Presented at IAQ '96; Nagoya, Japan; July 18,1996

File: Indoor Air Quality

BASELINE INFORMATION ON INDOOR AIR QUALITY IN LARGE BUILDINGS (BASE '95)

8/14

H.S. Brightman,[1] S.E. Womble,[2] E.L. Ronca,[2] and J.R. Girman,[2]

[1] Harvard School of Public Health, Boston, MA, USA
[2] U.S. Environmental Protection Agency, Office of Radiation and Indoor Air, Washington, DC, USA

ABSTRACT

A significant data gap exists regarding baseline indoor air quality (IAQ) in public and commercial office buildings in the USA. The U.S. Environmental Protection Agency's (EPA) Office of Radiation and Indoor Air is conducting a major study, entitled the Building Assessment Survey and Evaluation (BASE) Program, to address this gap with the goal of defining the status of the existing building stock. This cross-sectional study has collected baseline data to characterize public and commercial office buildings with respect to key determinants of IAQ and occupant perceptions. For the study, buildings were randomly selected without regard to IAQ complaints. The core parameters and methodology specified in an EPA standardized protocol were used to make measurements in a representative space in each building. This paper presents a summary of building descriptions and the results of environmental pollutant measurements and occupant perceptions of IAQ in 16 buildings studied during 1995. The building descriptions include information about building age; location; number of floors; floor area; heating, air-conditioning and ventilation system type; occupancy; and smoking policy. Environmental measurements include concentrations of the sum of targeted volatile organic compounds including formaldehyde, PM_{10}, fungi and bacteria. Occupant perceptions from a self-administered questionnaire were used to calculate a six-symptom Building Symptom Index (BSI), which is reported as well as the prevalence of selected individual symptoms. The data collected have been coded for confidentiality and are in a soon-to-be publicly-accessible data base.

INTRODUCTION

The Building Assessment Survey and Evaluation (BASE) Program is an on-going, cross-sectional study which is designed to address a significant data gap by collecting baseline data to characterize public and commercial office buildings in the USA with respect to key characteristics of IAQ and occupant perceptions. Data from 29 randomly selected buildings currently reside in a soon-to-be publicly available database. The study design, random selection process for buildings and study areas, and selected data from 13 buildings studied during 1994 are contained in two papers presented at the Healthy Buildings '95 Conference.[1,2] This paper presents selected data from 16 buildings studied during 1995. It provides a summary of building descriptions including information about building age; size; heating, air-conditioning and ventilation (HVAC) system type; occupant number; and smoking policy. This paper also

Disclaimer: Any opinions expressed in this paper are those of the authors and do not necessarily reflect those of Harvard University or the U.S. Environmental Protection Agency nor is any official endorsement to be implied.

summarizes environmental pollutant measurements, and occupant perceptions of IAQ in the 16 buildings, including the sum concentration of volatile organic chemicals (VOCs), formaldehyde,PM_{10}), and bioaerosols (fungi and bacteria). Other parameters such as temperature, relative humidity, $PM_{2.5}$, radon, carbon monoxide, and visible fungal growth, were measured in this study but will not be reported in this paper due to limitations of time and space. Occupant perceptions as measured by a self-administered questionnaire were used to calculate a six-symptom Building Symptom Index (BSI), which is reported, as well as the prevalence of selected individual symptoms.

MEASUREMENT METHODS

A test space was randomly selected within each building with a target population of no less than 50 occupants served by no more than two air handling units. Samplers for VOCs, formaldehyde, PM_{10}, bacteria and fungi were co-located at each of the three indoor and one outdoor sampling sites. Duplicate samples were taken at one indoor and the outdoor site. VOC samples were collected in Summa canisters and analyzed by GC/MS. Formaldehyde samples were collected on DNPH cartridges and analyzed by HPLC. PM_{10} samples were collected on filters and analyzed gravimetrically with a microbalance. Bacteria and fungi were collected on six-stage Anderson samplers for two- and five-minute intervals and were cultured on TSA and MEA media respectively. The bacteria samples were cultured at 30°C and 55°C. Details on the collection and analysis of these parameters can be found in "A Standardized EPA Protocol for Characterizing Indoor Air Quality in Large Office Buildings."[3] QA/QC procedures as described in "The United States Environmental Protection Agency's Large Building Studies Quality Assurance Overview Document"[4] were followed.

The questionnaire requests information about occupants' symptoms, their perceptions of their buildings' IAQ and work environment, and about other stressors, both at home and at work. The questionnaire was self-administered by occupants of the sampled space on Thursday of the sampling week, with steps taken to maintain confidentiality. The occupants were asked to return the questionnaires by that afternoon, which allowed for any follow-up collection on Friday.

RESULTS

The database of information which now includes the 13 buildings from BASE '94 and the 16 buildings from BASE '95 is a major step in the study of relationships among building and HVAC features, pollutant concentrations and occupant perceptions, as well as toward establishing a baseline of IAQ information in office buildings nationwide. This paper provides a summary of selected information from BASE '95. Further analyses and hypothesis testing will be possible as the study progresses and more buildings are included. Data summaries are presented in Tables 1 through 4. Buildings are identified with a unique code which identifies the State (with the first two letters), the climatic region by the third letter, and the season (winter (W) or summer (S)), with the fourth letter. The last two digits are a building designation for the study. Table 1 provides summary information regarding the building characteristics.

Table 2 contains the results of bioaerosol and PM_{10} measurements. Bioaerosols, including both fungi and bacteria, were sampled in both the morning and the afternoon. While both mesophyllic (30°C) and thermophyllic (55°C) bacteria were cultured, only the results for mesophyllic bacteria and fungi collected in the afternoon are reported in Table 2. Indoor PM_{10} concentrations ranged from 5.3 ug/m^3 to 28.6 ug/m^3. As was seen in the results from BASE '94 the particulate concentrations were generally lower indoors than outdoors. The difference

between indoor and outdoor concentrations is more pronounced when outdoor concentratic.. are elevated, buildings seem to attenuate the outdoor concentrations. The variation across sites within a building was low.

TABLE 1: Building Characteristics. Data regarding building age, size, study area location, smoking policy, and ventilation type, are shown for the 16 BASE '95 buildings.

Building ID[1]	Date Built/ Renovated	Building Envelope	Gross Area (m^2)	No. of Floors	Floor(s) of Study Area	No. of Occu-pants	Smoking policy	Ventilation Type
LAGW04	1980	Stone	70,232	27	20	1500	NSC[2]	VAV/CV[8]
LAGW05	1959	Glass/ Masonry	26,128	14	5	680	NS[3]	CV
LAGW06	1979	Glass/ Aluminum	74,815	33	22	1700	NSC/S[4]	VAV
SCDW01	1900/1985	Masonry	36,752	4	1	600	NS/SL[5]	VAV
SCDW02	1965/1970	Masonry	20,686	4	3	900	NS	VAV
NVAW02	1986	Masonry/ Glass	31,122	6	2	792	NS	VAV
NVAW01	1974	Concrete/ Glass	8,191	6	2	259	NS	VAV
NVAW03	1870/1963	Masonry	14,892	5	1	200	NS	CV
CAEW09	1963	Glass/ Concrete	6,775	2	1,2[6]	197	NS	VAV
CAEW07	1962	Concrete	4,134	4	2,3	95	NS/NE[7]	CV
AZHS04	1980	Masonry	1,950	1	1[6]	165	NS	VAV
AZHS02	1983/1993	Stucco	17,820	7	1	800	NS	VAV
FLGS04	1967	Concrete	8,243	7	4,5	200	NS	CV
FLGS01	1982	Masonry	4,538	3	1,2	120	NS	VAV
PABS04	1972	Concrete/ Glass	23,225	3	1	490	NS	VAV
PABS03	1963	Concrete	6,375	6	2,3	350	NS	VAV

[1]The buildings are identified with a unique code as follows: the first two letters represent the State abbreviation (e.g., LA represents Louisiana); the third letter represents the climatic region for the BASE study; the fourth letter designates a building studied in winter (W) or summer (S); and the two digits are a building designation for the study.
[2] Non-smoking common areas
[3] Non-smoking
[4] Smoking
[5] Smoking lounge, or designated smoking area
[6]Study area included the entire building
[7] Non -smoking building but policy not enforced
[8]Variable Air Volume (VAV)/Constant Volume(CV)

In general, both indoor VOC and formaldehyde concentrations tended to be approximately equal or higher than the outdoor concentrations. In addition, both the indoor and outdoor formaldehyde concentrations tended to be relatively low for this set of buildings, suggesting that formaldehyde sources were not strong. The high sum VOC value for one Nevada building was due overwhelmingly to high dichlorodifluoromethane concentrations. Table 4 presents the results of the self-administered occupant questionnaire. Building occupants were asked to report

Presented at IAQ '96; Nagoya, Japan; July 18,1996

File: Indoor Air Quality

BASELINE INFORMATION ON INDOOR AIR QUALITY IN LARGE BUILDINGS (BASE '95)

8/14

H.S. Brightman,[1] S.E. Womble, [2] E.L. Ronca,[2] and J.R. Girman,[2]

[1] Harvard School of Public Health, Boston, MA, USA
[2] U.S. Environmental Protection Agency, Office of Radiation and Indoor Air, Washington, DC, USA

ABSTRACT

A significant data gap exists regarding baseline indoor air quality (IAQ) in public and commercial office buildings in the USA. The U.S. Environmental Protection Agency's (EPA) Office of Radiation and Indoor Air is conducting a major study, entitled the Building Assessment Survey and Evaluation (BASE) Program, to address this gap with the goal of defining the status of the existing building stock. This cross-sectional study has collected baseline data to characterize public and commercial office buildings with respect to key determinants of IAQ and occupant perceptions. For the study, buildings were randomly selected without regard to IAQ complaints. The core parameters and methodology specified in an EPA standardized protocol were used to make measurements in a representative space in each building. This paper presents a summary of building descriptions and the results of environmental pollutant measurements and occupant perceptions of IAQ in 16 buildings studied during 1995. The building descriptions include information about building age; location; number of floors; floor area; heating, air-conditioning and ventilation system type; occupancy; and smoking policy. Environmental measurements include concentrations of the sum of targeted volatile organic compounds including formaldehyde, PM_{10}, fungi and bacteria. Occupant perceptions from a self-administered questionnaire were used to calculate a six-symptom Building Symptom Index (BSI), which is reported as well as the prevalence of selected individual symptoms. The data collected have been coded for confidentiality and are in a soon-to-be publicly-accessible data base.

INTRODUCTION

The Building Assessment Survey and Evaluation (BASE) Program is an on-going, cross-sectional study which is designed to address a significant data gap by collecting baseline data to characterize public and commercial office buildings in the USA with respect to key characteristics of IAQ and occupant perceptions. Data from 29 randomly selected buildings currently reside in a soon-to-be publicly available database. The study design, random selection process for buildings and study areas, and selected data from 13 buildings studied during 1994 are contained in two papers presented at the Healthy Buildings '95 Conference.[1,2] This paper presents selected data from 16 buildings studied during 1995. It provides a summary of building descriptions including information about building age; size; heating, air-conditioning and ventilation (HVAC) system type; occupant number; and smoking policy. This paper also

Disclaimer: Any opinions expressed in this paper are those of the authors and do not necessarily reflect those of Harvard University or the U.S. Environmental Protection Agency nor is any official endorsement to be implied.

summarizes environmental pollutant measurements, and occupant perceptions of IAQ in the 16 buildings, including the sum concentration of volatile organic chemicals (VOCs), formaldehyde,PM_{10}), and bioaerosols (fungi and bacteria). Other parameters such as temperature, relative humidity, $PM_{2.5}$, radon, carbon monoxide, and visible fungal growth, were measured in this study but will not be reported in this paper due to limitations of time and space. Occupant perceptions as measured by a self-administered questionnaire were used to calculate a six-symptom Building Symptom Index (BSI), which is reported, as well as the prevalence of selected individual symptoms.

MEASUREMENT METHODS

A test space was randomly selected within each building with a target population of no less than 50 occupants served by no more than two air handling units. Samplers for VOCs, formaldehyde, PM_{10}, bacteria and fungi were co-located at each of the three indoor and one outdoor sampling sites. Duplicate samples were taken at one indoor and the outdoor site. VOC samples were collected in Summa canisters and analyzed by GC/MS. Formaldehyde samples were collected on DNPH cartridges and analyzed by HPLC. PM_{10} samples were collected on filters and analyzed gravimetrically with a microbalance. Bacteria and fungi were collected on six-stage Anderson samplers for two- and five-minute intervals and were cultured on TSA and MEA media respectively. The bacteria samples were cultured at 30°C and 55°C. Details on the collection and analysis of these parameters can be found in "A Standardized EPA Protocol for Characterizing Indoor Air Quality in Large Office Buildings."[3] QA/QC procedures as described in "The United States Environmental Protection Agency's Large Building Studies Quality Assurance Overview Document"[4] were followed.

The questionnaire requests information about occupants' symptoms, their perceptions of their buildings' IAQ and work environment, and about other stressors, both at home and at work. The questionnaire was self-administered by occupants of the sampled space on Thursday of the sampling week, with steps taken to maintain confidentiality. The occupants were asked to return the questionnaires by that afternoon, which allowed for any follow-up collection on Friday.

RESULTS

The database of information which now includes the 13 buildings from BASE '94 and the 16 buildings from BASE '95 is a major step in the study of relationships among building and HVAC features, pollutant concentrations and occupant perceptions, as well as toward establishing a baseline of IAQ information in office buildings nationwide. This paper provides a summary of selected information from BASE '95. Further analyses and hypothesis testing will be possible as the study progresses and more buildings are included. Data summaries are presented in Tables 1 through 4. Buildings are identified with a unique code which identifies the State (with the first two letters), the climatic region by the third letter, and the season (winter (W) or summer (S)), with the fourth letter. The last two digits are a building designation for the study. Table 1 provides summary information regarding the building characteristics.

Table 2 contains the results of bioaerosol and PM_{10} measurements. Bioaerosols, including both fungi and bacteria, were sampled in both the morning and the afternoon. While both mesophyllic (30°C) and thermophyllic (55°C) bacteria were cultured, only the results for mesophyllic bacteria and fungi collected in the afternoon are reported in Table 2. Indoor PM_{10} concentrations ranged from 5.3 ug/m^3 to 28.6 ug/m^3. As was seen in the results from BASE '94 the particulate concentrations were generally lower indoors than outdoors. The difference

between indoor and outdoor concentrations is more pronounced when outdoor concentratic... are elevated, buildings seem to attenuate the outdoor concentrations. The variation across sites within a building was low.

TABLE 1: Building Characteristics. Data regarding building age, size, study area location, smoking policy, and ventilation type, are shown for the 16 BASE '95 buildings.

Building ID[1]	Date Built/ Renovated	Building Envelope	Gross Area (m^2)	No. of Floors	Floor(s) of Study Area	No. of Occu-pants	Smoking policy	Ventilation Type
LAGW04	1980	Stone	70,232	27	20	1500	NSC[2]	VAV/CV[8]
LAGW05	1959	Glass/ Masonry	26,128	14	5	680	NS[3]	CV
LAGW06	1979	Glass/ Aluminum	74,815	33	22	1700	NSC/S[4]	VAV
SCDW01	1900/1985	Masonry	36,752	4	1	600	NS/SL[5]	VAV
SCDW02	1965/1970	Masonry	20,686	4	3	900	NS	VAV
NVAW02	1986	Masonry/ Glass	31,122	6	2	792	NS	VAV
NVAW01	1974	Concrete/ Glass	8,191	6	2	259	NS	VAV
NVAW03	1870/1963	Masonry	14,892	5	1	200	NS	CV
CAEW09	1963	Glass/ Concrete	6,775	2	1,2[6]	197	NS	VAV
CAEW07	1962	Concrete	4,134	4	2,3	95	NS/NE[7]	CV
AZHS04	1980	Masonry	1,950	1	1[6]	165	NS	VAV
AZHS02	1983/1993	Stucco	17,820	7	1	800	NS	VAV
FLGS04	1967	Concrete	8,243	7	4,5	200	NS	CV
FLGS01	1982	Masonry	4,538	3	1,2	120	NS	VAV
PABS04	1972	Concrete/ Glass	23,225	3	1	490	NS	VAV
PABS03	1963	Concrete	6,375	6	2,3	350	NS	VAV

[1]The buildings are identified with a unique code as follows: the first two letters represent the State abbreviation (e.g., LA represents Louisiana); the third letter represents the climatic region for the BASE study; the fourth letter designates a building studied in winter (W) or summer (S); and the two digits are a building designation for the study.
[2] Non-smoking common areas
[3] Non-smoking
[4] Smoking
[5] Smoking lounge, or designated smoking area
[6]Study area included the entire building
[7] Non -smoking building but policy not enforced
[8]Variable Air Volume (VAV)/Constant Volume(CV)

In general, both indoor VOC and formaldehyde concentrations tended to be approximately equal or higher than the outdoor concentrations. In addition, both the indoor and outdoor formaldehyde concentrations tended to be relatively low for this set of buildings, suggesting that formaldehyde sources were not strong. The high sum VOC value for one Nevada building was due overwhelmingly to high dichlorodifluoromethane concentrations. Table 4 presents the results of the self-administered occupant questionnaire. Building occupants were asked to report

symptoms for the last week and for the last month. The occupant response rate for completing questionnaires was high, 83%.

Table 2. Fungi, Bacteria, and PM_{10}. The range for the sum of 36 genus/species of fungi and 7 classifications of bacteria for three indoor sites, two-minute, afternoon samples and the arithmetic mean (AM) and standard deviation (ASD) for duplicates at the outdoor site, afternoon, two minute samples taken for the 16 '95 BASE buildings. PM_{10} measurements at each of the indoor sites and the AM and ASD for the outside measurements. $PM_{2.5}$ measurements were made at one indoor site and outdoor but are not reported due to space limitations.

Building ID	Fungi[1] - cfu/m³		Bacteria[1] - cfu/m³		PM_{10}-µg/m³				
	Indoor	Outdoor	Indoor	Outdoor	Indoor			Outdoor	
	Range	AM (ASD)	Range	AM (ASD)	Site 1	Site 2	Site 3	P[2]	D[3,4]
LAGW04	35-371	575(112)	18-203	292(37)	13.4	4.7	6.2	15.8	14.7
LAGW05	0-88	300(0)	18-124	362(87)	11.3	-[5]	12.0	51.4	48.8
LAGW06	0-35	159(50)	18-124	159(25)	-[6]	19.3	11.3	12.1	6.7
SCDW01	35-194	159(26)	88-194	106(25)	15.2	17.6	11.0	9.1	8.4
SCDW02	0-18	NC[7]	35-124	NC	10.6	12.0	8.5	18.6	15.6
NVAW02	0-106	NC	71-124	NC	12.4	9.6	12.3	5.8	7.1
NVAW01	0-53	115(38)	132-230	283(175)	12.5	12.9	12.6	51.2	48.0
NVAW03	18-88	115(13)	124-159	168(62)	11.3	16.8	12.3	10.6	12.1
CAEW09	265-530	1281(163)	230-389	1387(13)	10.7	11.8	6.0	19.9	22.7
CAEW07	0-88	247(0)	106-212	327(237)	6.9	7.1	9.1	13.6	14.1
AZHS04	53-3462	221(38)	71-247	265(150)	6.7	7.4	8.0	31.5	35.3
AZHS02	35-141	168(13)	97-336	141(50)	9.0	12.1	31.1	34.0	33.6
FLGS04	0-177	813(150)	106-813	1025[7]	5.3	7.4	9.3	7.6	8.4
FLGS01	0-106	353(150)	159-177	62(13)	12.6	23.9	28.6	102.8	98.6
PABS04	53-194	1405(112)	27-495	327(187)	16.1	14.3	16.0	38.1	38.1
PABS03	0-53	865(175)	133-177	53(0)	15.0	14.8	11.7	25.4	26.4

[1]Samples cultured at 30°C, colony forming units (cfu)
[2]Primary Sample
[3]Duplicate Sample
[4]Average relative standard deviation for duplicates was 8.5%.
[5]$PM_{2.5}$ was measured instead of PM_{10}
[6]Sample voided by lab
[7]Sample not collected due to very heavy rain.
[8]Duplicate below detection limit

The symptom prevalences reported in Table 4 are unadjusted for gender, job classification or age, although this information was collected for future analysis. The symptoms for each individual were used to calculate a Personal Symptoms Index (PSI) by summing the number of the six symptoms reported by each occupant. Symptoms were counted in the PSI only if that symptom "got better" when the respondent was away from work. These PSI values were then averaged for each building to create a Building Symptom Index (BSI), which can range from 0 to 6.

SUMMARY

This data set represents the first step toward obtaining baseline data to characterize public and commercial office buildings in the U.S. with respect to IAQ and occupant perceptions toward it. This is a rich data set which allows examination of possible relationships among building and HVAC features, pollutant concentrations and occupant symptoms. In addition, the data will provide a sound basis for hypothesis development in subsequent studies. As more buildings are studied (five additional buildings have already been studied during the 1995-6 winter season), data will become more representative of the current status of the U.S. building stock and occupant perceptions.

Table 3. VOCs and Formaldehyde. Sum of volatile organic chemicals in ug/m^3 measured using the EPA TO-14 standard test method and the concentrations of formaldehyde also in ug/m^3.

Building ID	VOCs ug/m^3					Formaldehyde ug/m^3				
	Indoor			Outdoor		Indoor			Outdoor	
	Site 1	Site 2	Site 3	P[1]	D[2,3]	Site 1	Site 2	Site 3	P	D[4]
LAGW04	462	424	515	28	32	9	1	BQL[6]	BQL	1
LAGW05	206	178	199	113	112	6	8	7	AQL[7]	BQL
LAGW06	284	212	223	14	58	16	23	19	2	1
SCDW01	144	140	313	38	39	7	9	8	AQL	AQL
SCDW02	101	199	149	32	33	12	15	17	BQL	BQL
NVAW02	1935[5]	1358[5]	2108[5]	204	248	9	6	8	1	1
NVAW01	69	64	160	47	38	4	4	5	BQL	1
NVAW03	58	70	119	38	26	3	3	4	1	1
CAEW09	63	83	103	35	97	8	9	10	3	1
CAEW07	47	33	53	23	23	5	6	5	4	2
AZHS04	174	159	191	297	24	17	21	21	2	2
AZHS02	69	126	94	49	33	8	12	9	2	3
FLGS04	441	394	440	72	45	21	29	27	BQL	AQL
FLGS01	-	119	146	81	53	9	11	11	8	7
PABS04	260	174	165	29	130	13	13	14	5	4
PABS03	388	371	460	44	57	15	16	15	5	5

[1]Primary Sample
[2]Duplicate Sample
[3]The average relative standard deviation for duplicates was 25%.
[4]The average relative standard deviation for duplicates was 20%.
[5]The reported concentration is mostly due to the contribution of dichlorodifloromethane.
[6]Below the quantitation limit of 0.4 ug/m^3.
[7]At the quantitation limit.

Table 4. Building Symptom Index (BSI), based on six self-reported symptoms that got better when occupants were away from work. BSI This Month is for the past four weeks preceding the study and BSI This Week is for the week of the study. The questionnaire was administered on Thursday. Also shown are the symptom prevalence for the six symptoms used to calculate the BSI for the sixteen BASE '95 buildings.

Building ID	BSI This Month	BSI This Week	Dry, Itching or Irritated Eyes This Week	Head-ache This Week	Sore or Dry Throat This Week	Unusual Tiredness, Fatigue or Drowsiness This Week	Stuffy or Runny Nose, or Sinus Congestion This Week	Dry or Itchy Skin This Week
LAGW04	0.89	0.56	0.06	0.27	0.03	0.11	0.08	0.02
LAGW05	2.02	1.52	0.46	0.22	0.11	0.28	0.37	0.07
LAGW06	0.81	0.55	0.09	0.19	0.04	0.08	0.11	0.04
SCDW01	1.18	0.96	0.18	0.19	0.13	0.18	0.21	0.07
SCDW02	0.78	0.74	0.26	0.26	0.04	0.13	0.04	0.00
NVAW02	1.49	1.06	0.27	0.31	0.08	0.24	0.08	0.08
NVAW01	1.23	0.98	0.20	0.23	0.10	0.25	0.20	0.00
NVAW03	2.22	1.67	0.42	0.40	0.16	0.33	0.31	0.04
CAEW09	1.84	1.39	0.39	0.29	0.16	0.30	0.20	0.05
CAEW07	0.81	0.47	0.06	0.25	0.03	0.06	0.06	0.00
AZHS04	1.46	1.08	0.22	0.27	0.19	0.19	0.16	0.05
AZHS02	1.22	0.83	0.14	0.22	0.11	0.19	0.11	0.06
FLGS04	1.44	0.74	0.22	0.16	0.10	0.16	0.06	0.04
FLGS01	1.26	1.02	0.28	0.20	0.08	0.20	0.18	0.08
PABS04	1.98	1.44	0.35	0.31	0.21	0.27	0.20	0.08
PABS03	1.58	1.24	0.29	0.29	0.13	0.31	0.18	0.04

ACKNOWLEDGMENT

We would like to acknowledge the efforts and care taken by the staff of Environmental Health & Engineering in conducting the field work and by the staff of ManTech in assuring the quality of the data.

