PEOPLE EVERY YEAR
SMOKING KILLS

• TOBACCO WILL KILL
  1 BILLION = 1 000 000 000
  PEOPLE

• IN THE 21st CENTURY
SMOKING KILLS PHYSICIANS

- British Medical Doctors Study (Doll, Lopez, Peto): smokers lost
- 5 YEARS OF LIFE - 1951-1971
- 10 YEARS OF LIFE – 1991-2006
SMOKING KILLS NON-SMOKERS

- MAIN STREAM
  - 800-900°C
  - 16% O₂
  - 6.0-6.7 pH

- SIDE STREAM
  - 600°C
  - 2% O₂
  - 6.7-7.5 pH
DANGER FOR NO-SMOKERS

- SECONDHAND SMOKE
- ENVIRONMENTAL TOBACCO SMOKE
- PASSIVE SMOKING
- INVOLUNTARY SMOKING

Side stream + smoker’s expiration + chemicals interaction
SS : MS - IRRITANTS

- ACROLEIN 8 – 15
- FORMALDEHYDE 10 – 15
- AMONIUM 73
- NITROGEN OXIDES 4 – 10
- FORMAMIC ACID 1,5
- NAFTALENE 16
SS : MS - TOXINS

- CARBON MONOXIDE  2 – 5
- TOLUENE  6 – 8
- NICOTINE  2,6-3,3
- NICKEL  13 – 30
- POLONIUM 210  1 – 4
- PCDD, PCDF  2
SS : MS - CARCINOGENS

- BENZENE 5 – 10
- NITROSAMINES 20 – 100
- 2-NAFTYLAMINE 30
- 4-AMINOBIFENYLE 30
- BENZO/A/PYRENE 2,5 – 3,5
- TAR 1,7
INDOOR CONCENTRATIONS OF NICOTINE

- WORK-PLACES: 20 ug/m$^3$
- CONFERENCE HALL: 40 ug/m$^3$
- RESTAURANTS: 26-28 ug/m$^3$
- CARS: 40 ug/m$^3$
- HOMES: 7-11 ug/m$^3$
- HOSPITALS: 0.01-4 ug/m$^3$
# INDOOR CONCENTRATIONS OF NITROSAMINE NNK

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<thead>
<tr>
<th>Location</th>
<th>Concentration</th>
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<tbody>
<tr>
<td>Bars</td>
<td>10 – 24 ug/m³</td>
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<tr>
<td>Restaurants</td>
<td>1 – 3 ug/m³</td>
</tr>
<tr>
<td>Trains</td>
<td>5 ug/m³</td>
</tr>
<tr>
<td>Cars</td>
<td>29 ug/m³</td>
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<tr>
<td>Offices</td>
<td>26 ug/m³</td>
</tr>
<tr>
<td>Homes</td>
<td>2 ug/m³</td>
</tr>
</tbody>
</table>
THIRDHAND SMOKE

- NICOTINE + NITRIC ACID + NO$_x$
- $\Rightarrow$ INTERACTIONS $\Rightarrow$
- NITROSAMINES NNK, NNA, NNN
- (mutagenic, carcinogenic)
- CONTAMINATION OF CLOTHES, SKIN, CARPETS, FORNITURE for many hours
EXPOSURE TO ETS - CHILDREN

- UNPLEASANT DYSCOMFORT
- IRRITATION
- IMPAIRED IMMUNITY
- RESPIRATORY INFECTIONS, ALLERGY
- SIDS
- LEUKEMIA, BRAIN TUMORS
EXPOSURE TO ETS - ADULTS

- UNPLEASANT DYSCOMFORT
- IRRITATION
- ACUTE CORONARY ISCHEMIA
- CHRONIC OBSTRUCTIVE PULMONARY DISEASE
- LUNG CANCER
HEALTH CONSEQUENCES OF INVOLUNTARY EXPOSURE TO ETS:

- AN HOUR A DAY IN A ROOM WITH SMOKER
- IS NEARLY A HUNDRED TIME MORE LIKELY TO CAUSE LUNG CANCER IN A NON-SMOKER
- THAN TWENTY YEARS SPENT IN A BUILDING CONTAINING ASBESTOS

Sir Richard Doll, 1989
ANTENATAL EXPOSURE

- GROWTH RETARDATION
- DELAYED LUNG DEVELOPMENT
- ACTIVATION OF nAChs (by NICOTINE) = NEUROTERRATOGENICITY (CONDUCT DISORDERS, ADHD, REDUCED MENTAL / SCHOOL PERFORMANCES)
PRENATAL PROGRAMING

- EXPOSURE TO MATERNAL SMOKING
- => CHANGES IN FETAL METABOLISM
- OUTLAST AFTER DELIVERY
- => OBESITY, HYPERTENSION, DAMAGES SERUM LIPIDS’ RATES in CHILDHOOD and ADULTHOOD
CONCLUSION

• CIGARETTE IS UNIQUE ARM KILLING BY ITS BOTH ENDS

• GLOBAL TOBACCO EPIDEMY IS WORSE TODAY THAN 50 YEARS AGO AND MAY BE WORSE IN ANOTHER 50 YEARS

• SMOKING IS THE MOST IMPORTANT PREVENTABLE RISK FACTOR