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EXPERIMENTAL BRONCHITIS IN ANIMALS DUE TO SULPHUR DIOXIDE AND CIGARETTE SMOKE: AN AUTOMATED QUANTITATIVE STUDY

INHALED PARTICLES 3(0): 509-526; 1971

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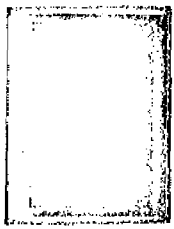
REVIEW: PREVIOUSLY PUBLISHED WORK CONCERNING INDUCED CHRONIC BRONCHITIS IN ANIMALS DUE TO SULFUR DIOXIDE AND CIGARETTE SMOKE EXPOSURES IS REVIEWED. THE SELECTION OF THE RAT AND THE RANK AS THE MOST USEFUL EXPERIMENTAL MODELS FOR STUDYING THE EFFECTS OF INHALATION ON THE LUNG AND THE QUANTITATIVE ASSESSMENTS OF THESE EFFECTS ARE ALSO DISCUSSED. (35 REFS)

DISCUSSION: "THE USE OF THE SPF TO DEMONSTRATE THE INCREASE IN TRACHEAL GLAND HYPERTROPHY FOLLOWING TOBACCO SMOKE HAS SHOWN THAT IT IS POSSIBLE TO MIMIC THE HUMAN CONDITION...IN PATIENTS WHO DIED OF CHRONIC BRONCHITIS. THIS CONDITION HAS BEEN REPRODUCED IN ANIMALS BEING SUBJECTED TO CIGARETTE SMOKE FOR A COMPARATIVELY SHORT PERIOD OF TIME AND INDICATES THE POTENTIAL DANGER OF CIGARETTE SMOKING IN RELATION TO BRONCHITIS. IT MAY BE THAT THIS ASPECT OF CIGARETTE SMOKING IS CONSIDERABLY MORE IMPORTANT THAN THE CARCINOGENIC PROPERTIES THAT HAVE BEEN THE SUBJECT OF SO MUCH CONCERN. THE METHODS HAVE BEEN EVOLVED TO PRODUCE BIO-ASSAYS OF IRRITATION WHICH MEAN IT IS NOW POSSIBLE TO MEASURE EXACTLY THE IRRITANT EFFECT OF TOBACCO SMOKE IN SOME LABORATORY ANIMALS. THIS IS THE FIRST AND VITALLY IMPORTANT STAGE IN THE PRODUCTION OF LESS IRRITANT CIGARETTES."

"RESPIRATORY IRRITANTS ARE FREQUENTLY CONTRIBUTORY CAUSES OF CHRONIC BRONCHITIS OR LUNG CANCER. EPIDEMIOLOGICAL STUDIES HAVE BEEN USED TO DETERMINE THESE FACTORS MAINLY DUE TO THE INABILITY OF RESEARCHERS TO



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PROVIDE SOME RUMORS IN LABORATORY ANIMALS WERE CARCINOGENIC SUBSTANCES. RESEARCH INTO THE ROLE OF ARE POLYAMINES AS A CAUSE OF CHRONIC BRONCHITIS HAS ALSO PROVIDED INCONCLUSIVE RESULTS. A MAJOR PROBLEM IN THE EXPERIMENTAL PRODUCTION OF BRONCHITIS HAS BEEN ELIMINATION OF THE ROLE PLAYED BY BACTERIAL INFECTION ALLOWING ONLY THE PHYSIOLOGICAL CHANGE CAUSED BY THE NOXIOUS SUBSTANCE ADMINISTERED TO BE EVALUATED.