REFERENCES

1. Womble, S.E.;Girman, J.R.; Ronca, E.L.; et al. 1995. "Developing Baseline Information on Buildings and Indoor Air Quality (BASE '94): Part I-Study Design, Building Selection, and Building Descriptions." *Proceedings of Healthy Buildings '95, Milan, Italy*, Vol. 3, pp.1305-1310.

2. Girman, J.R.; Womble, S.E.; and Ronca, E.L. 1995. "Developing Baseline Information on Buildings and Indoor Air Quality (BASE'94): Part II - Environmental Pollutant Measurements and Occupant Perceptions." *Proceedings of Healthy Buildings '95, Milan, Italy*, Vol. 3, pp.1311-1316.

3. U.S. Environmental Protection Agency. 1994. "A Standardized EPA Protocol for Characterizing Indoor Air Quality in Large Office Building," Office of Research and Development and Office of Air and Radiation, U.S. Environmental Protection Agency, Washington, DC, USA.

4. U.S. Environmental Protection Agency. 1994. "The United States Environmental Protection Agency's Large Building Studies Quality Assurance Overview Document," Office of Research and Development and Office of Air and Radiation.

Author: John B. Cunningham at ~PITCCN4
Date: 7/10/96 5:39 PM
Priority: Normal
TO: Donald J. Moeslein at ~AMPCCN3
Subject: air quality at 2AC

---------- Message Contents ----------

Don,
How should we test for air quality?
John

File: INDOOR AIR QUALITY

Subject: air quality at 2AC
From: Kathleen M. Hovanec at ~PITCCN8
Date: 7/10/96 3:25 PM

John,

I'm still having a problem with the air quality here in 2AC. Persistent headaches and a general feeling of fatigue or sleepiness appear within an hour of arriving at the building, persist while I'm here and then just disappear after I'm out of here for about 20-30 minutes. One thing I did notice is that when I was here after 6PM (when the air circulation is off) on Monday, the headache went away by 6:30.

I know I've mentioned this before, but other people here on the 4th floor have experienced the same symptoms which generally disappear after they are out of the building for a short while. This surely presents a health/safety concern, not only from the standpoint of possible errors of judgment occurring, but also the regular consumption of aspirin, Tylenol, etc. and high levels or caffeine in the effort to overcome these symptoms isn't good for anyone's health.

In doing some reading, these symptoms have been linked to insufficient levels of oxygen, excessive levels of carbon dioxide or carbon monoxide; airborne pollutants (with all the construction going on in the building, this wouldn't surprise me); and mold/mildew from insufficiently/improperly cleaned air conditioning equipment (this can be particularly bad, as it can cause a severe form of pneumonia generally know as Legionnaire's disease). I think it has been dubbed "sick building syndrome."

Could we please have the air quality for these things (you're probably more aware than I am of things they test for) to see just what we are breathing every day?

Thanks!

and other airborne substances which may cause material impairment to employees working within the nonindustrial environment.

Assistant Secretary means the Assistant Secretary of Labor for Occupational Safety and Health, U.S. Department of Labor, or designee.

Building-related illness describes specific medical conditions of known etiology which can be documented by physical signs and laboratory findings. Such illnesses include sensory irritation when caused by known agents, respiratory allergies, asthma, nosocomial infections, humidifier fever, hypersensitivity pneumonitis, Legionnaires' disease, and the signs and symptoms characteristic of exposure to chemical or biologic substances such as carbon monoxide, formaldehyde, pesticides, endotoxins, or mycotoxins.

Comment: Support inclusion only of illness documented by physical signs and laboratory findings.

Building systems include but are not limited to the heating, ventilation and air-conditioning (HVAC) system, the potable water systems, the energy management system and all other systems in a facility which may impact indoor air quality.

Comment: Add "are systems that may have an impact on indoor air quality and" after "Building systems" above. Delete "potable water systems" and substitute "systems that could result in aerosolized microbial contaminants that could cause BRI."

Designated person means a person who has been given the responsibility by the employer to take necessary measures to assure compliance with this section and who is knowledgeable in the requirements of this standard and the specific building systems servicing the affected building or office.

Designated smoking area means a room, in a non-work area, in which smoking of tobacco products is permitted.

Director means the Director, National Institute for Occupational Safety and Health (NIOSH) U.S. Department of Health and Human Services or designee.

Employer means all persons defined as employers by Sec. 3(5) of the Occupational Safety and Health Act of 1970 including employers (such as building owners or lessees) who control the ventilation or maintenance of premises where employees of other employers work.

File: INDOOR AIR QUALITY

1910 Sunderland Place, N.W.
Washington, D.C. 20036
Tel: 202-293-2980
Fax: 202-293-2915

Organization Resources Counselors, Inc.

Memorandum

May 26, 1994

To: ORC Indoor Air Quality Task Force

From: Ann Brockhaus

Subject: Draft ORC Comments

Attached is a very preliminary draft of ORC comments on the OSHA IAQ proposal. I will send a more polished draft within the next two weeks. I look forward to getting your reactions.

OSHA has not yet made a decision on extending the comment period. A 60 day extension is likely. I will let you know when a decision is made.

If the comment period is not extended, I will need your comments by June 23, 1994.

AB/ab

HVAC system means the collective components of the heating, ventilation and air-conditioning system including, but not limited to, filters and frames, cooling coil condensate drip pans and drainage piping, outside air dampers and actuators, humidifiers, air distribution ductwork, automatic temperature controls, and cooling towers.

Nonindustrial work environment means an indoor or enclosed work space such as, but not limited to, offices, educational facilities, commercial establishments, and healthcare facilities, and office areas, cafeterias, and break rooms located in manufacturing or production facilities used by employees. Nonindustrial work environments do not include manufacturing and production facilities, residences, vehicles, and agricultural operations.

Comment: D.O. to send additional comment. Add "warehouses" to list of exemptions.

Renovation and remodeling means building modification involving activities that include but are not limited to: removal or replacement of walls, ceilings, floors, carpet, and components such as moldings, cabinets, doors, and windows; painting, decorating, demolition, surface refinishing, and removal or cleaning of ventilation ducts.

(c) Indoor air quality (IAQ) compliance program.

(1) All employers with workplaces covered by paragraph (a)(1) of this section shall establish a written IAQ compliance program.

(2) The employer shall identify a designated person who is given the responsibility to assure implementation of the IAQ compliance program.

Comment: Support (c)(1) and (2).

(3) Written plans for compliance programs shall include at least the following:

(i) A written narrative description of the facility building systems;

(ii) Single-line schematics or as-built construction documents which locate major building system equipment and the areas that they serve;

(iii) Information for the daily operation and management of the building systems, which shall include at least a description of normal operating procedures, special procedures such as seasonal start-ups and shutdowns, and a list of

operating performance criteria including, but not limited to minimum outside air ventilation rates, potable hot water storage and delivery temperatures, range of space relative humidities, and any space pressurization requirements;

(iv) A general description of the building and its function including but not limited to, work activity, number of employees and visitors, hours of operation, weekend use, tenant requirements and known air contaminants released in the space;

Comment: Delete (c)(3)(i)-(iii) and include in a non-mandatory appendix "Model Indoor Air Quality Management Plan."

(v) A written maintenance program for the maintenance of building systems which shall be preventive in scope and reflect equipment manufacturer's recommendations and recommended-good-practice as determined by the building systems maintenance industry. At a minimum, the maintenance program shall describe the equipment to be maintained, and establish maintenance procedures and frequency of performance;

(vi) A checklist for the visual inspection of building systems.

Comment: Support (c)(3)(v) and (vi).

(4) The following additional information, if available, shall be retained by the employer to assist in potential indoor air quality evaluations:

(i) As-built construction documents;

(ii) HVAC system commissioning reports;

(iii) HVAC systems testing, adjusting and balancing reports;

(iv) Operations and maintenance manuals;

(v) Water treatment logs; and

(vi) Operator training materials.

(5) The employer shall establish a written record of employee complaints of signs or symptoms that may be related to building-related illness to include at least information on the nature of the illness reported, number of employees affected, date of employee complaint, and remedial action, if any, taken to correct the source of the problem.

Comment: Oppose this requirement. BRI as defined by OSHA is recordable on the OSHA 200 Log. Complaints investigated and readily resolved, and not found to be consistent with BRI, should not have to be recorded. This section could instead require a written procedure for receiving and responding to IAQ complaints.

(d) Compliance program implementation.

Employers shall assure compliance with this section by implementing at least the following actions:

(1) Maintain and operate the HVAC system to assure that it operates up to original design specifications and continues to provide at least the minimum outside air ventilation rate, based on actual occupancy, required by the building code, mechanical code, or ventilation code applicable at the time the facility was constructed, renovated, or remodeled, whichever is most recent;

Comment: Change wording to the following:

(1) Maintain and operate the HVAC system to assure that it operates up to original design specifications and continues to provide at least the minimum outside air ventilation rate, based on actual occupancy, required by the applicable building code, mechanical code, or ventilation code;

(2) Conduct building systems inspections and maintenance in accordance with paragraph (c) of this section;

(3) Assure that the HVAC system is operating during all work shifts, except during emergency HVAC repairs and during scheduled HVAC maintenance;

Comment: Employers must have the flexibility to adjust the HVAC system appropriately during periods of reduced demand. P.O. to provide additional comment on this. Wording??

(4) Implement the use of general or local exhaust ventilation where housekeeping and maintenance activities involve use of equipment or products that could reasonably be expected to result in hazardous chemical or particulate exposures to employees working in other areas of the building or facility;

Comment: Needs clarification. D.E. and J.B. to provide additional comment. It has been suggested that this section and other similar sections [sections (e)(2)(ii), (f)(1), (f)(2), and (f)(3)] be deleted and placed in a non-mandatory appendix. Another approach is as follows:

(4) Implement the use appropriate controls such as local exhaust ventilation where housekeeping and maintenance activities involve use of equipment or products that could reasonably be expected to result in chemical or particulate exposures at levels that could cause BRI to employees working in other areas of the building or facility;

(5) Maintain relative humidity below 60% in buildings with mechanical cooling systems;

Comment: Delete; not defensible or always feasible. Need volunteer to write argument for this.

(6) The employer shall monitor carbon dioxide levels when routine maintenance under paragraph (d)(1) of this section is done. When the carbon dioxide level exceeds 800 ppm, the employer shall check to make sure the HVAC system is operating as it should. If it is not, the employer shall take necessary steps to correct deficiencies if they exist.

Comment: Recommend this be placed in a non-mandatory appendix "Model Indoor Air Quality Management Plan."

(7) Assure that buildings without mechanical ventilation are maintained so that windows, doors, vents, stacks and other portals designed or used for natural ventilation are in operable condition;

(8) Assure that mechanical equipment rooms and any non-ducted air plenums or chases that transport air are maintained in a clean condition, hazardous substances are properly stored to prevent spillage, and asbestos, if friable, is encapsulated or removed so that it does not enter the air distribution system;

Comment: Delete reference to asbestos, as this duplicates requirements likely to be soon to be published asbestos rule. New wording:

(8) Assure that mechanical equipment rooms and any non-ducted air plenums or chases that transport air are maintained in a clean condition, and hazardous substances are properly stored to prevent spillage.

(9) Assure that inspections and maintenance of building systems are performed by or under the supervision of the designated person;

(10) Establish a written record of building system inspections and maintenance required to be performed under this section;

(11) Assure that employees performing work on building systems are provided with and use appropriate personal protective equipment as prescribed in 29 CFR part 1926, subpart E, Personal Protective and Life Saving Equipment; 29 CFR part 1926.52, Occupational Noise Exposure; 29 CFR part 1910, subpart I, Personal Protective Equipment; and 29 CFR part 1910.95, Occupational Noise Exposure;

Comment: Delete; not necessary to refer to other standards. May be provided as information to employers in a non-mandatory appendix "Model Indoor Air Quality Management Plan."

(12) Evaluate the need to perform alterations of the building systems to meet the minimum requirements specified in paragraph (d) of this section in response to employee complaints of building-related illnesses; and

(13) Take such remedial measures as the evaluation shows to be necessary.

(e) Controls for specific contaminant sources.

(1) Tobacco smoke.

(i) In workplaces where the smoking of tobacco products is not prohibited, the employer shall establish designated smoking areas and permit smoking only in such areas;

(ii) The employer shall assure that designated smoking areas are enclosed and exhausted directly to the outside, and are maintained under negative pressure (with respect to surrounding spaces) sufficient to contain tobacco smoke within the designated area;

(iii) The employer shall assure that cleaning and maintenance work in designated smoking areas is conducted only when no smoking is taking place;

(iv) The employer shall assure that employees are not required to enter designated smoking areas in the performance of normal work activities;

(v) The employer shall post signs clearly indicating areas that are designated smoking areas;

(vi) The employer shall post signs that will clearly inform anyone entering the workplace that smoking is restricted to designated areas; and

(vii) The employer shall prohibit smoking within designated smoking areas during any period that the exhaust ventilation system servicing that area is not properly operating.

Comment: Support as written (1)(i)-(vii), consistent with ORC comments in response to the RFI.

(2) Other indoor air contaminants.

(i) The employer shall implement measures such as the relocation of air intakes and other pathways of building entry, where necessary, to restrict the entry of outdoor air contaminants such as vehicle exhaust fumes, into the building;

Comment: F.G. to improve wording.

(ii) When general ventilation is inadequate to control air contaminants emitted from point sources within workspaces the employer shall implement other control measures such as local source capture exhaust ventilation or substitution.

Comment: Reword to be consistent with (d)(4). Suggest the following wording: "Implement the use of other control measures such as local source capture exhaust ventilation or substitution when necessary to prevent accumulation of air contaminants emitted from point sources within workspaces at levels that could reasonably be expected to result in building related illness."

(3) Microbial contamination.

(i) The employer shall control microbial contamination in the building by routinely inspecting for, and promptly repairing, water leaks that can promote growth of biologic agents;

(ii) The employer shall control microbial contamination in the building by promptly drying, replacing, removing, or cleaning damp or wet materials; and

Comment: Improve wording as follows: "The employer shall control microbial contamination in the building by promptly using effective means such as drying, replacing, removing, or cleaning damp or wet materials; and"

(iii) The employer shall take measures to remove visible microbial contamination in ductwork, humidifiers, other HVAC and building system components, or on building surfaces when found during regular or emergency maintenance activities or during visual inspection.

(4) Use of cleaning and maintenance chemicals, pesticides, and other hazardous chemicals in the workplace.

(i) The employer shall assure that these chemicals are used and applied according to manufacturers' recommendations; and

(ii) The employer shall inform employees working in areas to be treated with potentially hazardous chemicals, at least within 24 hours prior to application, of the type of chemicals intended to be applied.

Comment: Help!!! We considered recommending that this be deleted because we thought HazCom might take care of this, but now I'm not so sure. It may be defensible to leave this in. What do you think?

(f) Air quality during renovation and remodeling.

(1) General. During renovation or remodeling, the employer shall assure that work procedures and appropriate controls are utilized to minimize degradation of the indoor air quality of employees performing such activities and employees in other areas of the building.

Comment: Vague wording about "degradation" needs to be improved. Sections (d)(4), (e)(2)(ii), (f)(1), (f)(2), and (f)(3), should all be consistent.

Suggest the following wording:

(1) General. During renovation or remodeling, the employer shall assure that work procedures and appropriate controls are utilized where equipment or products are used that could reasonably be expected to result in chemical or particulate exposures at levels that could cause BRI to employees working in other areas of the building or facility;

(2) Work plan development.

(i) Before remodeling, renovation, or similar activities are begun the employer shall meet with the contractor or individual(s) performing the work and shall develop and implement a work plan designed to minimize entry of air contaminants to other areas of the building during and after performance of the work; and

Comment: Change to be consistent with Sections (d)(4), (e)(2)(ii), and (f)(1), as follows:

(i) Before remodeling, renovation, or similar activities are begun the employer shall meet with the contractor or individual(s) performing the work and shall develop and implement a work plan designed to assure that work procedures and appropriate controls are utilized where equipment or products are used that could reasonably be expected to result in chemical or particulate exposures at levels that could

cause BRI to employees working in other areas of the building or facility;

(ii) The work plan shall consider all of the following where appropriate:

(A) Requirements of this standard.

(B) Implementation of means to assure that HVAC systems continue to function effectively during remodeling and renovation activities.

(C) Isolation or containment of work areas and appropriate negative pressure containment.

(D) Air contaminant suppression controls or auxiliary air filtration/cleaning.

(E) Controls to prevent air contaminant entry into the HVAC air distribution system.

Comment: (E) Should be reworded to be consistent with Sections (d)(4), (e)(2)(ii), and (f)(1), and (f)(2) as follows:

(E) Other work procedures and appropriate controls as necessary where equipment or products are used that could reasonably be expected to result in chemical or particulate exposures at levels that could cause BRI to employees working in other areas of the building or facility;

(3) Prior notification of employees who work in the building.

(i) The employer shall notify employees at least 24 hours in advance, or promptly in emergency situations, of work to be performed on the building that may introduce air contaminants into their work area;

Comment: Revise wording as follows:

(i) The employer shall notify employees at least 24 hours in advance, or promptly in emergency situations, of work to be performed on the building that may result in potentially hazardous exposures in their work area;

(ii) Notification shall include anticipated adverse impacts on indoor air quality or workplace conditions.

(g) Employee information and training.

(1) The employer shall provide training for maintenance workers and workers involved in building system operation and maintenance which shall include at least the following:

(i) Training in the use of personal protective equipment (PPE) needed in operating and maintaining building systems;

Comment: Delete; covered by PPE standard.

(ii) Training on how to maintain adequate ventilation of air contaminants generated during building cleaning and maintenance; and

(iii) Training of maintenance personnel on how to minimize adverse effects on indoor air quality during the use and disposal of chemicals and other agents.

(2) All employees shall be informed of:

(i) The contents of the standard in this section and its appendices; and

(ii) Signs and symptoms associated with building-related illness and the requirement under paragraphs (d)(12) and (d)(13) of this section directing the employer to evaluate the effectiveness of the HVAC system and to take remedial measures to the HVAC system if necessary, upon receipt of complaints from employees of building-related illness.

Comment: Delete. Change wording to "Employees should be informed of the employer's procedures for receiving employee indoor air quality concerns." This procedure should be included in the employer's written compliance program.

(3) Availability of training material. The employer shall make training materials developed in response to paragraph (g), including the standard in this section and its appendices, available for inspection and copying by employees, designated employee representatives, the Director, and the Assistant Secretary.

(h) Recordkeeping.

(1) Maintenance records. The employer shall maintain inspection and maintenance records required to be established under paragraph (d) of this section, which shall include the specific remedial or maintenance actions taken, the name and affiliation of the individual performing the work, and the date of the inspection or maintenance activity.

(2) Written IAQ compliance program. The employer shall maintain the written compliance program and plan required to be established under paragraph (c) of this section.

(3) Employee complaints. The employer shall maintain a record of employee complaints of signs or symptoms that may be associated with building-related illness required to be established under paragraph (c)(5) of this section. These complaints shall be promptly transmitted to the designated person for resolution.

Comment: Delete and include in non-mandatory appendix to be consistent with (c)(5).

(4) Retention of records. The employer shall retain records required to be maintained under this section for at least the previous three years, except that records required to be maintained under paragraphs (h)(1) and (h)(2) of this section need not be retained for three years if rendered obsolete by the establishment and replacement of more recent records, or rendered irrelevant due to HVAC system replacement or redesign.

(5) Availability. The records required to be maintained by this paragraph shall be available on request to employees and their designated representative and the Assistant Secretary for examination and copying.

(6) Transfer of records. Whenever the employer ceases to do business, records that are required to be maintained by paragraph (h) of this section shall be provided to and retained by the successor employer.

(i) Dates. (1) Effective date. This section is effective [DATE 60 DAYS FROM PUBLICATION OF THE FINAL RULE]

(2) Start-up dates.

Employers shall have implemented all provisions of this standard no later than one year from [THE EFFECTIVE DATE OF THE FINAL RULE].

VI. Factors influencing the dose for aerosols

a. Factors influencing total dose (total deposition)

b. Factors influencing regional deposition

i) sedimentation

ii) impaction

iii) diffusion

iv) electrostatic forces

v) interception

vi) quick summary

VII. Retention - Clearance

a. Model

b. Input

c. Absorption - translocation processes

d. implication of the model

e. Man vs. laboratory animals

VIII. Factors influencing the dose for gases, vapors

1. High water solubility and reactivity

o Importance in toxicological studies, man vs. mouse

2. High reactivity, low water solubility

3. Low reactivity, no metabolism

a. Physical parameters

b. Physiological parameters

c. Influence of metabolism

4. Quick summary

o Application in toxicology

5. Practical use, alveolar air

o Example of industrial exposure

o Breath analysis

IX. Effects on the respiratory tract

A. Sensory irritants

B. Pulmonary irritants

C. Bronchoconstrictors

D. Respiratory irritants

E. Pulmonary sensitizers

F. Tissue reactions

1. Obstructive pulmonary disease, chronic bronchities

2. Centrilobular emphysema

3. Asthma

4. Oxidant injury

5. Pulmonary edema

G. Specific Occupational Pulmonary Disease

1. Cadmium and Beryllium

2. Silicosis

3. Silicotuberculosis

4. Asbestosis

5. Coal Worker's pneumoconiosis

6. Kaolin

7. Siderosis, Nickel

8. Metal fume fever, zinc, cadmium

9. Teflon fume fever

H. Lung Carcinoma

1. Classification

2. Human Carcinogens

3. Mesothelioma

X. Standards for Airborne Contaminants

A. Definitions, Promylgating Agencies

i) TLV-TWA

ii) TLV (C)

iii) STEL

iv) PEL

v) EEL

vi) AQS

B. OSHA Health Hazard Categories

i) System

ii) Examples

C. NIOSH/OSHA

i) Pocket guide to chemical hazards

D. Air Quality Standards

E. Establishing TLVs

a) Type of data

b) Type of effects

c) TLV are not toxic indices

XI. Federal Hazardous Substances Act

a) Toxic

b) Highly toxic

I. DESCRIPTION OF CONTAMINANTS, TERMS USED

A. GAS: A STATE OF MATTER IN WHICH THE MOLECULES ARE PRACTICALLY UNRESTRICTED BY COHESIVE FORCES. A GAS HAS NEITHER SHAPE NOR VOLUME FOR OUR USE, IT IS A SUBSTANCE WHICH HAS A CRITICAL TEMPERATURE BELOW 20^{O} C AND THUS CANNOT BE CONDENSED AT ANY PRESSURE AT THIS TEMPERATURE. EXAMPLES: METHANE (-82), FLOURINE (-129) HELIUM (-268).

(cannot exist as a liquid at room temperature 20°C

B. VAPOR: SUBSTANCE DISPERSED IN AIR AS INDIVIDUAL MOLECULES, BELOW ITS CRITICAL TEMPERATURE AND THUS COULD BE CONDENSED TO A LIQUID AT 20^{O} C BY INCREASING THE PRESSURE. THE WORDS VAPOR AND GAS ARE OFTEN USED INTER-CHANGEABLY. VAPOR IS MORE FREQUENTLY USED FOR A SUBSTANCE WHICH, THOUGH PRESENT IN THE GASEOUS PHASE AT 20^{O} C, GENERALLY EXISTS AS A LIQUID OR SOLID AT THIS TEMPERATURE AND NORMAL ATMOSPHERIC PRESSURE. EXAMPLES: IODINE (512), BENZENE (289), CARBON DISULFIDE (279). WE CAN ALSO SAY THAT SO_2 (157), CL_2 (144) NO_2 (158) AND CO_2 (289) CAN BE OBTAINED AS "VAPOR" SINCE AT 20^{O} C THEY CAN BE CONDENSED IN THE LIQUID PHASE BY INCREASING THE PRESSURE. THE DIFFERENCE BETWEEN THE TWO SETS OF EXAMPLES IS SIMPLY THAT FOR THE FIRST SET THEY ARE SOLID OR LIQUID AT ATMOSPHERIC PRESSURE AND 20^{O} C WHILE FOR THE SECOND SET THEY ARE NOT.

