

Smoke inhalation survey (-/1207)

Background

This survey presents the results from various cigarette smoke inhalation experiments. For each parameter studied in the animals, the statistical difference was calculated between the control and exposed groups. The degree of significance (0.001, 0.01 and 0.5) was given a weighted value (3, 2 and 1 respectively). Positive values were given when an increase was present, negative for a decrease relative to control. The "average" value was then calculated for each parameter in all exposure groups including high and low exposure levels.

For the evaluation of histological changes in the respiratory tract a scale from 0 to 2 was used to classify the alterations (normal to the most severe effect). For 3 typical histological changes the gradings were averaged over different sites of the respiratory tract. This value was related to the TPM dose used in the experiments.

Hematological data

The results from the hematological parameters used in the experiments are reported in diagram 1. It ^{can be} seen that the highest averaged significance for differences between control and exposed groups ~~was~~ ^{is} present for erythrocyte number, hematocrit and the number of mature neutrophils in bone marrow.

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Clinical_chemical_data

The results from the evaluation of the clinical chemical

- parameters are given in diagram 2. It ^{can be} seen that the highest
- averaged significance for differences between control and exposed
- groups ^{is} was present for GPT activity, acid phosphatase, alpha 1 globulin, cholesterol, triglycerate and total lipid concentration in serum.

Organ_weights

The results from the evaluation of organ weights in the control and exposed groups are given in diagrams 3.1 and 3.2 where the

- averaged statistical difference between control and exposed groups is expressed for the absolute and relative weight of the respective organ.

Histology_of_the_respiratory_system

The density of goblet cells and hyper/metaplasia of the epithelium in the nasal cavity, larynx, trachea, bifurcation, main bronchi and terminal bronchi was graded separately. The grading of each site was averaged over all exposed groups. From this evaluation it became apparent that the density of goblet cells in the nasal cavity, bifurcation and bronchioli gave the highest grading. For hyper/metaplasia the highest gradings were received from preparations of the nasal cavity, larynx, trachea and bifurcation.

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For the goblet cells and hyper/metaplasia the changes in the above preparations were averaged for each group separately and compared with values in control animals. In addition the presence of ~~a~~ pigment containing macrophages and foam cells was graded in lung preparations and compared to the controls. The results are reported in table 1 to 4.

Within each experiment the hyper/metaplasia index (HMI) shows a good correlation to the total TPM dose (TPM-concentration x daily exposure duration, x exposure days). When different experiments are compared a relatively poor dose response relationship is present ($r_{xy} = 0.51$). If the dose is transformed to the following dose where D.E is the daily exposure and E.D number of exposure days: $\text{Dose} = \text{TPM}^4 \times \text{D.E}^4 \times \text{E.D}$, the resulting dose response improves and shows a correlation coefficient of .96.

The above transformation of the TPM dose is based upon the experience from experiments where certain of the variables in the suggested expression for the dose only showed relatively minor variations. The validity of the dose concept must therefore be further tested in future experiments. At present it can however, be concluded that high daily doses seem to be more important for the induction of epithelial cell changes than a prolonged duration of the experiment. The TPM concentration and daily duration exposure are almost equivalent with regard to epithelial changes.

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Comments

Based upon the above results, the following criteria are suggested for standard evaluation of cigarette smoke exposure effects in future short time inhalation experiments (about 100 d).

Blood

erythrocyte number
leukocyte number

Bone marrow or blood

mature neutrophils
leukocytes

Serum

GPT activity
acaline phosphatase
alpha-1-globulin
cholesterol
triglyceride
glucose

Respiratory tract histology

-nasal cavity
-larynx
-trachea and bifurcation
for each preparation evaluate hyper/metaplasia
index and goblet cell index

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