"MEASUREMENT OF RESPIRATORY PHYSIOLOGY BY TRADITIONAL PNEUMOGRAPH OF THOSE CHANGES WHICH CAN BE DETECTED IN THE LIVING ANIMAL PROVIDE LITTLE EVIDENCE OF THE MORE SIGNIFICANT CHANGES OCCURRING IN THE RESPIRATORY TRACT. HYPERTROPHY OF MUCUS SECRETING ELEMENTS, THE ACCEPTED PATHOLOGICAL DESCRIPTION OF BRONCHITIS, IS MEANINGLESS IN THE CONTEXT OF CHANGES PRODUCED IN LABORATORY MODELS UNLESS SOME METHOD OF QUANTITATION SUPERIOR TO THE SUBJECTIVE ASSESSMENT OF THE HUMAN EYE CAN BE APPLIED. THE TECHNIQUES DESCRIBED IN THIS PAPER MAKE SUCH MORE OF IT POSSIBLE TO QUANTITATE CHANGES ASSOCIATED WITH BRONCHITIS TO A DEGREE OF ACCURACY HITHERTO UNPRECEDENTED."

"IT IS POSSIBLE THAT THE NORMAL DEFENCE MECHANISMS OF THE BODY TO ATMOSPHERIC POLLUTANTS ARE ABLE TO PROVIDE SOME DEGREE OF PROTECTION WITHOUT CAUSING PERMANENT DAMAGE. THE STAGE AT WHICH PERMANENT DAMAGE OCCURS IS AN UNKNOWN FACTOR AND ANY INCREASE IN SUBMICRON DUST IN OUR ATMOSPHERE MUST CONSTITUTE A CONSIDERABLE HAZARD.

"WHILST IT IS COMPARATIVELY EASY TO ASSESS A CELLULAR RESPONSE TO A NOXIOUS AGENT AS DELETERIOUS, A SENSE OF REALITY MUST BE APPLIED TO THIS CONCLUSION. THE RESPONSE COULD JUST AS EASILY BE ASSESSED, INITIALLY, AS AN EXTENDED PHYSIOLOGICAL SECRETION WHICH MIGHT EVEN BE BENEFICIAL. THE POINT AT WHICH AN EXTENDED PHYSIOLOGICAL REACTION BECOMES A PATHOLOGICAL ONE IS NOT EASILY ESTABLISHED."

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(PRESENTED AT THE PROCEEDINGS OF AN INTERNATIONAL SYMPOSIUM ORGANIZED BY THE BRITISH OCCUPATIONAL HYGIENE SOCIETY, LONDON UK, SEPT. 21-23, 1970)

(PART OF A SERIES: SEE ALSO DOCUMENT NOS. 31220-31235)

HUNT RES CENT, HUNTINGDON, UK/
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REVIEW, QUANTITATIVE STUDY A, AIR POLLUTION STUDY A, HISTOPATHOLOGICAL STUDY A, INHALATION STUDY A, ANIMAL MODEL STUDY, METHODOLOGY STUDY A, SPECIES SUSCEPTIBILITY A, CHRONIC BRONCHITIS INDUCTION A, CHRONIC BRONCHITIS SULFUR DIOXIDE ASSOC A, CHRONIC BRONCHITIS CIGARETTE SMOKE ASSOC A, CIGARETTE SMOKE EXPOSURE A, SULFUR DIOXIDE EXPOSURE A, ANIMAL MODEL EXTRAPOLATION/