Chemical name:

37

- THE SMALLER THE ANIMAL THE LARGER THE PROBABILITY OF NASAL RETENTION. A 2um PARTICLE: SAME PROBABILITY OF BEING RETAINED IN THE MOUSE NOSE AS AN 8um PARTICLE IN MAN. IMPORTANT FOR LARGE PARTICLES.
- THE LARGER THE PARTICLES ARE ABOVE 1um THE MORE CHANCE OF DIFFERENCE IN REGIONAL DEPOSITION WITH MAN. TOTAL NET DOSE MAY BE THE SAME BUT BIOLOGICAL EFFECTS WILL BE DIFFERENT.
- TO HAVE THE SAME RELATION WITH MAN BETWEEN ATMOSPHERIC PARTICULATE CONCENTRATION AND RATE OF DEPOSITION OF PARTICLES IN THE LUNGS, FAIRLY UNIFORM PARTICLES AROUND 1-3 um (MMAD) SEEMS TO BE HIGHEST TO USE WITH SMALL RODENTS.

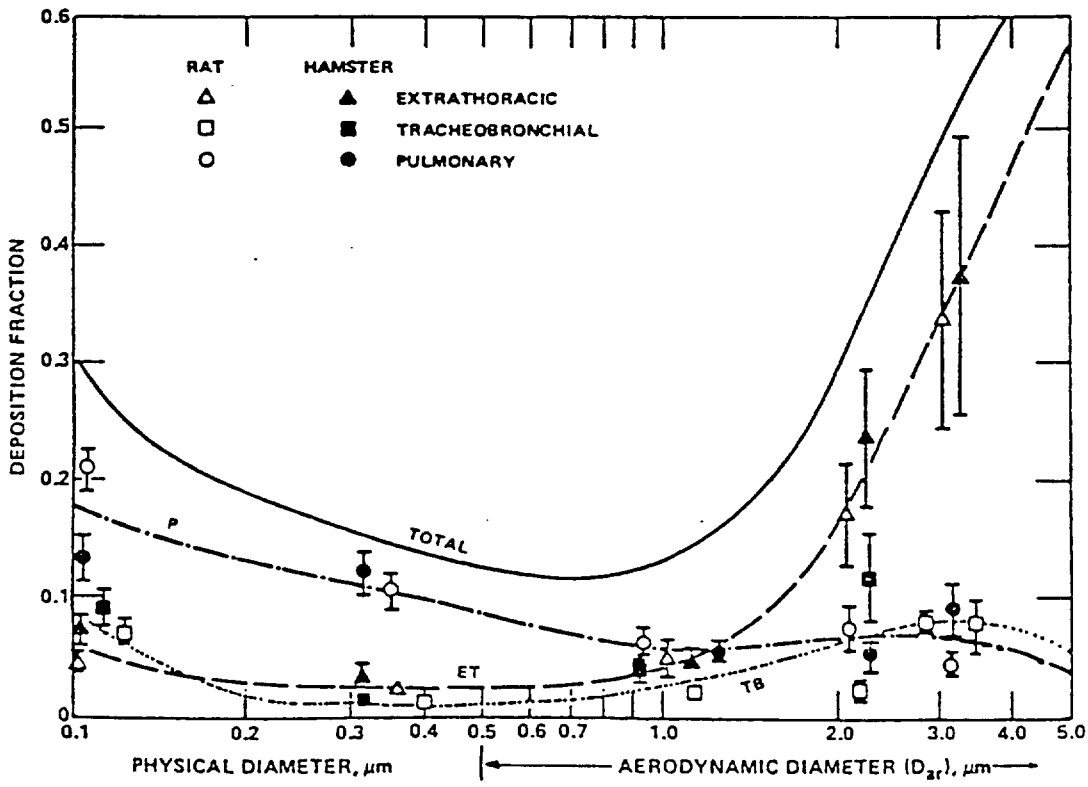


Figure 11-11. Deposition of inhaled monodisperse aerosols of fused aluminosilicate spheres in small rodents showing the deposition in the extrathoracic (ET) region, the tracheobronchial (TB) region, the pulmonary (P) region, and in the total respiratory tract based upon Raabe et al. (1977).

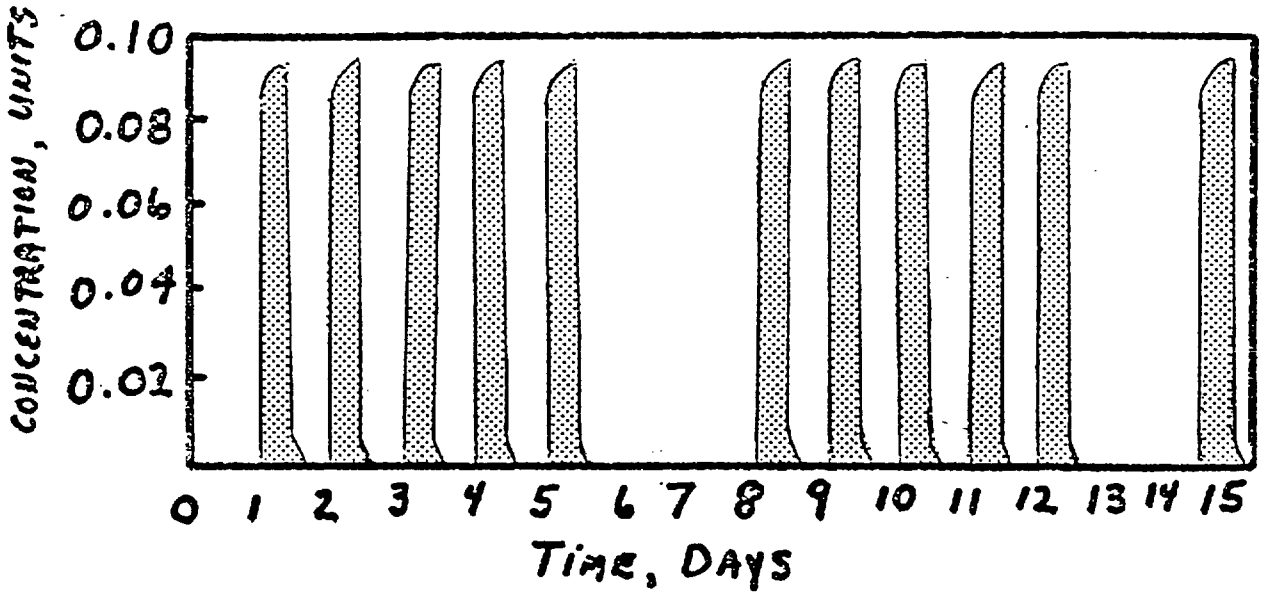
Compare this figure with the previous one given for man.

794961 0025

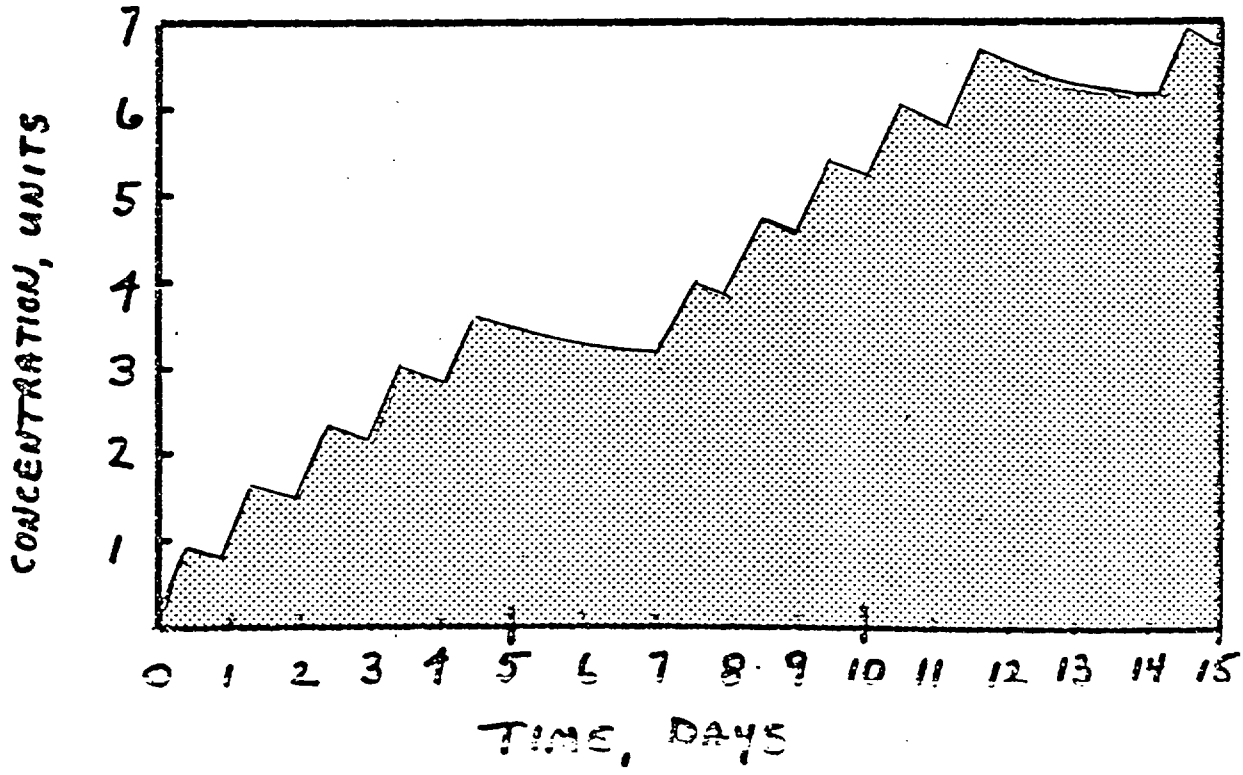
MAN VS. LABORATORY ANIMALS

IN AEROSOL EXPOSURE WITH LABORATORY ANIMALS IT IS IMPORTANT TO RECOGNIZE THAT ALTHOUGH THE SAME PARTICLE SIZE IS USED, DEPOSITION AND RETENTION IS LIKELY TO BE DIFFERENT. FEW STUDIES HAVE BEEN MADE (SEE. PALM ET. AL. ARCH. IND. HLTH. 13, 355, 1956, MCMAHON ET AL. INHALED PARTICLES, VOL. IV , 23, 1977). SOME GENERAL CONCLUSIONS:

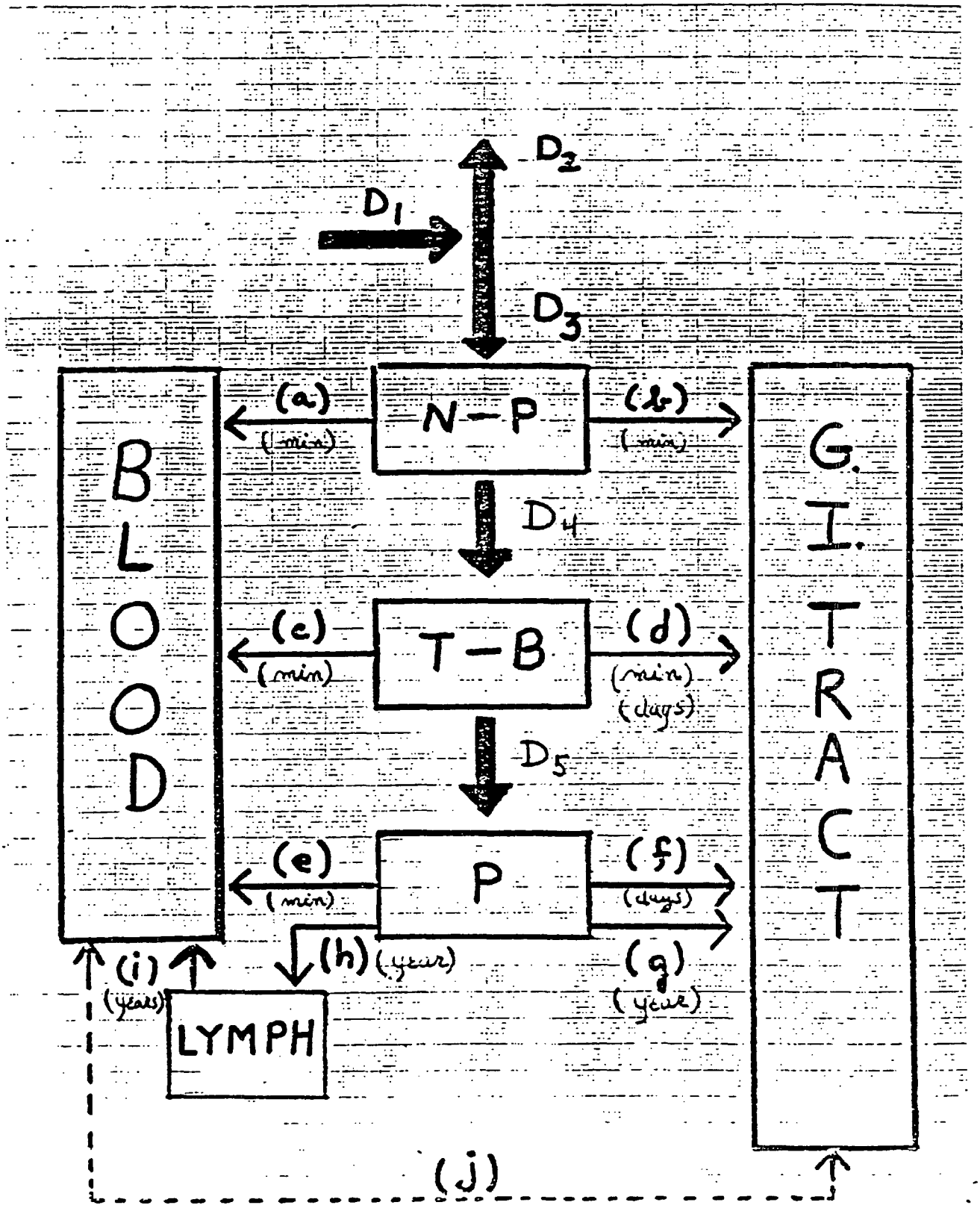
- THE MAJOR FACTOR CONTROLLING NET DOSE RECEIVED SEEMS TO BE MINUTE VENTILATION AND THEREFORE THE SMALL ANIMALS WILL RECEIVE A HIGHER TOTAL DOSE BECAUSE OF THEIR HIGHER VENTILATION TO BODY WEIGHT RATIO. HOWEVER THERE IS A LARGE VARIATION BETWEEN ANIMALS OF SAME SPECIES.



(HIGH TRANSLOCATION TO BLOOD)



(LOW TRANSLOCATION TO BLOOD)


D1
D2
D3
D4
D5
N-P
T-B
P
(a) (min)
(b) (min)
(c) (min)
(d) (min) (days)
(e) (min)
(f) (days)
(g) (year)
(h) (year)
(i) (years)
(j)
BLOOD
G.I. TRACT
LYMPH

VII. RETENTION - CLEARANCE

A. MODEL

A MODEL PROPOSED BY THE TASK GROUP ON LUNG DYNAMICS IS USED. THIS MODEL INCLUDES THE FOLLOWING AS PRESENTED IN THE NEXT FIGURE AND TABLE.

B. INPUTS

D_1: TOTAL DUST CONCENTRATION IS INHALED AIR

D_2: TOTAL DUST CONCENTRATION IN EXHALED AIR

D_3: TOTAL DUST DEPOSITED IN N-P COMPARTMENT

D_4: TOTAL DUST DEPOSITED IN T-B COMPARTMENT

D_5: TOTAL DUST DEPOSITED IN P COMPARTMENT

C. ABSORPTION - TRANSLOCATION PROCESSES

a: UPTAKE INTO SYSTEMIC BLOOD

b: UPTAKE FROM CILIARY MUCUS TRANSPORT

c: UPTAKE INTO SYSTEMIC BLOOD

d: UPTAKE FROM CILIARY MUCUS TRANSPORT

e: UPTAKE FROM DIRECT TRANSLOCATION TO SYSTEMIC BLOOD

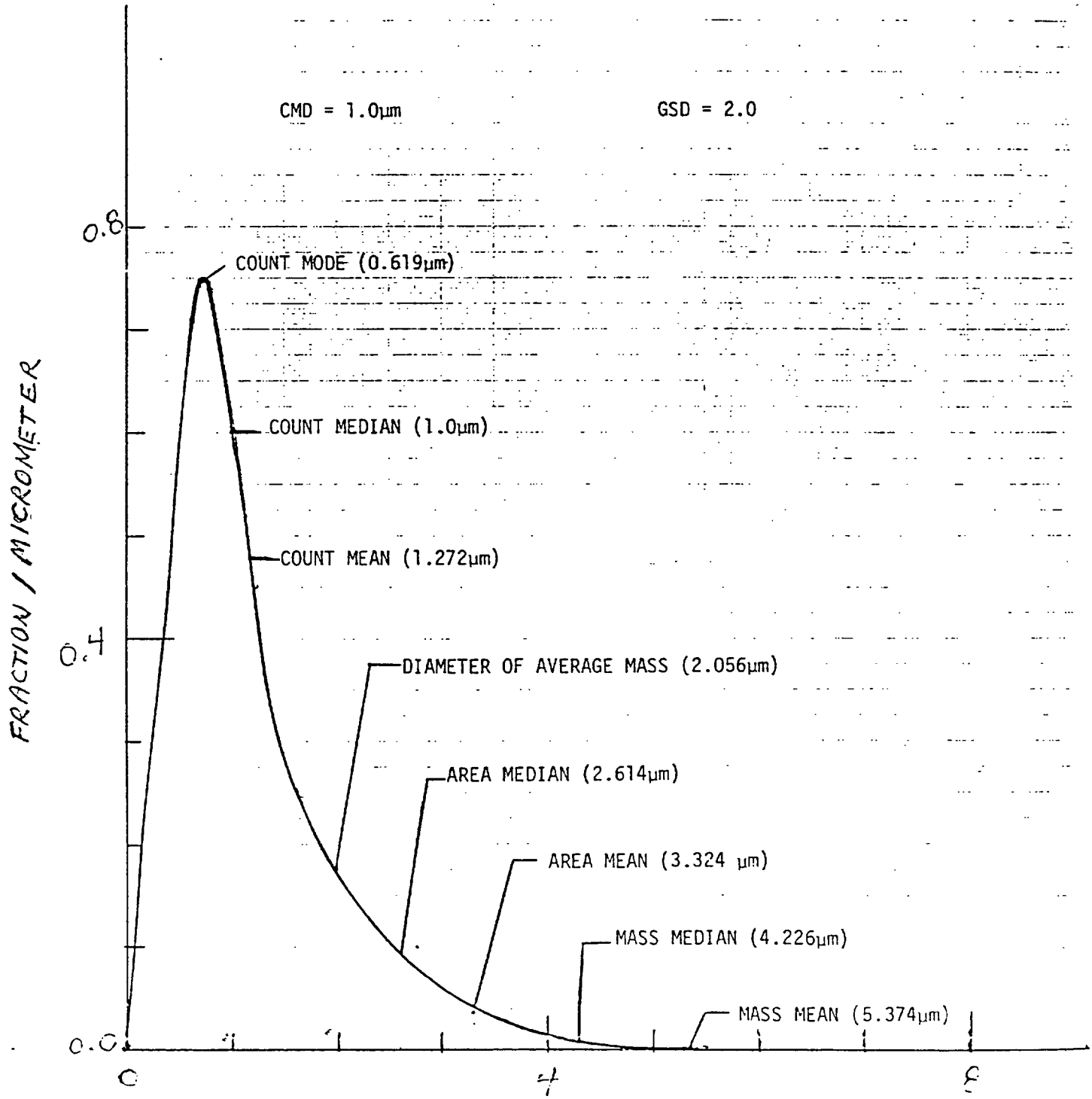
f: UPTAKE FROM RELATIVELY RAPID CLEARANCE DEPENDENT ON RECRUITABLE MACROPHAGES AND COUPLED TO CILIARY - MUCUS TRANSPORT

g: UPTAKE MUCH SLOWER THAN f, STILL DEPEND ON ENDOCYTOSIS AND CILIARY - MUCUS FOR CLEARANCE

h: UPTAKE BY SLOW REMOVAL VIA LYMPHATIC SYSTEM

i: UPTAKE FROM LYMPH TO LYMPH MODES TO BLOOD

j: UPTAKE FROM g.i. TRACT TO BLOOD


CMD = 1.0μm
GSD = 2.0
COUNT MODE (0.619μm)
COUNT MEDIAN (1.0μm)
COUNT MEAN (1.272μm)
DIAMETER OF AVERAGE MASS (2.056μm)
AREA MEDIAN (2.614μm)
AREA MEAN (3.324 μm)
MASS MEDIAN (4.226μm)
MASS MEAN (5.374μm)
0.8
0.4
0.0
FRACTION / MICROMETER
PARTICLE DIAMETER MICROMETERS

VI. CHARACTERISTICS OF THE AEROSOL, INFLUENCING ON TOXICITY

WE NEED TO KNOW:

1. MASS CONCENTRATION: mg/m^3, DIRECT SAMPLING, GRAVIMETRIC OR OTHER ANALYSIS

2. SIZE AND DISTRIBUTION
   SIZE OR MASS ARE GIVEN AS COUNT MEDIAN DIAMETER (CMD) AND MASS MEDIAN DIAMETER (MMD) WITH THE GEOMETRIC STANDARD DEVIATION (gsd). SINCE TOXICITY IS MORE LIKELY TO BE RELATED TO MASS THE MMD IS THE EXPRESSION OF CHOICE. WE ALSO LIKE TO DEFINE IT AS AN "AERODYNAMIC DIAMETER" WHICH TAKES INTO ACCOUNT SHAPE AND DENSITY OF THE PARTICLES WHICH INFLUENCE THEIR BEHAVIOR (SEE ABOVE) AND THIS IS OBTAINED EXPERIMENTALLY.

3. SOLUBILITY IN BODY FLUID WILL AFFECT RETENTION, SYSTEMIC EFFECT. STRICTLY SPEAKING IT IS NOT THE SOLUBILITY IN WATER, UNLESS MATERIAL IS HIGHLY WATER SOLUBLE AND NON-REACTIVE, BUT INCLUDES OTHER PARAMETERS SUCH AS REACTION WITH BIOLOGICAL MOLECULES WHICH MAY INCREASE TRANSPORT (CARRIERS ETC.) AND WILL ALSO VARY WITH PARTICLE SIZE. THEREFORE THE TERM "TRANSLOCATION" IS MORE APPROPRIATE.

NASOPHARYGEAL
TRACHEO-BRONCHIAL
PULMONARY
Aerodynamic Diameter (μm)
Mass median
Fractional deposited
1.0
0.8
0.6
0.4
0.2
0.0
10.0
5.0
1.0
0.5
0.1
0.05
0.01
46 5730
KE SEMI-LOGARITHMIC 3 CYCLES x 84 DIVISIONS
KEUFFEL & ESSER CO. MADE IN U.S.A.

