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
- MIDLE- 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

ACETYLCHOLINE RECEPTORS - nAChRs

- TWO UNITES: 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 BEEING (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 testimory 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 COCCAINE
- 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
- IMPAIRED 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 SYMPATIC NERVOUS SYSTÉM
- 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 cyanid HCN)

IN PREGNANCY

- LOCAL PLACENTAL NECROSIS (caused byl 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-(methylnitrosamino)-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/PANCRETIC 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
- 8 YEARS OF LIFE – 1971-1991
- 10 YEARS OF LIFE – 1991-2006

SMOKING KILLS NON-SMOKERS

- MAIN STREAM
- 800-900^{o} C
- 16% O_2
- 6,0-6,7 pH

- SIDE STREAM
- 600^{o} C
- 2% O_2
- 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

- BARS 10 – 24 ug/m^3
- RESTAURANTS 1 – 3 ug/m^3
- TRAINS 5 ug/m^3
- CARS 29 ug/m^3
- OFFICES 26 ug/m^3
- HOMES 2 ug/m^3

THIRDHAND SMOKE

- NICOTINE + NITRIC ACID + NO_X
- = > INTERACTIONS = >
- 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, ALERGY
- SIDS
- LEUKEMIA, BRAIN TUMORS

EXPOSURE TO ETS - ADULTS

- UNPLEASANT DYSCOMFORT
- IRRITATION
- ACCUTE CORONARY ISCHEMIA
- CHRONIC OBSTRUCTIVE PULMONARY DISEASE
- LUNG CANCER

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

CONCLUSSION

- 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