LUNG CHANGES REVERSIBILITY A, CHRONIC BRONCHITIS HISTOPATHOLOGY A, AIR POLLUTANTS INHALATION A, LUNG DEFENSE MECHANISMS A, CIGARETTE SMOKE IRRITANT EFFECTS A, RATS, SHEEP, SULFUR DIOXIDE POSITIVE DOSE RESPONSE A, GOBLET CELL HYPERPLASIA A, BRONCHUS EPITHELIUM CHANGES A, TRACHEA EPITHELIUM CHANGES A, TRACHEOBRONCHIAL TREE A, LUNG MACROPHAGES ENZYMIC CHANGES A, CIGARETTE SMOKE EXPOSURE DURATION A, CIGARETTE SMOKE EXPOSURE A HI, INDIVIDUAL SUSCEPTIBILITY A HI, METHODOLOGY ANALYSIS A, CIGARETTE SMOKE RESPIRATORY EFFECTS A HI, ACID PHOSPHATASE INCREASE A, MUCUS HYPERSECRETION A, MUCUS VISCOSITY CHANGES A, MUCOUS GLAND HYPERTROPHY A, READ SMOKE A, LUNG CANCER INDUCTION A HI, RESPIRATORY FUNCTION TEST VALIDITY A HI, CIGARETTE SMOKE PHYSIOLOGICAL EFFECTS A HI, CHRONIC BRONCHITIS SMOKING CAUSATION 1, LUNG CANCER SMOKING CAUSATION 1, CIGARETTE SMOKE CARCINOGENICITY, RESPIRATORY IRRITATION, CHRONIC BRONCHITIS IRRITATION CAUSATION 2, LUNG CANCER LUNG IRRITATION CAUSATION 2, CHRONIC BRONCHITIS AIR POLLUTION CAUSATION 2, CHRONIC BRONCHITIS INFECTION CAUSATION 2/

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CHEMICAL CARCINOGENESIS: A LONG-NEGLECTED FIELD BLOSSOMS

Science 192(4246): 940-943, 1976

Maugh, TH .

MAIN REPORT: THIS PAPER REVIEWS RECENT PROGRESS IN CHEMICAL CARCINOGENESIS AND DISCUSSES THE ACTION MECHANISM OF CHEMICAL CARCINOGENS.

"ALTHOUGH ACTIVATION OF THE CARCINOGEN [BY CELLULAR ENZYMES] AND ITS REACTION WITH CELLULAR MACROMOLECULES ARE ONLY THE FIRST OF MANY STEPS LEADING TO TUMOR FORMATION, THEY OFFER SEVERAL HIGHLY SPECULATIVE POSSIBILITIES FOR ASCERTAINING THE EFFECT OF CARCINOGENS.... THE GREATEST BENEFIT FROM THE DISCOVERIES, IN FACT, MIGHT COME FROM USING THEM TO IDENTIFY INDIVIDUALS WHO SHOULD LIMIT THEIR EXPOSURE TO CERTAIN TYPES OF CARCINOGENS. THE CAPACITY FOR ENZYME INDUCTION IS NOT UNIFORM, SO SOME INDIVIDUALS HAVE A GREATER CAPACITY THAN OTHERS....

"PRELIMINARY RESULTS SUGGEST THAT ABOUT 9 PERCENT OF THE WHITE POPULATION IN THE UNITED STATES HAS THE CAPACITY FOR INDUCTION OF HIGH CONCENTRATIONS [illegible] AHH [ARYL HYDROCARBON HYDROXYLASE]; MODERATE CONCENTRATIONS CAN BE INDUCED IN ABOUT HALF OF THE OTHERS, AND ONLY LOW CONCENTRATIONS IN THE REST.... [I]NITIAL FINDINGS ALSO INDICATE THAT THE INCIDENCE OF LUNG CANCER IS ABOUT 36 TIMES HIGHER IN CIGARETTE SMOKERS WITH HIGH AHH INDUCIBILITY THAN IN THOSE WITH LOW INDUCIBILITY, AND ABOUT 16 TIMES HIGHER IN CIGARETTE SMOKERS WITH MODERATE AHH INDUCIBILITY.... [ALSO,] IT ... APPEARS THAT INDIVIDUALS WITH A VITAMIN A DEFICIENCY FORM A SECOND POPULATION SUBGROUP THAT IS MORE SUSCEPTIBLE TO CARCINOGENS IN TOBACCO SMOKE....

"PRESUMABLY, THEN, THE GREATEST INCIDENCE OF LUNG CANCER MIGHT BE FOUND IN CIGARETTE SMOKERS WHO HAVE HIGH AHH INDUCIBILITY AND WHO ARE DEFICIENT IN VITAMIN A.... [I]T MIGHT FOR THE FIRST TIME BE POSSIBLE TO IDENTIFY INDIVIDUALS WHO ARE AT A GREATER RISK FROM

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