C. AEROSOL: STABLE OR QUASI-STABLE SUSPENSION OF SOLID OR LIQUID PARTICLES IN A GAS. VARIOUS TERMS ARE USED TO BETTER DEFINE AN AEROSOL DEPENDING ON ITS ORIGIN OR STATE. THESE ARE:

rain is not an aerosol

- o FUMES: SOLID PARTICLES FORMED BY CONDENSATION GENERALLY USED FOR METALS SUCH AS Cd, Pb, ETC., BUT CAN BE USED FOR ANY SOLID AFTER HEAT TREATMENT SUCH AS TEFLON OR PVC FUMES. USUALLY BELOW 1um AND FAIRLY HOMOGENOUS.
- o DUSTS: SOLID PARTICLES, FORMED FROM DISINTEGRATION PROCESSES OF A MECHANICAL NATURE, MINING, GRINDING, ETC. USUALLY ABOVE 1um, HETEROGENOUS, UNSTABLE, POLYDISPERSED.
- o MISTS: REFER TO LIQUID PARTICLES, FORMED BY CONDENSATION OF A VAPOR (SMALL PARTICLE HOMOGENEOUS AND STABLE) OR BY ATOMIZATION OF A LIQUID (LARGE PARTICLE HETEROGENOUS AND LESS STABLE).
- o FOG: A MIST WHICH APPRECIABLY REDUCES VISIBILITY.
- o SMOKE: PARTICLES IN SUSPENSION IN AIR RESULTING FROM COMBUSTION OR PYROLYSIS OF ORGANIC MATERIALS.

gases + aerosols combined

- o HAZE: COMBINATION OF VAPOR, DUST, FUME, MIST.
- o SMOG: COMBINATION OF SMOKE AND FOG BUT MORE COMMONLY USED TO DESCRIBE THE RESULTING COMBINATION OF GASES AND AEROSOLS FORMED DURING U-V IRRADIATION OF HYDROCARBONS AND OXIDES OF NITROGEN, OZONE, ETC., L.A. SMOG.

- HOMOGENOUS: REFERS TO CHEMICAL CONSTITUTION, I.E. SULFURIC ACID.
- HETEROGENOUS: REFERS TO CHEMICAL CONSTITUTION, I.E. COAL DUST.
- MONODISPERSED: REFERS TO DISTRIBUTION OF PARTICLES AROUND THE GEOMETRIC MEAN OR MEDIAN, USUALLY WHEN GEOMETRIC STANDARD DEVIATION IS 1.2 OR LESS AEROSOL IS SAID TO BE MONODISPERSED.
- POLYDISPERSED: AS ABOVE, GEOMETRIC STANDARD DEVIATION LARGER THAN 1.2, HETERODISPERSED ALSO USED.

NOTE: AEROSOLS CAN BE HOMOGENOUS AND POLYDISPERSED, HOMOGENOUS AND HETERODISPERSED, ETC. SOME AUTHORS ALSO USE HOMOGENOUS FOR MONODISPERSED, BE CAREFUL.

II. CONCENTRATION UNITS

A. mg/m^3: MILLIGRAMS OF POLLUTANT PER CUBIC METER OF AIR, CAN BE USED FOR GAS, VAPOR, AEROSOL.

B. ppm: PARTS PER MILLION = VOLUME OF GAS/VOLUME OF AIR RELATIONSHIP.

$$\frac{\text{VOLUME OF VAPOR OR GAS POLLUTANT} \times 10^6}{\text{TOTAL VOLUME OF CONTAINER OR TOTAL VOLUME OF AIR SAMPLE}}$$

C. VOLUME PERCENT: SAME VOLUME/VOLUME RELATIONSHIP AS ppm, USED FOR HIGH CONCENTRATION, I.E, 1% OR 0.1% INSTEAD OF 10,000 OR 1,000 ppm RESPECTIVELY.

D. mg/m^3 to ppm= $mg/m^3 \times \frac{24.5}{M.W.} = ppm$ (AT 25°C, 760 mmHg)(22.4 AT 0°C, 760 mmHg

E. ppm to mg/m^3 = $\frac{ppm \cdot \text{molecular weight}}{24.5} = mg/m^3$ (AT 25°C, 760 mmHg)(22.4 AT 0°C, 760 mmHg)

F. FIBERS/CC: NUMBER OF FIBERS/CUBIC CENTIMETER OF AIR, ASBESTOS

G. 1 ft^3 = 28.32 LITERS

mppcf =

H. INDUSTRIAL AND TOXICOLOGICAL APPLICATIONS

- DILUTION TO TLV

  ASSUME 1 GRAM OF TOLUENE DIISOCYANATE (TDI), (SPECIFIC GRAVITY $\approx$ 1.2) EVAPORATES COMPLETELY

  THRESHOLD LIMIT VALUE (TLV), 1979 IS 0.02ppm, 0.14 mg/m^3

  FOR DILUTION TO 1 ppm: NEED 141 m^3

  FOR DILUTION TO 0.02 ppm: NEED 7,000 m^3

  EQUIVALENT TO A BUILDING OF 30 X 15 X 420 FEET

- A LITTLE GOES A LONG WAY

  ASSUME TDI IS STORED AT ABOUT 100°F. WHEN A 55 GALLON DRUM IS FILLED, 55 GALLONS OF "SATURATED" TDI VAPOR ARE LIBERATED.

  55 GALLONS $\approx$ 200l OR 200,000 ml

  DILUTION TO 1 ppm: NEED 200,000 ml

  DILUTION 0.02 ppm: NEED $10^7 m^3$, A HUGE BUILDING!

o SATURATION CONCENTRATION (C_S)

$$C_S = \frac{MW \cdot 273 \cdot p \cdot 10^6}{22.4 \cdot T \cdot 760} = mg/m^3$$

MW: MOLECULAR WEIGHT

p: VAPOR PRESSURE (TORR OR mmHg)

T: TEMPERATURE ^oK

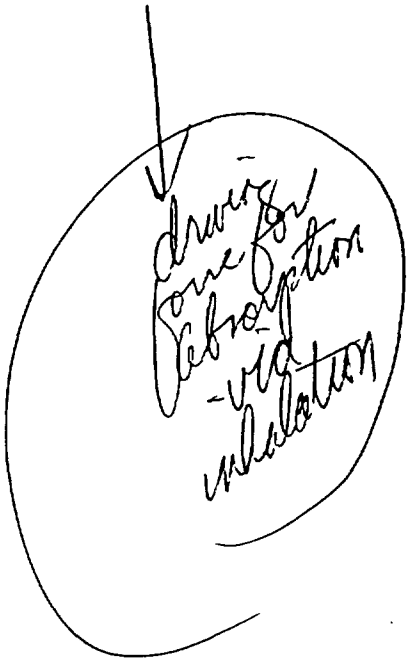
22.4: VOLUME OCCUPIED BY 1 MOLE OF GAS a 0^oC,1.

FOR TDI, AT 25^oC, $= 2 \times 10^{-2}$

$$C_{S,25^oC} = \frac{174.2 \cdot 273 \cdot 2X10^{-2} \cdot 10^6}{24.5 \cdot 298 \cdot 760} = 171 \text{ mg/m}^3 \text{ OR } 24.5 \text{ ppm.}$$

III. OTHER CONCENTRATION UNITS

A. PARTIAL PRESSURE: FRACTION (VOLUME/VOLUME COMPOSITION) OF THE TOTAL PRESSURE OF A MIXTURE EXERTED BY A COMPONENT OF THE MIXTURE.



FOR EXAMPLE, AT SEA LEVEL, 1 ATMOSPHERE (760 mmHg, 760 TORRS, 1,013 BAR, 1.03 kg/cm^2 OR 14.7 p.s.i.a.). IF WE KNOW THE VOLUME COMPOSITION OF EACH COMPONENT IN THE MIXTURE WE CAN CALCULATE THE PARTIAL PRESSURE OF EACH. ASSUMING THE FOLLOWING COMPOSITION:

N_2	=	78.6%	=	597 mm Hg PARTIAL PRESSURE
O_2	=	20.8%	=	159 mm Hg PARTIAL PRESSURE
CO_2	=	0.04%	=	0.3 mm Hg PARTIAL PRESSURE
H_2O	=	0.5 %	=	3.7 mm Hg PARTIAL PRESSURE
TOTAL		100%	=	760 mm Hg TOTAL PRESSURE

THE VOLUME COMPOSITION CAN BE IN % OR ppm, SEE ABOVE, SINCE BOTH ARE VOLUME/VOLUME UNIT. THEREFORE, 0.1% OR 1,000ppm = 0.76mmHg AT SEA LEVEL.

B. $pV = nRT$ IF THE CONCENTRATION IS GIVEN AS MOLES/LITER (n/V), THE PARTIAL PRESSURE p(in mm Hg) CAN BE OBTAINED USING THE VALUE OF THE GAS CONSTANT R AS 62 AND THE TEMPERATURE T IN DEGREE KELVIN.

C. HENRY'S LAW OSTWALD COEFFICIENT THE AMOUNT (MOLES) OF A GAS DISSOLVED IN A LIQUID IS DIRECTLY PROPORTIONAL TO THE PARTIAL PRESSURE OF THE GAS IN THE GAS PHASE ABOVE THE LIQUID. AT EQUILIBRIUM THE PARTIAL PRESSURE IN BOTH PHASES IS EQUAL BUT THE AMOUNT, IN MOLES, WILL VARY ACCORDING TO EACH GAS. THIS RATIO, S, IS CALLED THE SOLUBILITY COEFFICIENT.

S = CONCENTRATION IN MOLES (OR MILLIGRAMS) IN LIQUID/ CONCENTRATION (SAME UNITS) IN GAS PHASE.

$$S = \frac{Cl}{Cg}$$

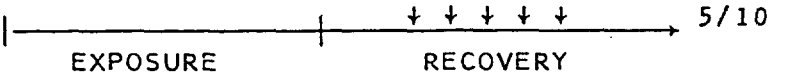
SOME EXAMPLES*:

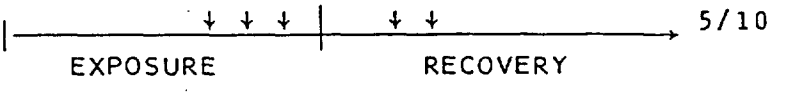
$\frac{Cl}{Cg} = \frac{1}{100}$	$= 0.01S$	=	LOW: NITROGEN, HELIUM OXYGEN
$\frac{Cl}{Cg} = \frac{50}{100}$	$= 0.5S$	=	MODERATE: CO_2, N_2O
$\frac{Cl}{Cg} = \frac{150}{100}$	$= 1.5S$	=	MODERATE: VINYL ETHER
$\frac{Cl}{Cg} = \frac{1500}{100}$	$= 15S$	=	HIGH: DIETHYL ETHER
$\frac{Cl}{Cg} = \frac{110000}{100}$	$= 1{,}100S$	=	VERY HIGH: ETHANOL

* LIQUID = BLOOD (WATER) T = $37^{o}C$

IV. ACUTE INHALATION TOXICOLOGY

A. LC_{50}: ATMOSPHERIC CONCENTRATION, STATISTICALLY ESTIMATED, TO KILL 50% OF THE ANIMALS EXPOSED FOR A FIXED TIME, WITHIN A SPECIFIED POST-EXPOSURE PERIOD.





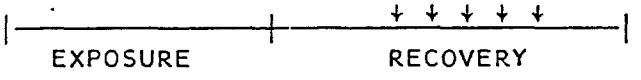
normal parameters for LC50 determination

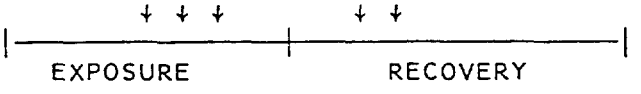
EXPOSURE: 1 HOUR, RECOVERY 14 DAYS
EXPOSURE: 4 HOUR, RECOVERY 14 DAYS

TIME: FIXED
CONCENTRATIONS: VARIABLE
LC_{50}: mg/m^3 OR ppm

B. LT50: TIME FOR 50% OF THE ANIMALS TO DIE AT A PARTICULAR CONCENTRATION. OFTEN USED FOR SATURATED VAPORS, NOT A MEASURE OF TOXICITY.

Always put a odd number here





TIME: VARIABLE
CONCENTRATION: FIXED
FAST ACTING, SLOW ACTING, HAZARD CONCEPT. RESEMBLES ANESTHETIC GASES COMPARISONS ON THEIR POTENCY (mg/ml OF BLOOD) AND SPEED OF INDUCTION (TIME FOR A PARTICULAR LEVEL OF ANESTHESIA).

C. CONCENTRATION X TIME: LCT50: mg · min/m^3 or ppm · min
USE TO COMPARE APPLES AND ORANGES

D. HABER'S RULE, WORKS WITHIN LIMITED RANGE

RESPONSE: C · T
C OR T WITHIN 2 OR 3, WILL NOT WORK WHEN WITH SUBSTANCED HAVING OBVIOUS TRESHOLD (CO) UNLESS QUITE ABOVE TRESHOLD, WORKS BETTER WITH PROGRESSIVE, CUMMULATIVE EFFECT.

E. EXPRESSION OF: TOXICITY — DOSE: $\frac{mg}{kg}$: NONE OF THE ABOVE, RATHER, INTENSITY OF EXPOSURE IS INVOLVED.

HABER'S RULE

50% MORTALITY AT 10 mg/m^3 · 10 min, C · T = 100

50% MORTALITY AT 5 mg/m^3 · 20 min, C · T = 100

50% MORTALITY AT 1 mg/m^3 ·100 min, C · T = 100: INCORRECT

Further reading on concept of dose in inhalation toxicology: MacFarland, H.N., Respiratory Toxicology, Chapter 5 in Essays in Toxicology, Vol. 7 pp. 121-154, 1976, Academic Press.

F. BEST: FIX DURATION OF EXPOSURE, ACCORDING TO SITUATIONS (i.e. SPILLS, WORKDAY ETC.) VARIOUS CONCENTRATIONS, TRY TO GET DEATHS TOWARD END OF EXPOSURE OR BEGINNING OF A SHORT POST-EXPOSURE PERIOD (NO MORE THAN 1/3 OF DURATION OF EXPOSURE), CALCULATE LC_{50} AND ALSO OBSERVE ANIMALS FOR 14 DAYS AND CALCULATE LC_{50} INCLUDING THIS POST-EXPOSURE PERIOD. RATIO OF THE TWO GIVES INDICATION OF DELAYED TOXICITY.

G. SECOND BEST: WHEN IT IS MECHANICALLY IMPOSSIBLE TO GENERATE CONCENTRATIONS HIGH ENOUGH FOR ACUTE TOXICITY DURATION OF EXPOSURE CAN BE INCREASED. HOWEVER COMPARISON OF LC_{50} FOR TWO MATERIALS WHEN THE DURATION OF EXPOSURE IS DIFFERENT BY MORE THAN A FACTOR OF 2 IS RISKY (SEE ABOVE).

H. COMPARING: LC_{50}

i) REGARDLESS OF STATISTICAL SIGNIFICANCE, LC_{50} FOR TWO MATERIALS ARE COMPARABLE IF WITHIN A FACTOR OF 3.

ii) IF ABOVE A FACTOR OF 3: START TO THINK ABOUT IT.

iii) IF ABOVE A FACTOR OF 10: WILL DEFINITIVELY MAKE A DIFFERENCE IN REAL LIFE SITUATIONS.

J. COMPARING: LT_{50} NO GOOD GENERAL RULE, A FACTOR OF MAYBE 0.5 OF THE ABOVE. USE LT_{50} TO COMPARE RAPIDITY OF EFFECT OF TWO MATERIALS AT SIMILAR CONCENTRATION OR FOR TWO MATERIALS FOR THE SAME SITUATION, i.e. SATURATED VAPOR, IDEA OF TENABILITY LIMITS.

WHEN COMPARING LT_{50}, MAKE SURE THAT YOU ARE COMPARING THE SAME LEVEL OF EFFECT. FOR EXAMPLE, 99 RATS ARE EXPOSED FOR 4 HOURS TO A SATURATED VAPOR ATMOSPHERE OF MATERIAL A AND MATERIAL B. FOR MATERIAL A THE 50^{TH} DEATH OCCURRED AT 2 HOURS AND 66 DEATHS OCCURRED BY 4 HOURS. FOR MATERIAL B THE 50^{TH} DEATH OCCURRED AT 2 HOURS AND ALL THE ANIMALS WERE DEAD BY 3 HOURS. COMPARING LT_{50} IS A TRICKY BUSINESS.

K. COMPARING BOTH LC_{50} AND LT_{50}:

THIS CAN BE DONE BUT REQUIRES THAT A "STANDARD" BE USED AND THEN COMPARISONS ARE MADE TO THE STANDARD. ANYTHING CAN BE USED AS THE STANDARD OR REFERENCE MATERIAL. FIRST A PERIOD OF TIME MUST BE SELECTED, RELEVANT TO THE SITUATION TO BE INVESTIGATED. IN THE EXAMPLE BELOW 30 MINUTES WAS SELECTED. THEN THE LC_{50} IS DETERMINED, ARRANGING SO THAT 50% OF THE ANIMALS DIE CLOSE TO THE END OF THAT PERIOD, THE TIME WILL BE THE LT_{50} (22 MINUTES IN THE EXAMPLE GIVEN BELOW FOR WOOD SMOKE AS THE REFERENCE MATERIAL). THEN THE OTHER MATERIALS ARE TESTED. IN THIS PROTOCOL, THE LEVEL OF EFFECT IS FIXED, I.E. 50% LETHALITY AND WE ASK WHAT WILL BE THE CONCENTRATION TO KILL 50% (LC_{50}) AND THE TIME TO DO THIS (LT_{50}). HOWEVER, REMEMBER THAT A FIXED MAXIMUM TIME WAS SELECTED AND THAT RANKING CAN CHANGE IF ANOTHER TIME PERIOD IS SELECTED. THIS CONCEPT OF CONCENTRATION AND TIME DOES NOT BELONG ONLY TO INHALATION EXPERIMENTS. IT IS ALSO OF IMPORTANCE IN CHRONIC STUDIES WHEN CONSIDERING THE DOSE TO PRODUCE 50% EFFECT (ANY EFFECT SUCH AS TUMORS ETC) AND THE TIME REQUIRED FOR THIS GIVEN LEVEL OF EFFECT TO OCCUR. THE SAME APPLIES IN AQUATIC TOXICOLOGY.

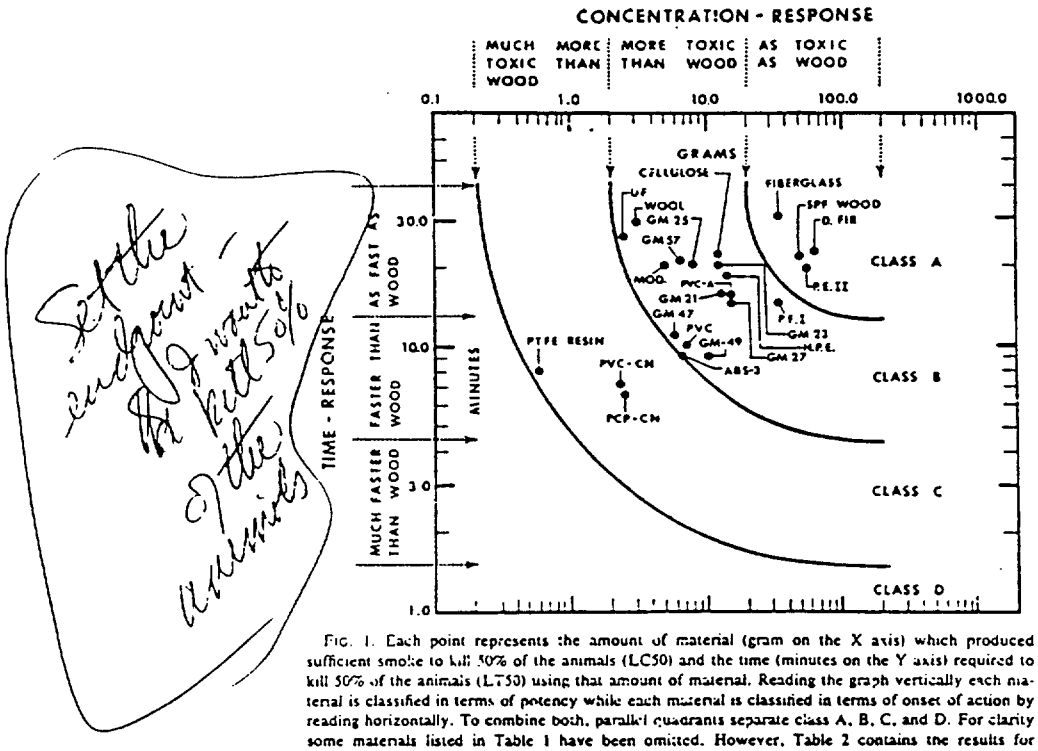


FIG. 1. Each point represents the amount of material (gram on the X axis) which produced sufficient smoke to kill 50% of the animals (LC50) and the time (minutes on the Y axis) required to kill 50% of the animals (LT50) using that amount of material. Reading the graph vertically each material is classified in terms of potency while each material is classified in terms of onset of action by reading horizontally. To combine both, parallel quadrants separate class A, B, C, and D. For clarity some materials listed in Table 1 have been omitted. However, Table 2 contains the results for all materials.

From Toxicol. Appl. Pharmacol. 51, 181-188, 1981.

always best to operate with single layer

V. CHAMBER

ALL THERE IS TO KNOW ABOUT INHALATION CHAMBERS WAS WRITTEN BY SILVERS IN 1964 (SILVER, S.D. - CONSTANT GASSING CHAMBERS: PRINCIPLES INFLUENCING DESIGN AND OPERATION. J. LAB. CLIN. MED. 31, 1153-1161, 1946). ANYONE STARTING AN INHALATION STUDY WITHOUT READING IT IS MAKING A BIG MISTAKE.

A. BEST DESIGN

THERE IS NO SUCH THING AS "BEST DESIGN" CHAMBER TO ANSWER ALL THE NEEDS OF INHALATION TOXICOLOGY STUDIES. THE "BEST DESIGN" IS A CHAMBER THAT WORKS ACCORDING TO THE FOLLOWING CRITERIA:

- FAIRLY UNIFORM DISTRIBUTION OF CONTAMINANTS, VARIATION OF 10-15% BETWEEN SAMPLING PORTS ARE QUITE ACCEPTABLE.
- AIRFLOW (LITERS/MINUTE) EQUAL TO THE TOTAL VOLUME (LITER) OF CHAMBER IS A GOOD BET TO RUN A CHAMBER, THIS IS GENERALLY SUFFICIENT TO PREVENT TEMPERATURE RISE IF CHAMBER IS CONSTRUCTED WITH METAL, KEEP CO_2 AND AMMONIA LEVEL LOW. AMMONIA LEVEL SHOULD BE VERIFIED WITH HIGH ANIMAL LOAD PARTICULARLY WHEN REACTION WITH POLLUTANTS IS POSSIBLE, Cl_2, SO_2, NO_2, ETC. IF THIS AIRFLOW PRESENTS A PROBLEM (HIGH COST OF POLLUTANT, AVAILBILITY OF POLLUTANT, CLEANING, ETC) IT CAN BE REDUCED BUT PROBABLY NOT BELOW 0.2 THE TOTAL VOLUME OF THE CHAMBER WITHOUT CREATING PROBLEMS WITH TEMPERATURE, AMMONIA, ETC.

MacFarland has reviewed Silver's article and expanded it, see previous page for reference.

- ANIMAL LOAD SHOULD BE LOWER THAN 1% TO 5% OF CHAMBER VOLUME. CALCULATE AS FOLLOWS: TAKE BODY WEIGHT OF EACH ANIMAL TO BE SAME AS ITS VOLUME (i.e. 200 GRAMS RAT = .2 LITER) AND MULTIPLY BY NUMBER OF ANIMALS. THUS TO EXPOSE 100 RATS OF 200 GRAMS (20 LITERS OF RATS) YOU NEED A CHAMBER VOLUME OF MINIMUM 2,000 LITERS AND PREFERABLY THERE WILL BE ONLY ONE LAYER OF ANIMALS. THIS CAN BE REDUCED TO A 400 LITER CHAMBER (5%) BUT LIKELY TO NEED 2 LAYERS. THIS ONE LAYER IS PREFERABLE IF WORKING WITH HIGHLY REACTIVE GASES WHICH WILL REACT WITH FUR OF ANIMALS OR WITH LARGE PARTICLES BUT IS NOT NECESSARY WITH AREOSOL AROUND 1um AND WITH NON REACTIVE GASES SUCH AS CO ETC. OR VAPORS SUCH AS BENZENE, CARBON TETRACHLORIDE ETC.
- DO NOT USE THE CHAMBER FOR MIXING. THE ADDED POLUTANT SHOULD BE MIXED WITH THE INCOMING DILUTING AIR IN A MIXING DEVICE PRIOR TO ENTERING THE CHAMBER OR MIXED AT THE TOP OR ENTRANCE OF THE CHAMBER. THE IDEA OF PLACING BAFFLES ETC. IN A CHAMBER FOR BETTER MIXING IS ABSURD. THE GOLDEN RULE: MIX YOUR MARTINI BEFORE YOU DRINK IT, NOT AFTER.
- DO NOT USE FAN IN A CHAMBER FOR MIXING A FAN WILL CREASE TURBULANCE WHICH WILL INCREASE AEROSOL COAGULATION AND STRATIFICATION.

- WITH REACTIVE GASES "CONDITIONING" OF THE CHAMBER SHOULD BE DONE PRIOR TO LOADING ANIMALS IN THE CHAMBER. ONCE THIS IS DONE ADDITION OF ANIMALS WILL DROP THE CONCENTRATION BY AT LEAST 50% AND SOMETIMES BY AS MUCH AS 95%. THIS IS NOT SERIOUS FOR A LONG-TERM CHRONIC STUDY. INDEED DURING THE FIRST WEEK OF SUCH STUDY ADJUSTMENT CAN BE MADE TO THE DELIVERY SYSTEM TO BRING THE CONCENTRATION UPWARD TO THE DESIRED LEVEL. IN CASES OF ACUTE STUDIES, IF YOU WANT TO KNOW WHAT THE ANIMALS ARE LIKELY TO "SOAK" COLLECT DEAD ANIMALS, KEEP THEM REFRIGERATED AND THEN PLACE IN YOUR CHAMBER. THERE WILL BE NO DIFFERENCE BETWEEN LIVE AND DEAD ANIMALS SINCE THE AMOUNT OF POLLUTANT INHALED BY THE LIVING ANIMALS IS EXTREMELY SMALL, THE MAJOR CONTRIBUTION COMES FROM REACTION WITH THE FUR. PROBABLY THE BEST DESIGN IS HEAD ONLY EXPOSURE.

- PERMITTED DAILY VARIATION

REACTIVE GASES	≈	20% OF DESIRED
NON-REACTIVE GASES	≈	15% OF DESIRED
AEROSOL < 1 um	≈	20% OF DESIRED
AEROSOL 1-5 um	≈	20% OF DESIRED
AEROSOL > 5 um	≈	DON'T USE THEM IN LARGE CHAMBER, HEAD ONLY EXPOSURE, RELEVANCE IS IN QUESTION. RATS DO NOT INHALE ROCKS!

→ BIG PROBLEM: CONSUMER SPRAY CAN PRODUCTS. SPRAY PAINTS.

POSSIBLY: REDUCE TO SMALLER SIZE SET-UP ELUTRIATION SYSTEMS.

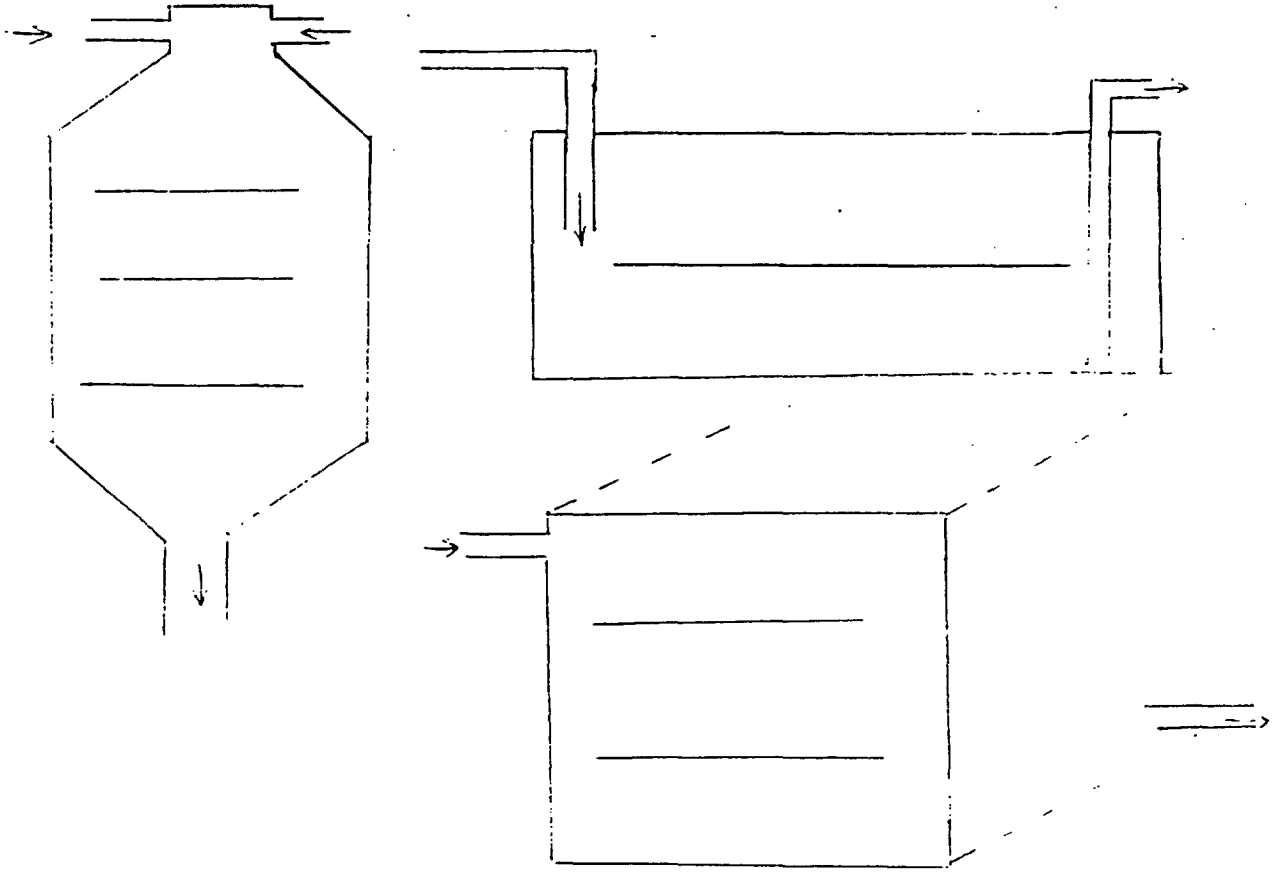
B. DESIGN FOR VERY HIGH LEVEL OF AEROSOL EXPOSURE

THE DECISION TO USE A CHAMBER OR HEAD ONLY EXPOSURE IS IMPOSSIBLE TO MAKE WITHOUT SOME PRELIMINARY WORK WITH MATERIAL. THIS WORK CAN BE DONE USING A SMALL CHAMBER AND A FEW ANIMALS. IN GENERAL CONCENTRATION OF > THAN 50 mg/m^3 ARE DIFFICULT TO WORK WITH UNLESS THE PARTICLE SIZE IS SMALL, HEAD ONLY EXPOSURE IS INDICATED. THIS PRESENTS SOME PROBLEMS, CAGE CONTROL AND HEAD ONLY EXPOSURE CONTROL MUST BE USED, HIGH LABOR, BUT IT CAN BE DONE WELL AND HAS BEEN DONE WELL.

THERE HAS BEEN SOME TALK ABOUT AN EPA RECOMMENDED LEVEL OF 5 GRAM/LITER OF AEROSOL. THIS IS IMPOSSIBLE TO ACHIEVE FOR MOST SOLID OR LIQUID AND KEEPING THE PARTICLE SIZE REASONABLY SMALL FOR RATS TO INHALE AND AT THE SAME TIME USING AN INHALATION CHAMBER. DON'T WASTE YOUR TIME TRYING THIS.

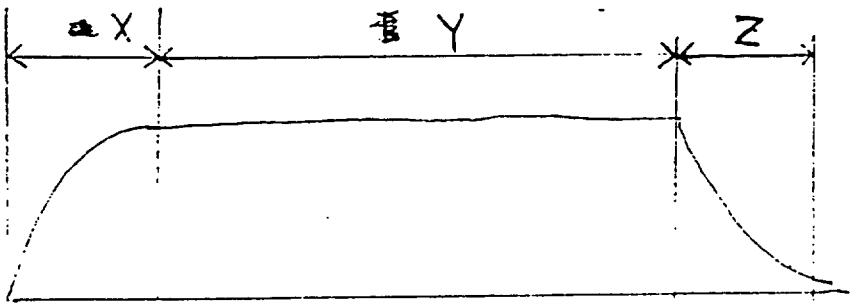
C. CHEAP CHAMBER, GOOD RESULTS

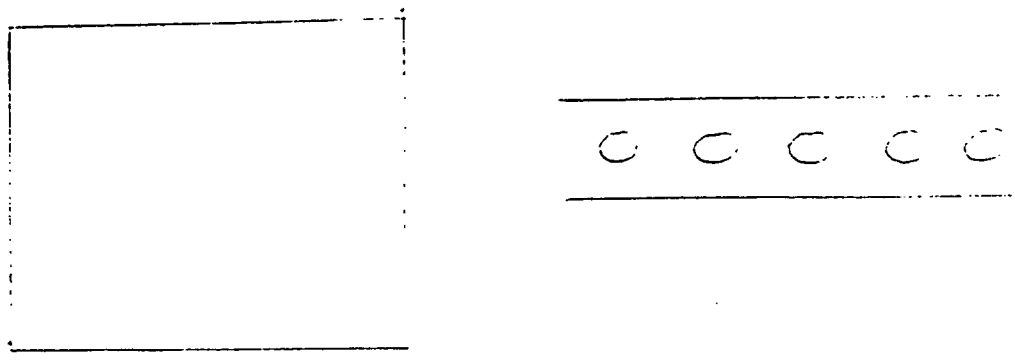
FOR ACUTE OR SUB-ACUTE WORK USING 10-20 RATS OR 20-50 MICE AN ALL-GLASS 100-LITER AQUARIUM IS JUST PERFECT. A COVER CAN BE MADE OUT OF PLYWOOD OR PLEXIGLASS WITH THE INSIDE OF THE COVER LINED WITH TEFLON. SUCH A CHAMBER COST ABOUT $100 WITH ALL FITTINGS. OPERATED AT 100 LITERS/MIN EQUILIBRIUM CONCENTRATION WILL BE REACHED IN ABOUT 5 MINUTES WITH UNIFORM DISTRIBUTION OF CONTAMINANTS, GASES OR AEROSOLS. (SEE TAP, 49, 89-95, 1979)



D. VERY SHORT EXPOSURE (10-15 MINUTES)

FOR VERY SHORT-EXPOSURE A CHAMBER OPERATED AS ABOVE WOULD BE INAPPROPRIATE UNLESS THE AIRFLOW WAS RAISED TO ABOUT 500 LITERS/MINUTE TO REDUCE EQUILIBRATION TIME. THIS MAY PRESENT SOME PROBLEMS. INSTEAD A CHAMBER HAVING A VOLUME OF 10 LITERS CAN BE MADE OUT OF A GLASS CYLINDER AND USE FOR HEAD ONLY EXPOSURE WITH AN AIRFLOW OF 50 LITERS/MINUTE. (SEE ARCH. ENV. HLTH. 32, 68-76, 1977).





E. DON'T EXPOSE ANIMALS UNLESS YOU ARE SURE

PRIOR TO EXPOSING ANIMALS YOU SHOULD HAVE GOOD EXPERIENCE WITH AN EMPTY CHAMBER, INCLUDING THE HOUSING CAGES. YOU SHOULD KNOW HOW LARGE A DIFFERENCE THERE IS BETWEEN THE NOMINAL CONCENTRATION AND ACTUAL CONCENTRATION.

$$\text{NOMINAL CONCENTRATION} = \frac{\text{AGENT FLOW IN MILLIGRAMS/MINUTE}}{\text{AIRFLOW IN LITERS/MINUTE}}$$

ACTUAL CONCENTRATION = OBTAINED FROM SAMPLING AND ANALYSIS

F. RAPID GUIDE FOR EQUILIBRATION TIME AND ITS USE

AS A GAS OR AEROSOL IS INTRODUCED AT A UNIFORM RATE IN THE CHAMBER MAINTAINED AT A CONTINUOUS FLOW THE CONCENTRATION WITHIN THE CHAMBER INCREASES UNTIL IT IS PRACTICALLY CONSTANT. ASSUMING PERFECT MIXING

$$C = \frac{W}{b}\left(1-e^{\frac{-bt}{a}}\right) \qquad (1)$$

C = CONCENTRATION IN mg/liter AT TIME t

W = MILLIGRAMS OF AGENT INTRODUCE/MINUTE

a = VOLUME OF THE CHAMBER IN LITER

b = VOLUME OF AIR THROUGH THE CHAMBER IN LITERS/MIN.

e = THE BASE OF NATURAL LOG, 2.7182

THUS THE % OF THE DESIRED CONCENTRATION $\frac{W}{b}$ OBTAINED IN TIME t IS:

$$\% = 100\left(1-e^{\frac{-bt}{a}}\right) \qquad (2)$$

THE TIME REQUIRED FOR EQUILIBRATION OF THE CHAMBER TO 99% CAN BE CALCULATED BY SETTING EQUATION 2 EQUAL TO 99

$$99 = 100\left(1-e^{\frac{-bt}{a}}\right) \quad \text{OR} \quad e^{\frac{-bt}{a}} = \frac{100-99}{100} = .01$$

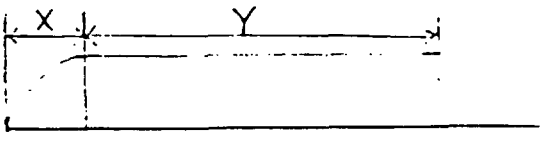
TRANSFORMED INTO LOGARITHIM FORM

$$-\frac{bt}{a} = \ln 0.01 = -4.6052 \qquad (3)$$

AND

$$t_{99}\ (\text{minutes}) = 4.6052\,\frac{a}{b}$$

t_{99} SHOULD BE CALCULATED FOR EACH SITUATION SO THAT THE TIME TO REACH EQUILIBRATION I'S VERY SHORT COMPARED TO THE DURATION OF EXPOSURE.



THUS WHEN a AND b ARE EQUAL X IS ABOUT 5 MINUTE.

G. AIR CHANGES

AN AIR CHANGE IS SAID TO OCCUR WHEN A VOLUME OF AIR EQUAL TO THE VOLUME OF THE CHAMBER HAS PASSED THROUGH THE CHAMBER. THIS IS A CONVENIENT TERM FOR VENTILATION ENGINEERS BUT IS NOT STRICTLY SPEAKING CORRECT. WHEN SUCH OCCURS, FROM EQUATION 2, ONLY 63% OF THE AIR HAS BEEN "CHANGED". FROM EQUATION 3, THE TIME FOR ONE "AIR CHANGED" MUST BE MULTIPLIED BY A FACTOR OF 4.6 BEFORE EVEN 99% OF THE EXPECTED CHANGE CAN BE DONE. THEREFORE IF a AND b ARE EQUAL THERE IS ONE "AIR CHANGE" EVERY 4.6 MINUTES OR 12/ HOUR. THE BEST THING TO DO IS TO FORGET ABOUT "AIR CHANGE" AND GIVE a AND b. THEN WE KNOW.

VI. FACTORS INFLUENCING THE DOSE FOR AEROSOLS Ø

A. FACTORS INFLUENCING TOTAL DOSE

i) CONCENTRATION IN AIR, C, mg/m^3 OR mg/l

ii) PARTICLE SIZE, α, WHICH WILL DETERMINE THE FRACTION OF AEROSOL DEPOSITED⁂

iii) MINUTE VENTILATION, MV, WHICH IS DETERMINED BY TIDAL VOLUME (VT) AND NUMBER OF BREATH PER MINUTE (f)

iv) DURATION OF EXPOSURE IN MINUTES (t)

v) BODY WEIGHT,kg

USEFUL VALUES AT REST

SPECIES	VT (ml)	f
MAN (70kg)	800	15
MOUSE (.02 kg)	0.1 - 0.2	250
RAT (.2 kg)	2	120
GUINEA-PIGS (.2 kg)	2	120
MONKEYS (3 kg)	40	35
MAN (MODERATE EXERCISE)	1,450	15

⁂ DEPOSITION: ALL FACTORS WHICH DETERMINE WHAT FRACTION OF THE INSPIRED AEROSOL WILL BE CAUGHT IN THE RESPIRATORY TRACT (NOSE TO ALVEOLI) AND FAIL TO EXIT WITH THE EXPIRED AIR.

Ø REQUIRED READING FOR ANYONE PLANNING TO WORK WITH AEROSOLS: DEPOSITION AND RETENTION MODELS FOR INTERNAL DOSIMETRY OF THE HUMAN RESPIRATORY TRACT. TASK GROUP ON LUNG DYNAMICS HEALTH PHYSICS 12, 173-207, 1966. RECENT REVIEW: J.D. BRAIN AND P.A. VALBERG, AMER. REV. RESP. DISEASE 120, 1325-1373, 1979.

amount retained

$$\text{DOSE} = \frac{\alpha \cdot VT \cdot f \cdot C \cdot t}{kg} = \text{mg/kg}$$

very important equation

REMEMBER: THIS GIVES ONLY TOTAL DEPOSITED. DOES NOT GIVE REGIONAL DEPOSITION WHICH IS HIGHLY IMPORTANT. THIS DOES NOT TAKE CLEARANCE INTO ACCOUNT.

TO GET A "BALL PARK" FIGURE, ASSUME 50% (0.5) FOR α

THUS:
$$\frac{0.5 \times 800\text{ml} \times \frac{15}{\text{min}} \times \frac{1\text{ mg}}{1{,}000\text{ ml}} \times 60\text{ min}}{70\text{ kg}} = \text{mg/kg}$$

AS CAN BE SEEN, WE NOW HAVE THE PROPER UNITS FOR TOXICITY INSTEAD OF JUST HAVING AN EXPOSURE CONCENTRATION IN mg/l OR mg/m^3. COMPARISONS OF TOTAL DOSE RECEIVED CAN BE MADE BETWEEN VARIOUS ANIMALS, EXPOSED AT THE SAME CONCENTRATION, ON THE BASIS OF mg/kg OF BODY WEIGHT OR mg/m^2 OF BODY SURFACE AREA.

B. FACTORS AFFECTING REGIONAL DEPOSITION: SIZE, SHAPE, DENSITY

i) SEDIMENTATION (GRAVITY), SETTLING

ALL PARTICLES WITH DENSITY GREATER THAN AIR EXPERIENCE A DOWNWARD FORCE DUE TO GRAVITY

$$F_{grav} = V_{part} (D_{part} - D_{air}) g$$

V_{part} = VOLUME OF THE PARTICLE
D = DENSITY
g = GRAVITATIONAL ACCELERATION

THUS THE PARTICLE ACCELERATES DOWNWARD UNTIL ITS VELOCITY INCREASES TO THE POINT WHERE THE RETARDING FORCE DUE TO ITS MOTION THROUGH AIR JUST BALANCES ITS WEIGHT. IF PARTICLE IS SPHERIC AND SMALL ENOUGH SO THAT VISCOUS FORCES ARE THE PRIMARY RESISTIVE FORCES STOKE'S LAW APPLIES TO PREDICT RETARDING FORCES.

$$F_{resist} = 3 \pi d n v$$

d = DIAMETER OF PARTICLE
n = VISCOSITY OF AIR
v = VELOCITY OF THE PARTICLE

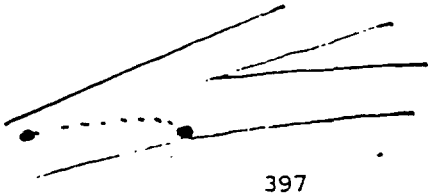
THE VELOCITY AT WHICH THIS RESISTIVE FORCE EQUALS THE GRAVITATIONAL FORCE IS THE TERMINAL VELOCITY, VT

$$VT = (D_{part} - D_{air}) \frac{gd^2}{18n}$$

EXAMPLE: 1 um PARTICLE, D = 1, VT = 33 um/s AND WOULD BE ESTABLISHED IN 10 us FOR PARTICLE STARTED FROM REST.

APPLIES TO PARTICLES 1-40 um, CORRECTION CAN BE MADE FOR 0.001 um TO 200 um BUT NOT RELEVANT FOR OUR USE.

FOR NON-SPHERICAL PARTICLES THIS CANNOT BE CALCULATED BUT MEASURED EXPERIMENTALLY AND CHARACTERIZED AS "AERODYNAMIC DIAMETER", IT HAS THE SAME SETTING VELOCITY OF A UNIT-DENSITY SPHERE.



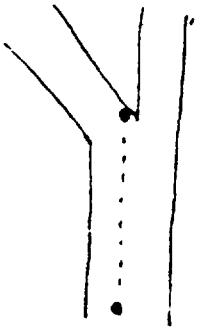
ii) IMPACTION, INERTIA

WHEN AN OBSTACLE IS PLACED IN THE PATH OF THE AIRFLOW OR BIFURCATIONS OR TORTUOUS PATHS SUCH AS IN THE NOSE OR TRACHEO-BRONCHIAL TREE ARE PRESENT SMALL PARTICLES WILL FOLLOW THE GAS FLOW LINES BUT LARGE PARTICLES, BECAUSE OF GREATER INERTIA ARE UNABLE TO CHANGE DIRECTION AND WILL IMPACT ON THE SIDE.

IMPACTION WILL DEPEND ON 4 FACTORS

- AIR VELOCITY
- DENSITY OF THE PARTICLE
- SQUARE OF THE PARTICLE DIAMETER
- ANGLE OF AIRSTREAM DEFLECTION

IMPORTANT: > 3 um, NASOPHARYNGEAL AREA, CENTRAL AIRWAYS



i) DIFFUSION, BROWNIAN MOVEMENT

MOTION CAUSED BY RANDOM MOLECULAR COLLISION THIS PROCESS CAN BE DESCRIBED AS FOLLOWS:

$$\Delta = \sqrt{6Dt}$$

Δ: ROOT-MEAN SQUARE DISPLACEMENT AFTER A TIME, t

D: DIFFUSION COEFFICIENT COEFFICIENT OF PARTICLES WHICH IS EXPRESSED AS FOLLOWS:

$$D = \frac{kT}{3\Pi\ nd}$$

T: TEMPERATURE, KELVIN

k: BOLTZMANN CONSTANT (1.38×10^{-16} ergs/K^{o})

n: GAS VISCOSITY

d: DIAMETER OF PARTICLE

IT IS IMPORTANT FOR PARTICLES < 1 um. IMPORTANT TO REMEMBER THAT PARTICLE DIAMETER IS THE PRIMARY FACTOR.

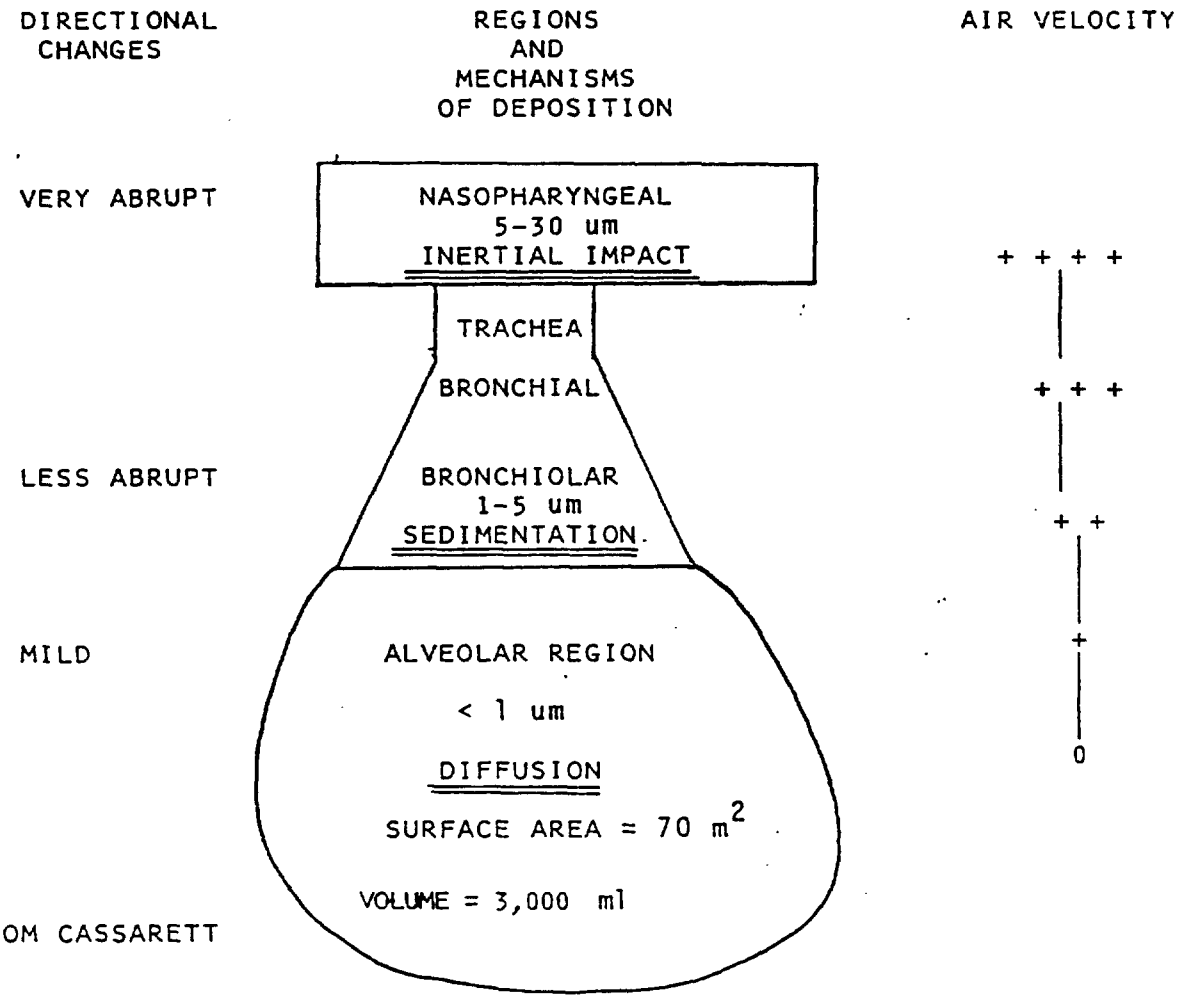
iv) ELECTROSTATIC FORCES ~~PARTICLES~~ negligible in particle deposition

ALL AEROSOL ~~PARTICLES~~ HAVE A + (NON-METALLIC) OR - (METALLIC) CHARGE WHICH MAY AFFECT DEPOSITION. HOWEVER, LITTLE IS KNOWN ABOUT THE EFFECT OF CHARGE.

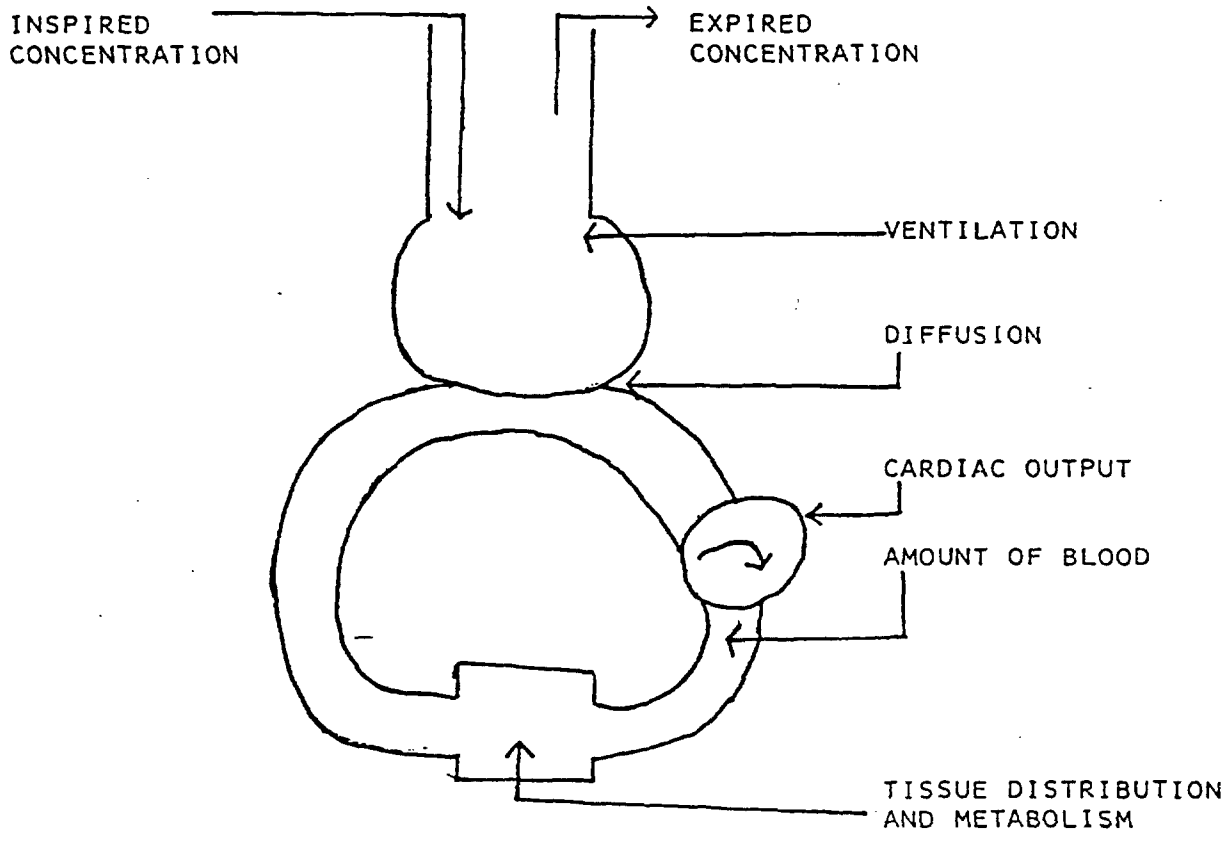
v) INTERCEPTION

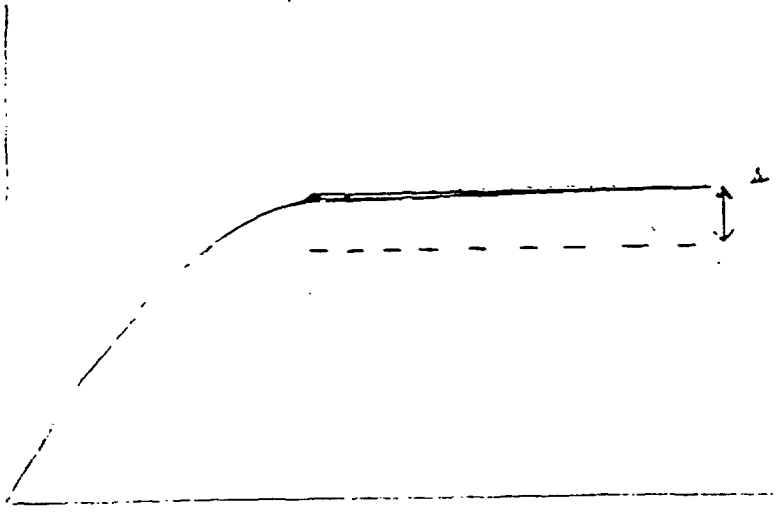
OF IMPORTANCE FOR FIBERS AS THE INSPIRED AIR COMES IN CLOSE CONTACT WITH A SURFACE. FIBER DEPOSITION MODELS ARE MUCH LESS WELL DEVELOPED THAN FOR PARTICLES.

VI. QUICK SUMMARY ⁂



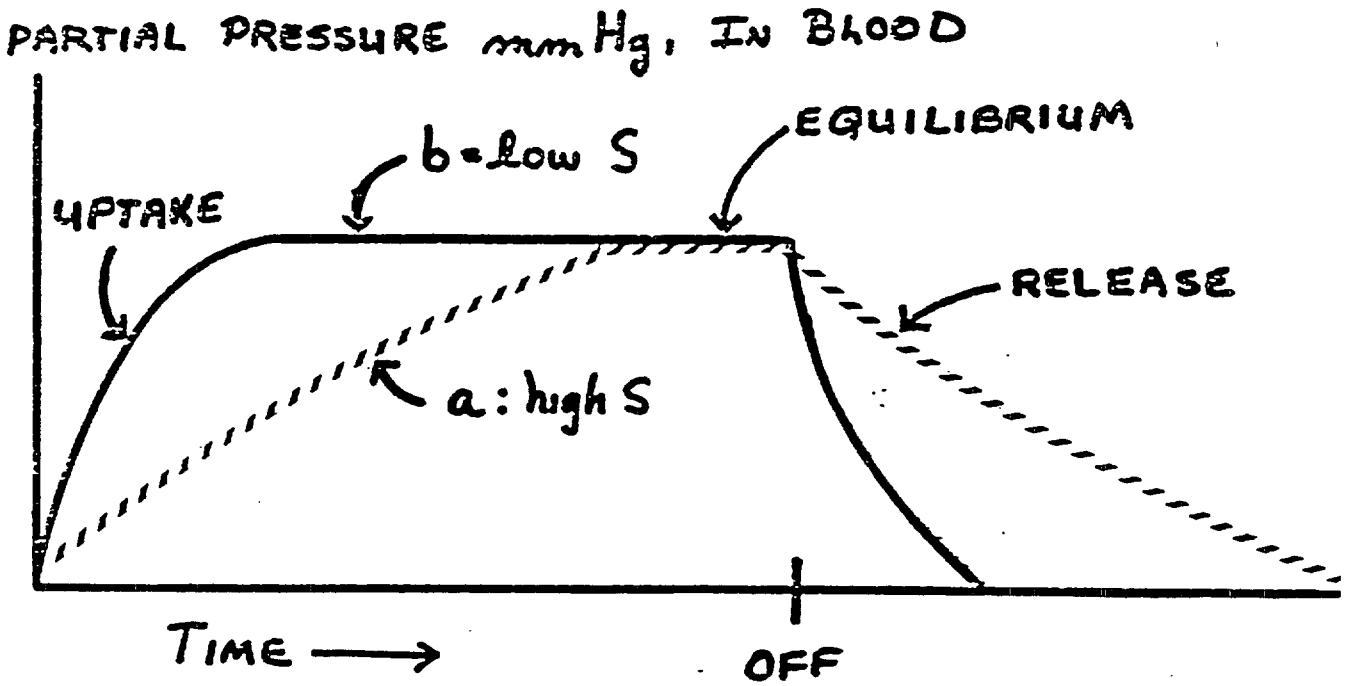
⁂ FROM CASSARETT

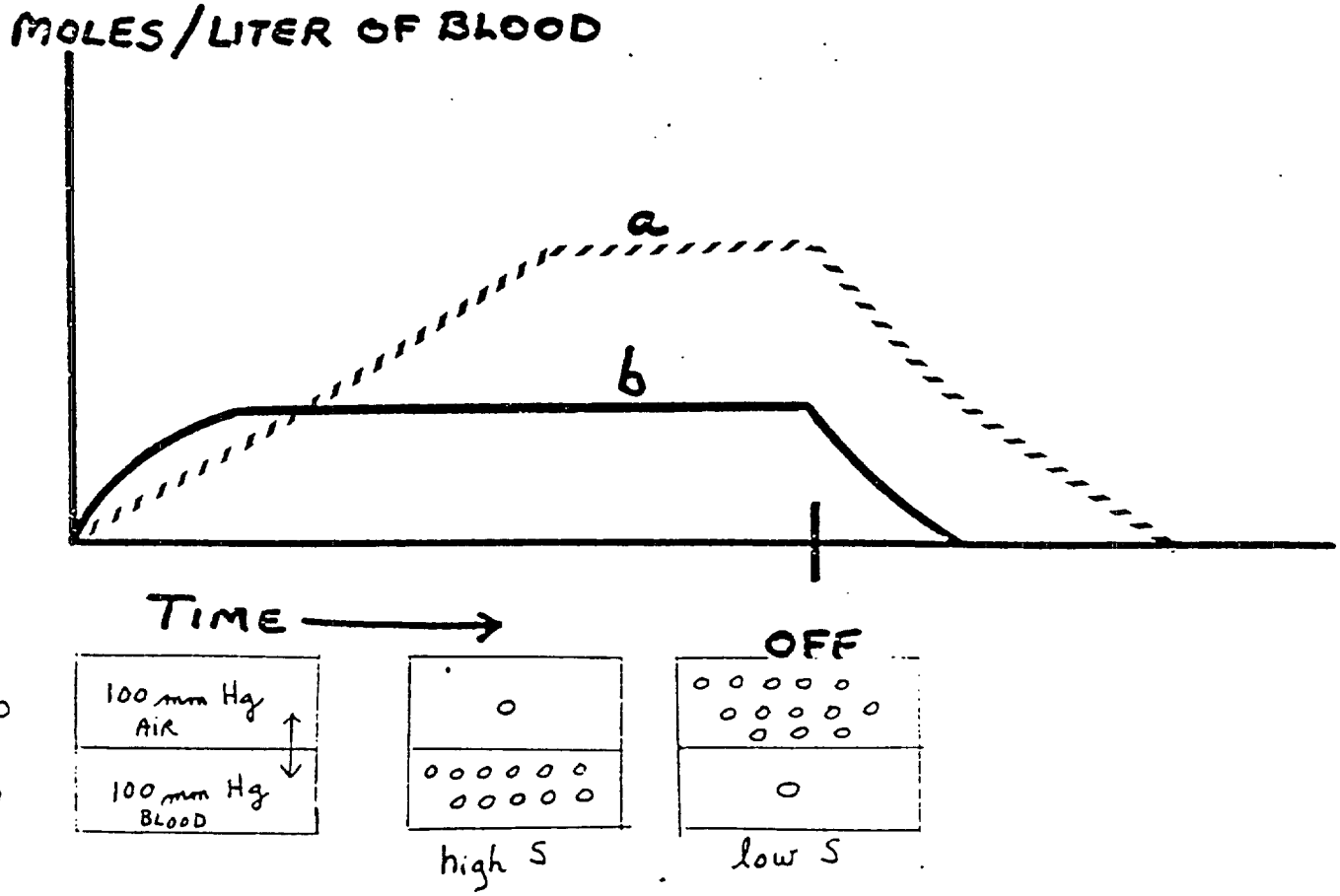




WATER: 40 LITERS

FAT: 15 LITERS


PARTIAL PRESSURE mm Hg, IN BLOOD
b = low S
EQUILIBRIUM
UPTAKE
RELEASE
a: high S
TIME
OFF


MOLES/LITER OF BLOOD
a
b
TIME
OFF
100
0
100 mm Hg AIR
100 mm Hg BLOOD
high S
low S

3. LOW REACTIVITY WITH SURFACE OF RESPIRATORY SYSTEM, ASSUME INERT GAS AND NO METABOLISM, USE THE FOLLOWING SYSTEM: ⁂

A: PHYSICAL PARAMETERS

i) CONCENTRATION IN AIR (mmHg) DETERMINES MAXIMUM CONCENTRATION (mmHg) IN BLOOD SINCE EQUILIBRIUM WILL BE ESTABLISHED AT THE SOME TIME.

ii) KNOWING S GIVES THE MAXIMUM CONCENTRATION IN MOLES OR MILLIGRAMS/LITER OF BLOOD WHICH CAN BE ACHIEVED, i.e. AT EQUILIBRIUM.

iii) SUBSTANCES WITH HIGH S WILL TAKE A LONG TIME TO REACH EQUILIBRIUM (METHANOL, ETHANOL, ACETONE, ETHER, ETC.). SUBSTANCES WITH LOW S (METHANE, ETC.) WILL REACH EQUILIBRIUM VERY QUICKLY. S VALUE CAN BE TAKEN FOR WATER AT $37^{o}C$.

B: PHYSIOLOGICAL PARAMETERS

i) MINUTE VENTILATION: IMPORTANT FOR HIGH S SUBSTANCES

ii) CARDIAC OUTPUT: IMPORTANT FOR LOW S SUBSTANCES

iii) AMOUNT OF BLOOD TO BE SATURATED, 5 LITERS AND TOTAL BODY WATER, 40 LITERS.

iv) OIL/WATER PARTITION COEFFICIENT: FROM BLOOD TO TISSUES.

⁂ Source: Goldstein et. al., Principles of drug action.

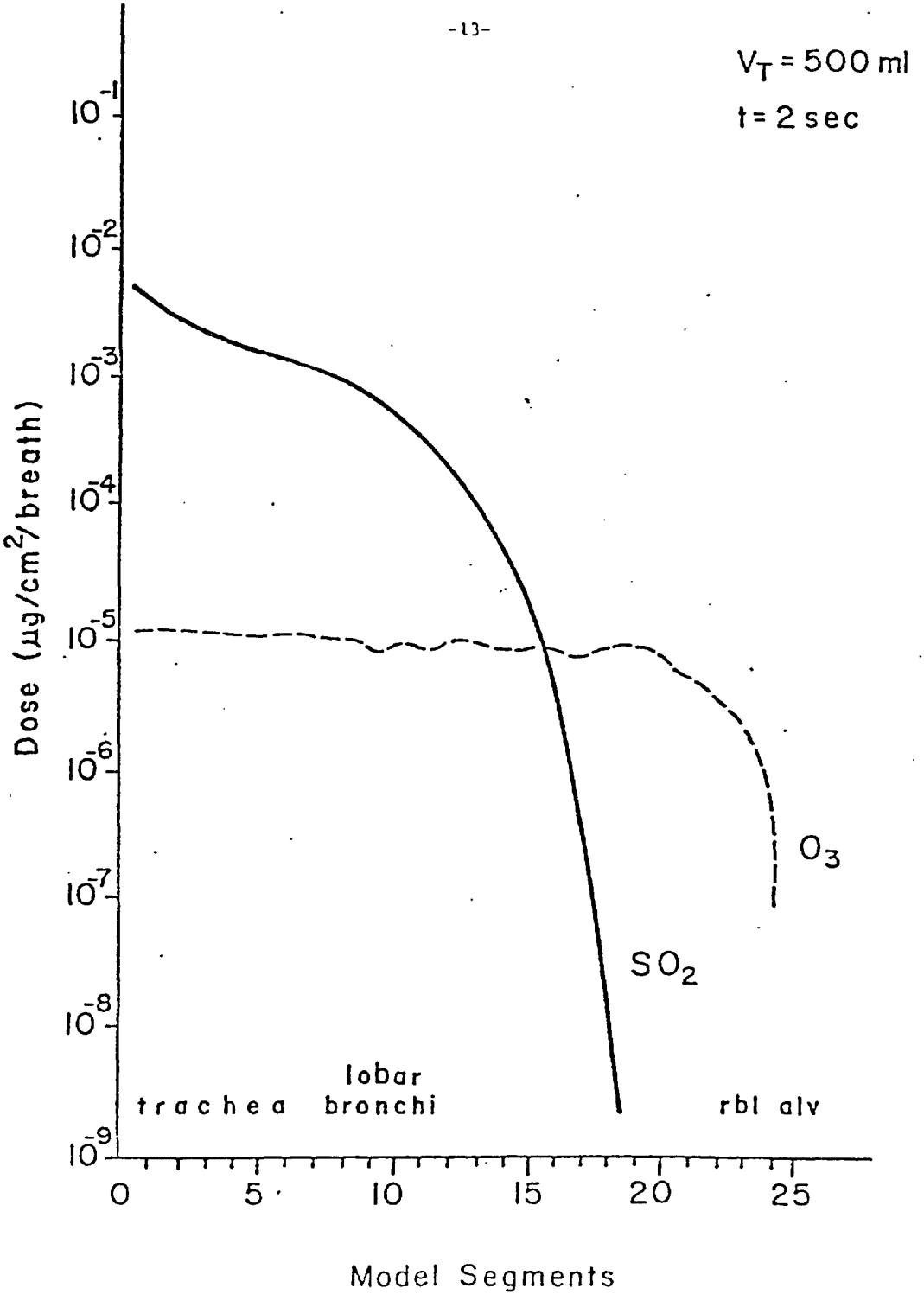


Figure 4. Reprinted from McJilton, C., Thielke, J., and Frank, R., 1972.

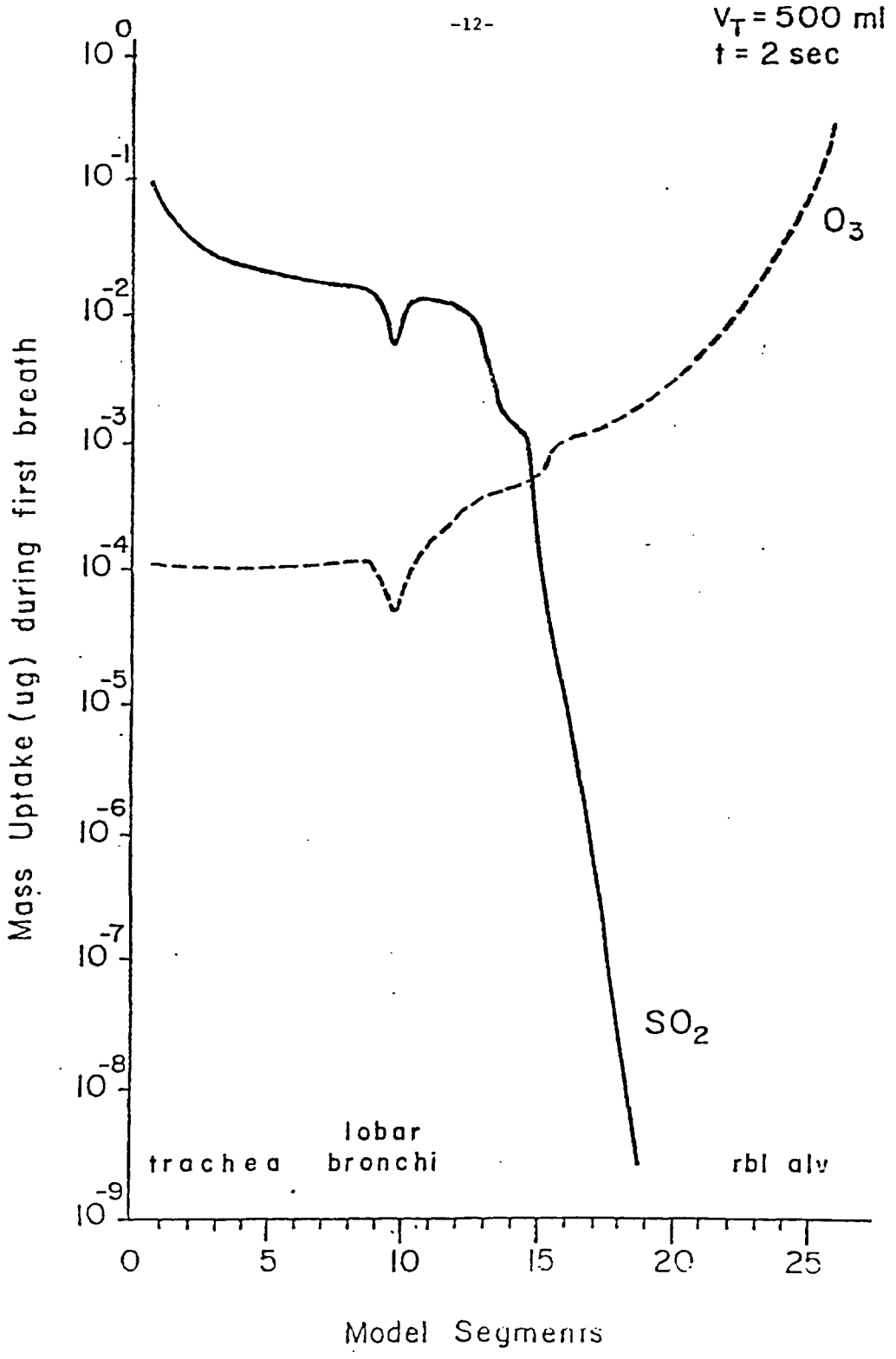


Figure 3. Reprinted from McJilton, C., Thielke, J., and Frank, R., 1972.

2. HIGH REACTIVITY, LOW WATER SOLUBILITY.

THESE WILL PENETRATE DEEPER INTO THE LUNG, NO_2, O_3, $COCl_2$, TDI, REACT WITH PULMONARY TISSUES, GENERALLY PRODUCE EDEMA. CALCULATE LIKE AEROSOL, ASSUME 100% FOR α.

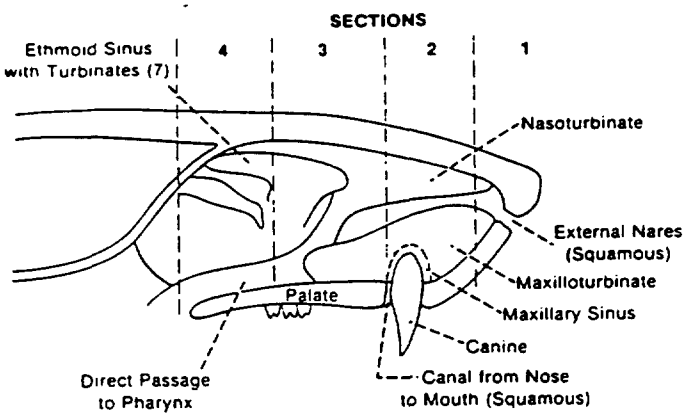


Figure 1. Parasagital view of the nose, showing the sections used in processing and for microscopic examination.

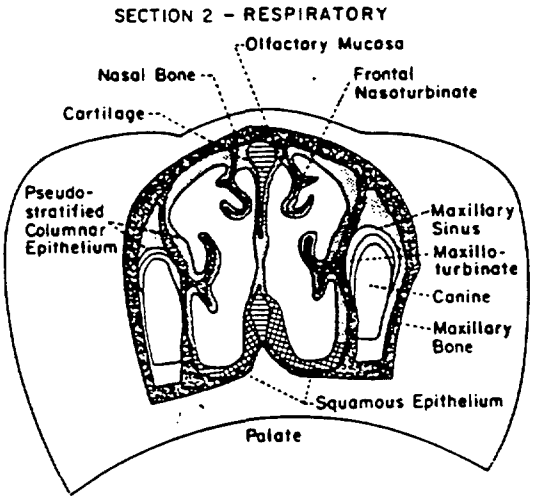


Figure 3. Coronal section =2, normal anatomy.

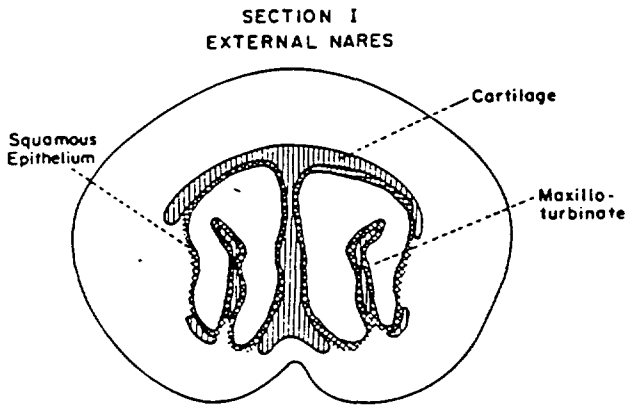


Figure 2. Coronal section =1, normal anatomy.

H. Lucia, C. S. Barrow, M. F. Stock and Y. Alarie

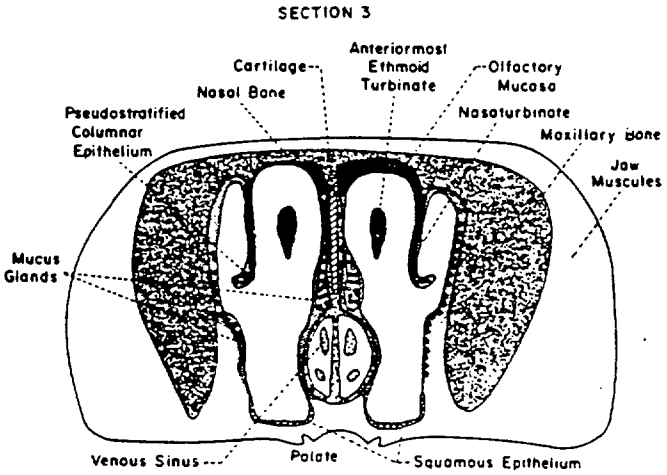


Figure 4. Coronal section =3, normal anatomy.

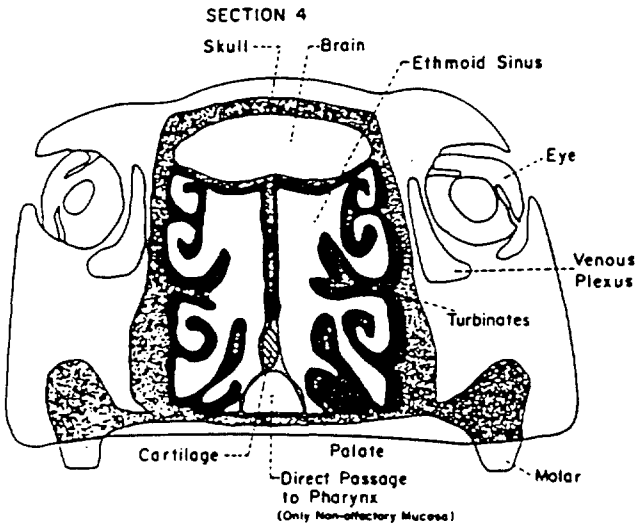


Figure 5. Coronal section =4, normal anatomy.

Table 1. Rating System for Evaluation of the Damage Due to Exposure to Airborne Chemicals in the Upper Respiratory Tract of Mice.

0	no damage seen at 24 hours
1+	1-50% of the mucosa is damaged, but underlying tissues are intact
2+	25-75% of the mucosa is destroyed, and some damage to the submucosa is noted
3+	50-99% of the mucosa is destroyed, and there is damage to the submucosa and underlying support structures
4+	100% of the mucosa is destroyed and there is extensive destruction of all underlying tissues

VIII FACTORS INFLUENCING THE DOSE FOR GASES, VAPORS ::

1. HIGH WATER SOLUBILITY AND REACTIVITY.

FOR THESE GASES, SO_2, HCl, HF, HCHO, CALCULATE LIKE AEROSOL ASSUME 100% FOR α. ESSENTIALLY COMPLETELY REMOVED BY SOLUTION AND REACTION AT THE SURFACES OF THE RESPIRATORY TRACT AND VERY EFFICIENTLY SCRUBBED BY THE UPPER RESPIRATORY TRACT, VERY LITTLE PENETRATION TO THE ALVEOLAR REGION UNTIL HIGH CONCENTRATIONS ARE REACHED. FEW GASES HAVE BEEN INVESTIGATED FOR REGIONAL PENETRATION, SO_2, O_3, SEVERAL ALDEHYDES.
HIGH WATER SOLUBILITY DOES NOT SEEM TO BE SUFFICIENT SINCE ACETONE IS NOT ENTIRELY REMOVED BY THE NOSE WHILE SO_2 IS.
WITH SO_2 THE REACTION WITH WATER AT pH 7.4 WILL YIELD

$$SO_2 + H_2O \rightleftarrows H_2SO_3 \rightleftarrows H^+ + HSO_3^-$$

$$HSO_3^- \rightleftarrows H^+ + SO_3^=$$

THEN REACTION OF HSO_3^- AND $SO_3^=$ WITH PROTEIN DISULFIDE BONDS TO YIELD SULFONATES.
SIMILAR SCHEMES CAN BE PRESENTED FOR SEVERAL WATER SOLUBLE AND REACTIVE CHEMICALS.

- IMPORTANCE IN TOXICOLOGICAL STUDIES: SINCE MICE, RATS, GUINEA-PIGS, HAMSTERS ARE OBLIGATORY NOSE BREATHERS, THE FIRST AREA AFFECTED BY THESE GASES WILL BE THE NOSE. NASAL CARCINOMA IN RATS AND MICE DUE TO FORMALDEHYDE IS A GOOD EXAMPLE.

5. PRACTICAL USE OF THE CONCEPT (ADAPTED FROM R.D. STEWART)

O BLOOD CONCENTRATION = ALVEOLAR AIR CONCENTRATION X S

HUMAN EXPOSURE TO TRICHLORETHYLENE, 200 ppm, 7 HRS/DAY FOR FOR 5 DAYS

ALVEOLAR AIR CONCENTRATION (ppm)

	1ST DAY	2ND DAY	3RD DAY	4TH DAY	5TH DAY
PRE-EXPOSURE (MORNING)	0.01	1.2	1.6	1.6	1.6
3 HOURS	76	75	76	79	76
30 MIN AFTER LUNCH	10.3	10.9	11.5	8.4	8.5
7 HOURS	76	75	76	79	76
1 HR. POST-EXPOSURE	8.3	9.4	9.0	7.7	8.7
3 HR. POST-EXPOSURE	5.1	4.4	3.5	3.5	3.6
6 HR. POST-EXPOSURE	3.3	2.8	2.4	2.9	2.9

90 HRS. POST-5 DAY EXPOSURE: 0.2

DOES NOT REACH EQUILIBRIUM WITH INSPIRED AIR

NO CUMMULATION

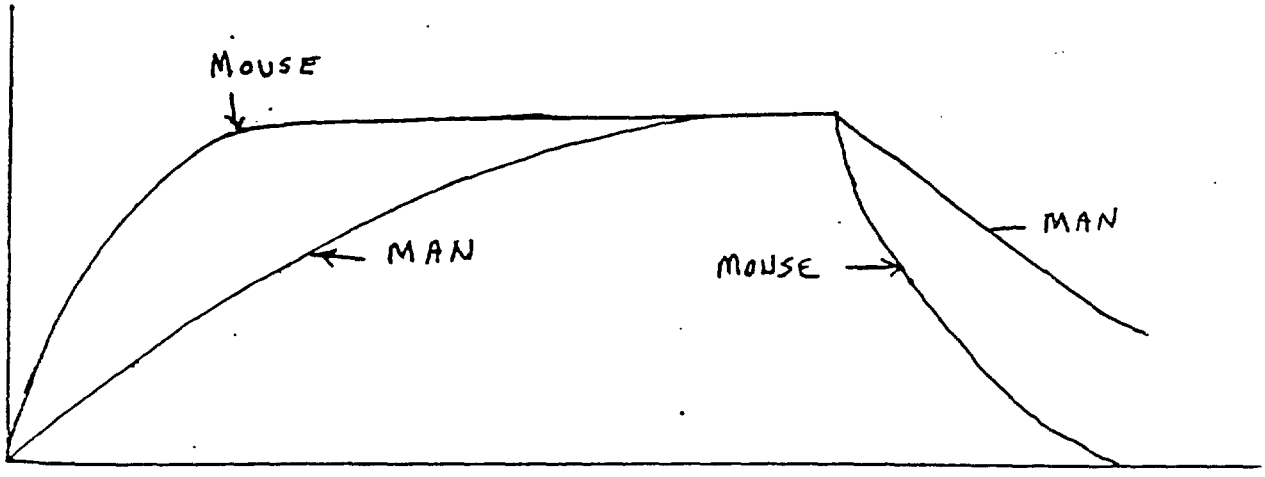
INCOMPLETE RELEASE

O ALCOHOL BREATH TEST ANALYSIS TO DETERMINE THE BLOOD CONCENTRATION FROM A SAMPLE OF ALVEOLAR AIR. SINCE ALVEOLAR AIR IS AT EQUILIBRIUM WITH CAPILLARY BLOOD, BY KNOWING THE AMOUNT IN ALVEOLAR AIR AND THE SOLUBILITY COEFFICIENT ONE KNOWS THE CONCENTRATION IN THE BLOOD.

4. QUICK SUMMARY (ADAPTED FROM A. GOLDSTEIN ET AL.)

AGENT	S	TIME TO EQUILIBRIUM	QUANTITY IN MOLES	PHYSIOLOGICAL FACTOR LIMITING UPTAKE
ETHYL ETHER	15	SLOW	LARGE	VENTILATION
CHLOROFORM	7.3	↓	↓	↑
HALOTHANE	2.5			
X	1.0			50/50
NITROUS OXIDE	0.5			↓
EHTYLENE	0.15	FAST	SMALL	CARDIAC OUTPUT

o Application in Toxicology: Man vs. Mouse, Why?



IX. EFFECTS ON THE RESPIRATORY TRACT ⁂

A - SENSORY IRRITANT

i) DEFINITION: CHEMICAL WHICH WHEN INHALED VIA THE NOSE WILL STIMULATE TRIGEMINAL NERVE ENDINGS, EVOKE A BURNING SENSATION OF THE NASAL PASSAGES AND INHIBIT RESPIRATION. ALSO MOST WILL INDUCE COUGHING FROM LARYNGEAL STIMULATION.

ii) OTHER CHARACTERISTICS: THESE CHEMICALS ARE ALSO CAPABLE OF STIMULATING TRIGEMINAL NERVE ENDINGS OF THE CORNEA AND INDUCE TEARING. AT HIGH CONCENTRATION, PARTICULARLY ON MOIST FACIAL SKIN, THEY ARE CAPABLE OF INDUCING A BURNING SENSATION. SOME HAVE ODORANT AND/OR GUSTATORY QUALITIES. MOST WILL INDUCE BRONCHOCONSTRICTION, USUALLY AT CONCENTRATIONS IN THE AIR HIGHER THAN REQUIRED FOR STIMULATION OF NERVE ENDINGS IN THE NASAL PASSAGES.

iii) EQUIVALENT TERMS TO DESCRIBE THEIR ACTION: UPPER RESPIRATORY TRACT IRRITANT, NASAL OR CORNEAL TRIGEMINAL STIMULANT, COMMON CHEMICAL SENSE STIMULANT, CHEMOGENIC PAIN STIMULANT, SUFFOCANT, LACHRYMATOR, STERNUTATOR.

iv) TYPICAL EXAMPLES: CHLORACETOPHENONE, O-CHLOROBENZYLIDENE MALONONITRILE, B-NITROSTYRENE, DIPHENYLAMINOCHLOROARSINE, SULFUR DIOXIDE, AMMONIA, ACROLEIN, FORMALDEHYDE.

⁂ Practical, Industrial Classification for A,B,C,D. - From Alarie, CRC, Crit. Rev. Toxicol., 2, 299, 1973.

B - PULMONARY IRRITANT

i) DEFINITION: CHEMICAL WHICH WHEN INHALED WILL STIMULATE SENSORY RECEPTORS WITHIN THE LUNG AND INCREASE RESPIRATORY RATE WITH A DECREASE IN TIDAL VOLUME RESULTING IN RAPID SHALLOW BREATHING. THEIR ACTION, AS OPPOSED TO THAT OF SENSORY IRRITANTS, OR BRONCHOCONSTRICTORS EVOKE A SENSATION OF DYSPNEA AND BREATHLESNESS RATHER THAN A CONSCIOUS PAINFUL SENSATION.

ii) OTHER CHARACTERISTICS: THESE CHEMICALS ARE CAPABLE OF INDUCING PULMONARY EDEMA WHICH IS THEN ACCOMPANIED BY PAINFUL BREATHING. THEY HAVE NO OR LITTLE ACTION AS SENSORY IRRITANTS OF THE EYE OR NASAL PASSAGES AT CONCENTRATION SUFFICIENT FOR PULMONARY IRRITATION AND, THEREFORE THEY PROVIDE LITTLE WARNING OF THEIR PRESENCE. SOME HAVE ODORANT OR GUSTATORY QUALITIES AND SOME EXERT A BRONCHOCONSTRICTING ACTION.

iii) EQUIVALENT TERMS TO DESCRIBE THEIR ACTION: LOWER RESPIRATORY IRRITANT, LUNG IRRITANT, DEEP LUNG IRRITANT.

iv) TYPICAL EXAMPLES: PHOSGENE, NITROGEN DIOXIDE, SULFURIC ACID MIST, OZONE, SULFUR AND NITROGEN MUSTARD, SULFUR PENTAFLUORIDE, CADMIUM FUMES.

C - BRONCHOCONSTRICTORS

i) DEFINITION: CHEMICAL WHICH WHEN INHALED WILL INDUCE AN INCREASE IN RESISTANCE TO AIRFLOW WITHIN THE CONDUCTING AIRWAYS OF THE LUNG. THE ACTION CAN BE VIA DIRECT EFFECT ON SMOOTH MUSCLES OF THE CONDUCTING AIRWAYS, BY AXONAL REFLEX, BY VAGO-VAGAL OR TRIGEMINAL-VAGAL REFLEXES FOLLOWING STIMULATION OF NERVE ENDINGS BELONGING TO THESE SYSTEMS OR BY LIBERATION OF HISTAMINE.

ii) OTHER CHARACTERISTICS: MOST OF THESE CHEMICALS ARE ALSO SENSORY IRRITANTS. THEIR ACTION ON THE BRONCHIAL MUSCOSA PRODUCES A PAINFUL SENSATION.

iii) TYPICAL EXAMPLES: SULFUR DIOXIDE, AMMONIA, INERT PARTICLES, SENSITIZATION BY ALLERGENS SUCH AS FOREIGN PROTEINS OR CHEMICALS ACTING AS HAPTEN SUCH AS TOLUENE DIISOCYANATE, AEROSOLS OF HISTAMINE OR CHOLINERGIC AGONISTS.

D - RESPIRATORY IRRITANTS

i) DEFINITION: CHEMICAL WHICH WHEN INHALED CAN ACT AS SENSORY IRRITANT, BRONCHOCONSTRICTOR AND PULMONARY IRRITANT. THESE CHEMICALS ARE CAPABLE OF ALL THREE ACTIONS AND THERE IS LITTLE DIFFERENCE BETWEEN THE CONCENTRATION AT WHICH THEY ARE SENSORY IRRITANT AND PULMONARY IRRITANTS.

ii) OTHER CHARACTERISTICS: SIMILAR TO SENSORY IRRITANTS AND LUNG IRRITANTS.

iii) EQUIVALENT TERM TO DESCRIBE THEIR ACTION: ANY OF THE TERMS MENTIONED IN THIS TABLE, DEPENDING ON THE EXPOSURE CONDITIONS INVOLVED.

iv) TYPICAL EXAMPLES: CHLORINE, KETENE, CHLOROPICRIN, DICHLOROMETHYL ETHER, CHLORINE PENTAFLUORIDE, DIEPOXYBUTANE.

E. PULMONARY SENSITIZERS (HYPERSENSITIVITY, DIFFERENT FROM HYPERSUSCEPTIBILITY)

i) DEFINITION: CHEMICALS WHICH WHEN INHALED STIMULATE IMMUNOLOGIC SYSTEM SUCH THAT UPON RE-EXPOSURE TO A VERY LOW CONCENTRATION A PULMONARY REACTION OCCURS.

a) FOREIGN PROTEINS: DEPENDENT ON MOLECULAR WEIGHT
EXAMPLE: SUBTILISINS (PROTEOLYTIC ENZYMES)
TLV = 6×10^{-5} mg/m^3 -- very potent

b) SIMPLE CHEMICALS WHICH ACT AS HAPTENS.
HAPTEN: ANY SMALL MOLECULE WHICH WHEN ATTACHED TO A MACROMOLECULE INDUCES FORMATION OF ANTIBODIES TO THE CHEMICAL AND WHICH CAN REACT WITH SPECIFIC ANTIBODIES.
EXAMPLE: TOLUENE DIISOCYANATE (TDI), TRIMELLITIC ANHYDRIDE, POTASSIUM CHLOROPLATINATE, PHTALLIC ANHYDRIDE.

ii) TYPE OF PULMONARY REACTIONS

a) IMMEDIATE HYPERSENSITIVITY: ASTHMA ATTACK, OCCURS WITHIN 1 HR OF EXPOSURE, CLASS OF ANTIBODY RESPONSIBLE MAINLY 1gE ALSO 1 gG4 POSSIBLY OTHERS.

b) LATE REACTION: STARTS AFTER 1 HR., LAST 2-3 HRS. OR START AFTER 3-4 HRS. LAST 24-36 HRS. MAINLY 1gG PRECIPITATING ANTIBODIES. BIRD FANCIERS DISEASE, FARMER'S LUNG DISEASE (THERMOPHYLLIC ACTINOMYCETES) ALLERGIC ALVEOLITIS.

c) GRANULOMA FORMATION: CELL-MEDIATED MECHANISM INSTEAD OF ANTIBODIES. TUBERCULOSIS, BERYLLIUM.

Table I. Respiratory Hypersensitivity from Industrial Chemicals

Industrial Compound	Symptoms	Reference
Amprolium hydrochloride	Asthma	Greene and Freedman, 1976
Beryllium	Rhinitis, cough, dyspnea, cyanosis	Hardy and Tabershaw, 1946
Cement dust	Asthma	Kobayashi, 1974
Chloramine	Asthma	Bourne et al., 1979
Diphenylmethane diisocyanate (MDI)		Zeiss et al., 1980; Konzen et al., 1966
Enflurane	Asthma	Schwettmann and Casterline, 1976
Ethylenediamine	Asthma	Lam and Chan-Yeung, 1980
Formalin	Asthma	Hendrick and Lane, 1975
Naphthylene diisocyanate	Asthma	Harries et al., 1979
Nickel sulfate	Asthma	McConnell et al., 1973
Persulfate salts	Asthma, dermatitis	Pepys et al., 1976 Baur et al., 1979
Phenylglycine acid chloride	Asthma	Kammermeyer and Mathews, 1973
Phenylmercuric proprionate	Asthma, urticaria	Koszewski and Hubbard, 1956; Mathews, 1968; Morris, 1960
Phthalic anhydride	Asthma, rhinitis	Kern, 1939; Maccia et al., 1976

Table I. (cont'd.)

Industrial Compound	Symptoms	Reference
Platinum salts	Asthma, dermatitis	Freedman and Krupey, 1968; Cleare et al., 1976
Sodium bichromate	Asthma	Kobayashi, 1974
Spiramycin	Asthma, dermatitis	Davies and Pepys, 1975
Tannic acid	Asthma, urticaria, rhinitis	Johnston et al., 1951
Tetracycline	Asthma	Menon and Das, 1977
Toluene diisocyanate (TDI)	Asthma, urticaria	Avery et al., 1969; Pepys et al., 1972; Karol et al., 1979b
Trimellitic anhydride	Asthma	Zeiss et al., 1977

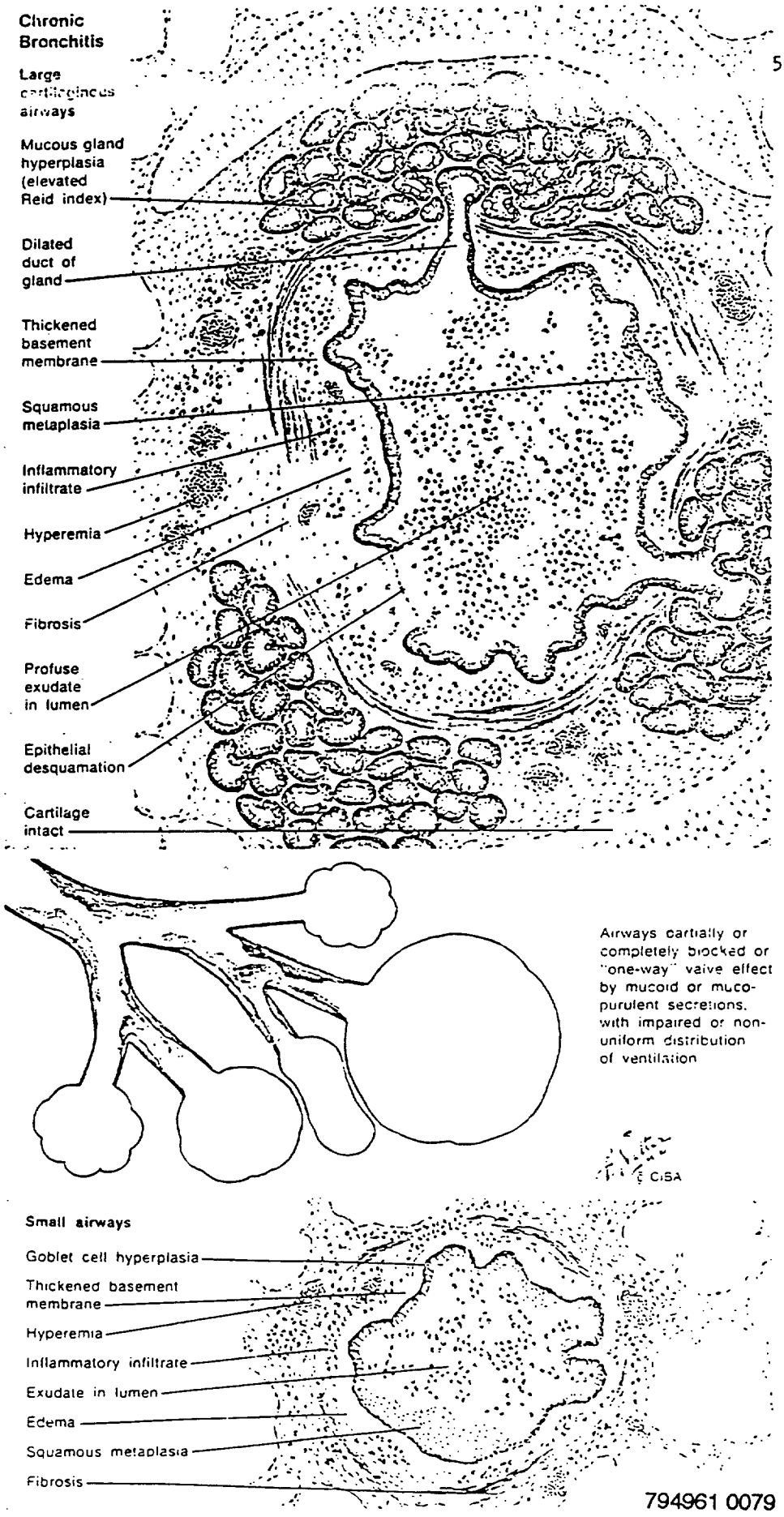
Etiologic Agents in Hypersensitivity Pneumonitis

Disease	Exposure	Antigen
Farmer's lung	Moldy hay or grain	*Micropolyspora faeni, Thermoactinomyces vulgaris*
Bagassosis	Stored sugar cane fiber (bagasse)	*T. saccharii* and possibly other organisms
Mushroom picker's disease	Moldy vegetable compost	*M. faeni, T. vulgaris*
Humidifier, air-conditioner or heating system disease	Contaminated forced air system	Thermophilic actinomycetes and other organisms
Fog fever (cattle)	Moldy hay	Same as farmer's lung
Maple bark stripper's disease	Maple tree logs or bark	*Cryptostroma corticale*
Sequoiosis	Redwood sawdust	*Graphium, Pullularia, Aureobasidium pullulans* and other fungi
Suberosis	Moldy cork dust	*Penicillium* species
Paper mill worker's disease	Moldy wood pulp	*Alternaria*
Pulpwood handler's disease	Moldy wood pulp	Same as above
Brewer's or malt worker's lung	Malt or barley dust	*Aspergillus clavatus, A. fumigatus*
Cheese washer's lung	Cheese mold	*P. casei*
Paprika slicer's disease	Moldy paprika pods	*Mucor stolonifer*
Wheat thresher's lung or grain measurer's lung	Wheat flour containing weevils	*Sitophilus granarius*
Pigeon breeder's disease	Pigeon serum and droppings	Avian proteins
Budgerigar fancier's disease	Contact with parakeets	Parakeet proteins
Chicken handler's or feather plucker's disease	Contact with chickens	Chicken proteins
Turkey handler's disease	Contact with turkeys	Turkey proteins
Pituitary snuff disease	Porcine, bovine pituitary gland (Pitressin snuff)	Porcine, bovine proteins
Smallpox handler's lung	Smallpox scabs	Unknown
Thatched roof disease (Papuan or New Guinea lung)	Dried grass and leaves	Unknown
Tobacco grower's disease	Tobacco plants	Unknown
Joiner's disease	Sawdust	Unknown
Tea grower's disease	Tea plants	Unknown
Bible printer's disease	Moldy typesetting water	Unknown
Coptic or mummy disease	Cloth wrappings of mummies	Unknown
Detergent disease (asthmalike symptoms—true pneumonitis not identified)	Enzyme detergents	*Bacillus subtilis*
Furrier's lung	Animal hairs	Unknown
Coffee worker's lung	Coffee beans	Coffee bean dust
Doghouse disease	Moldy straw	*Aspergillus versicolor*
Lycoperdonosis	Puffball spores (*Lycoperdon pyriform*)	Unknown
	water	

F. TISSUE REACTIONS

1) CHRONIC BRONCHITIS

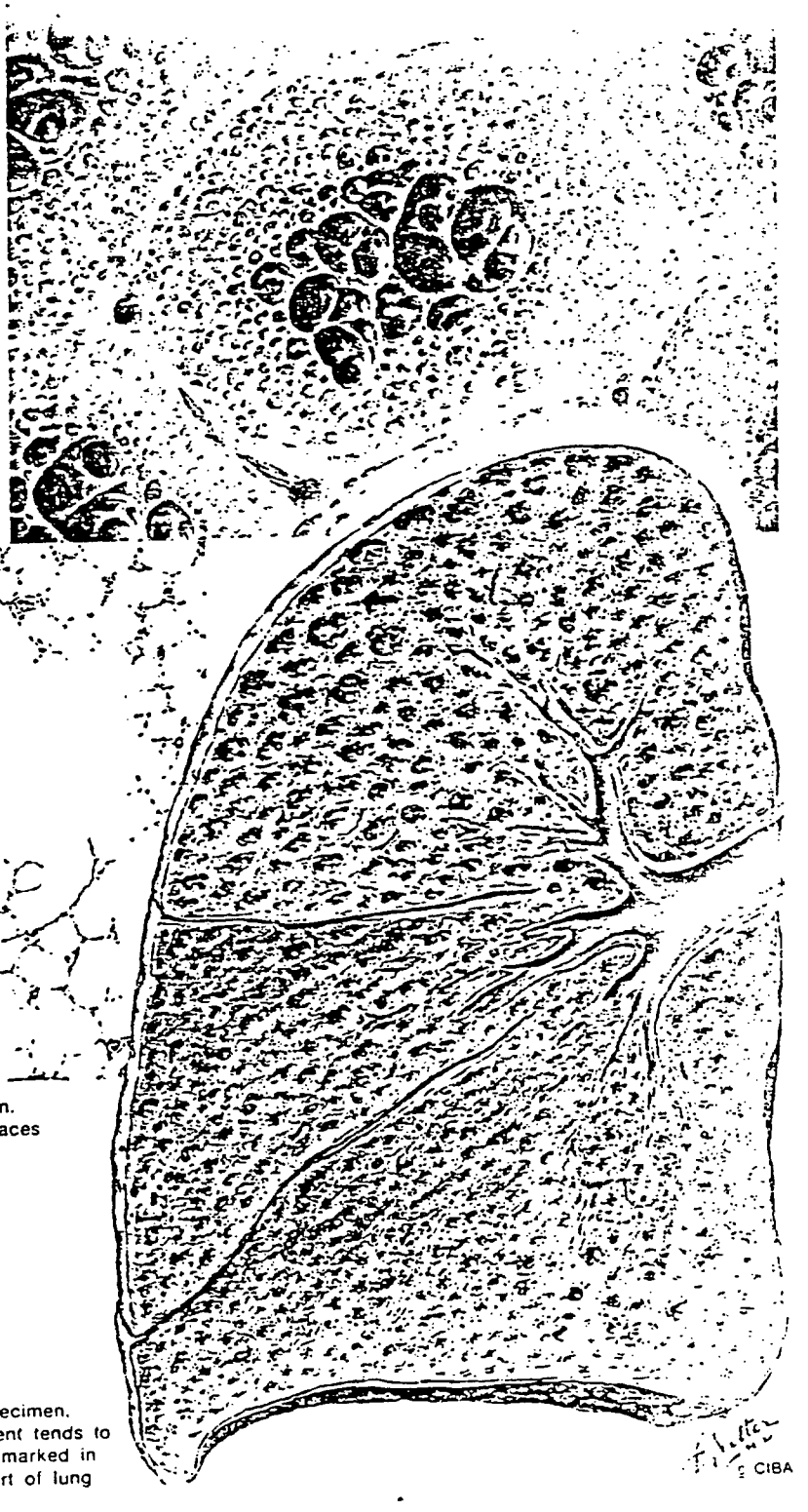
(SOURCE: CIBA COLLECTION, VOL.7)



794961 0079

2. CENTRILOBULAR EMPHYSEMA: SOURCE, CIBA COLLECTION, VOLUME 7.

Centriacinar
(Centrilobular)
Emphysema



Magnified section. Distended, intercommunicating, saclike spaces in central area of acini

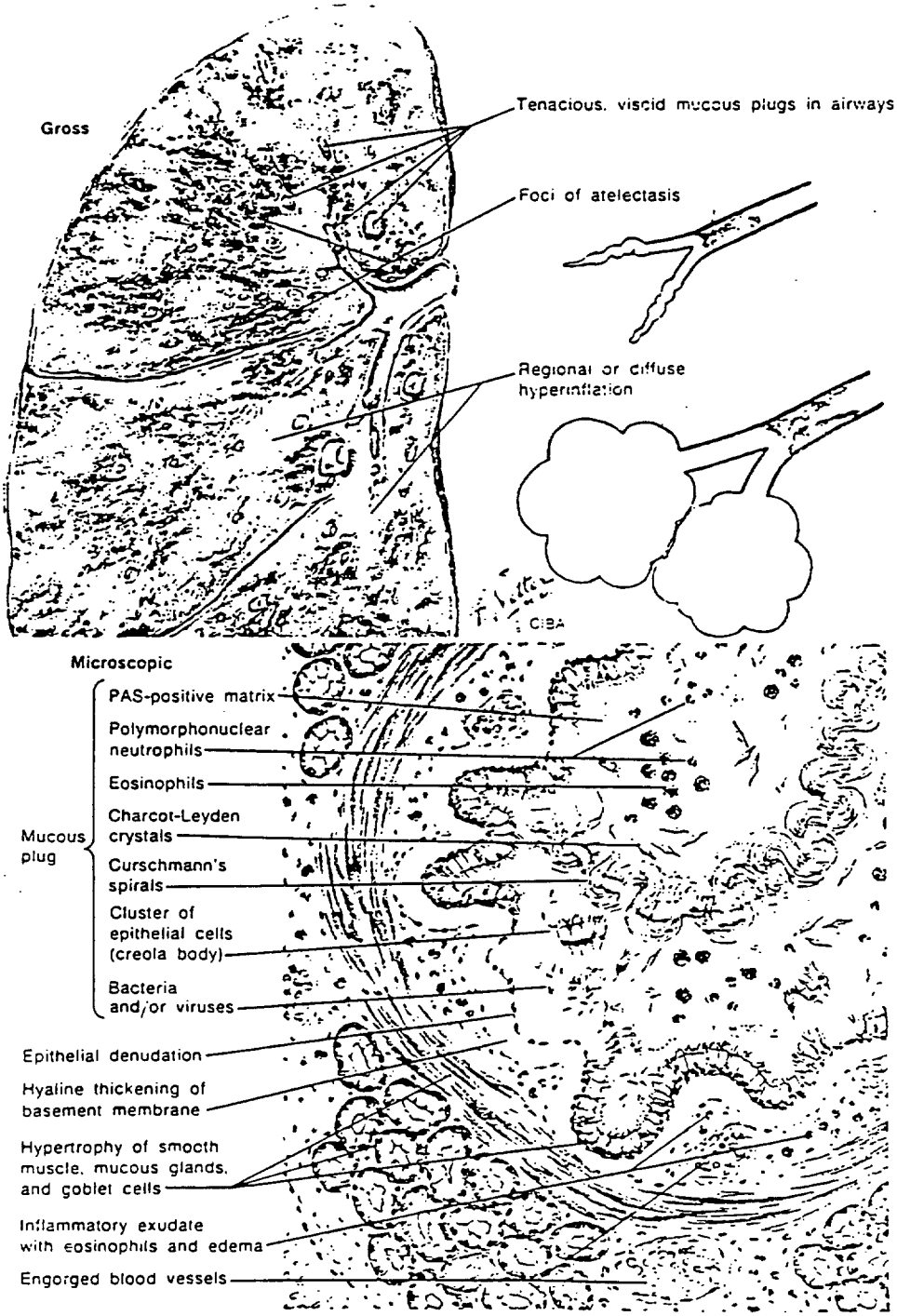
Microscopic section. Distention of airspaces with rupture of alveolar walls

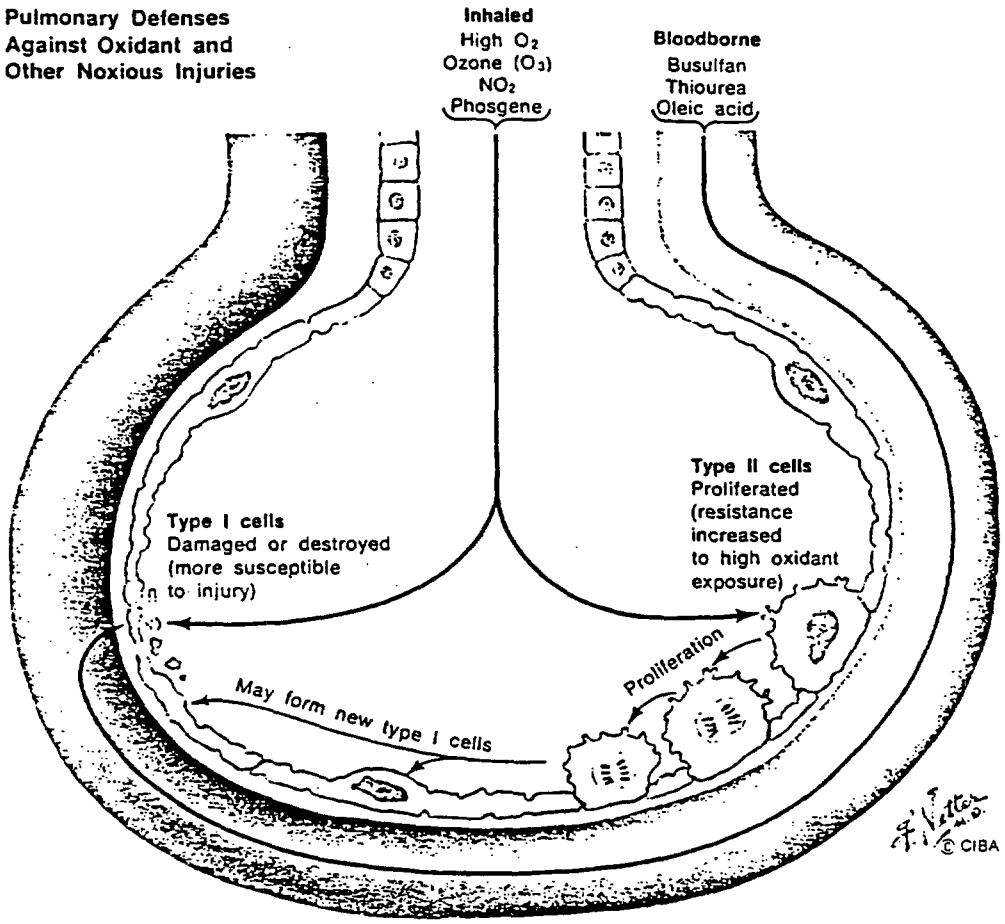
Gross specimen. Involvement tends to be most marked in upper part of lung

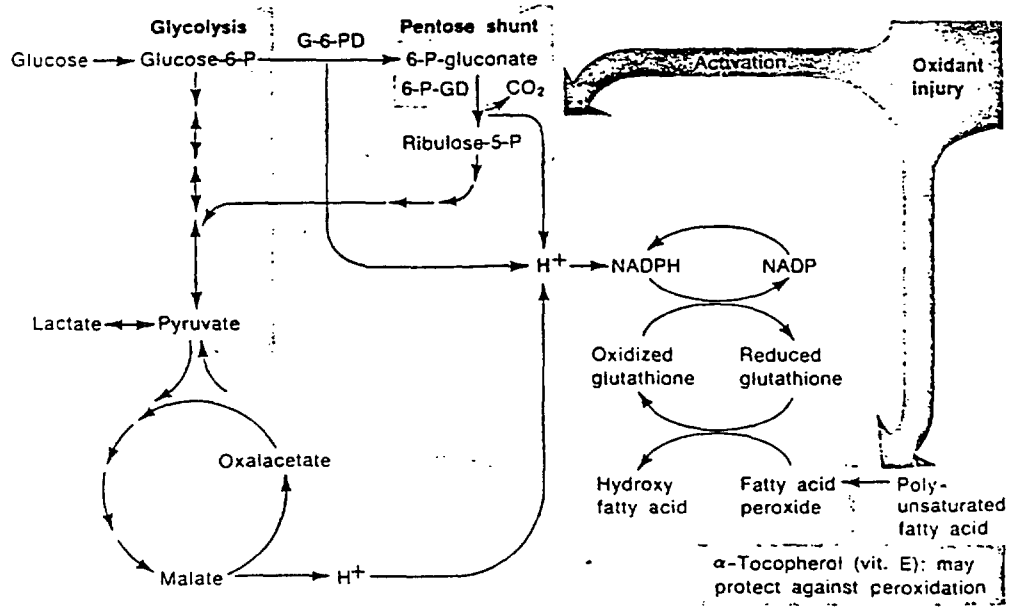
CIBA

3. ASTHMA: SOURCE, CIBA COLLECTION, VOLUME 7.

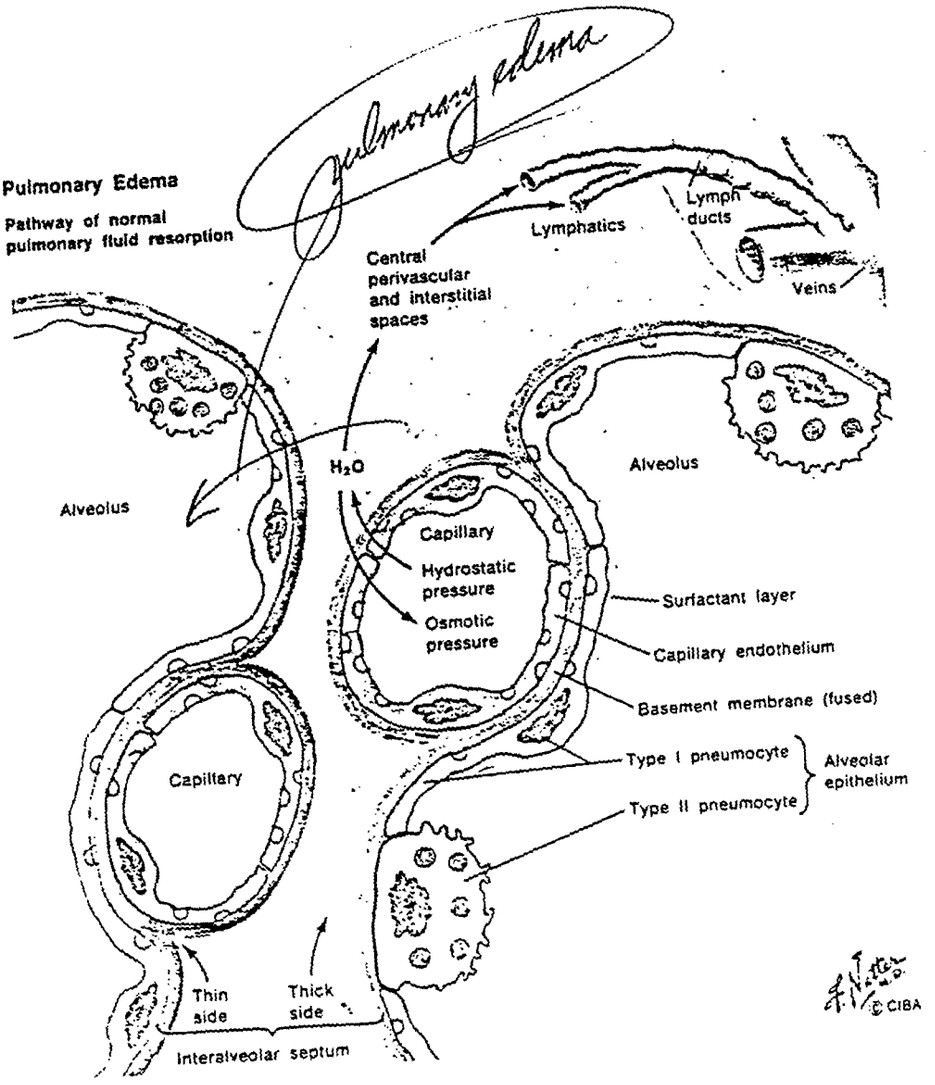
Pathology of Status Asthmaticus




Pulmonary Defenses Against Oxidant and Other Noxious Injuries
Inhaled
High O_2
Ozone (O_3)
NO_2
Phosgene
Bloodborne
Busulfan
Thiourea
Oleic acid
Type I cells
Damaged or destroyed
(more susceptible to injury)
Type II cells
Proliferated
(resistance increased to high oxidant exposure)
Proliferation
May form new type I cells
© CIBA


Glycolysis
Glucose
Glucose-6-P
G-6-PD
Pentose shunt
6-P-gluconate
6-P-GD
CO_2
Ribulose-5-P
Activation
Oxidant injury
H^+
NADPH
NADP
Lactate
Pyruvate
Oxidized glutathione
Reduced glutathione
Oxalacetate
Hydroxy fatty acid
Fatty acid peroxide
Poly-unsaturated fatty acid
Malate
H^+
α-Tocopherol (vit. E): may protect against peroxidation

5. PULMONARY EDEMA: SOURCE, CIBA COLLECTION, VOLUME 7.



G. SPECIFIC OCCUPATIONAL PULMONARY DISEASE

SOURCE, CIBA CLINICAL SYMPOSIUM, VOLUME 30, L978

1. CADMIUM AND BERYLLIUM

Plate 2

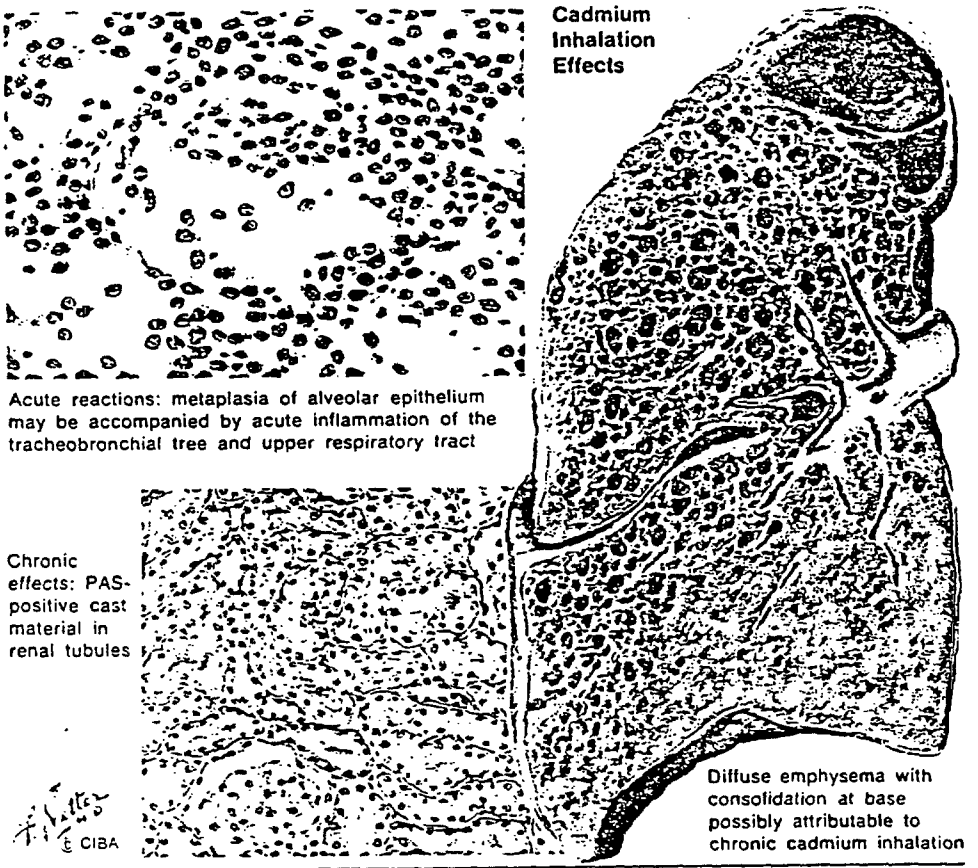
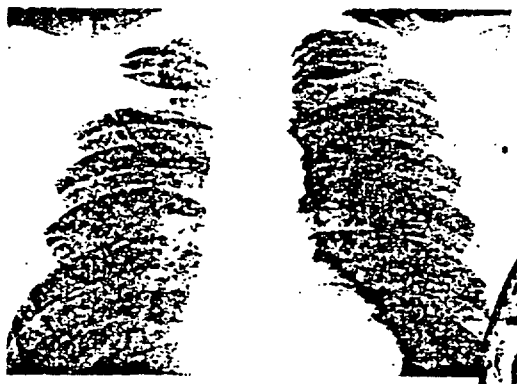
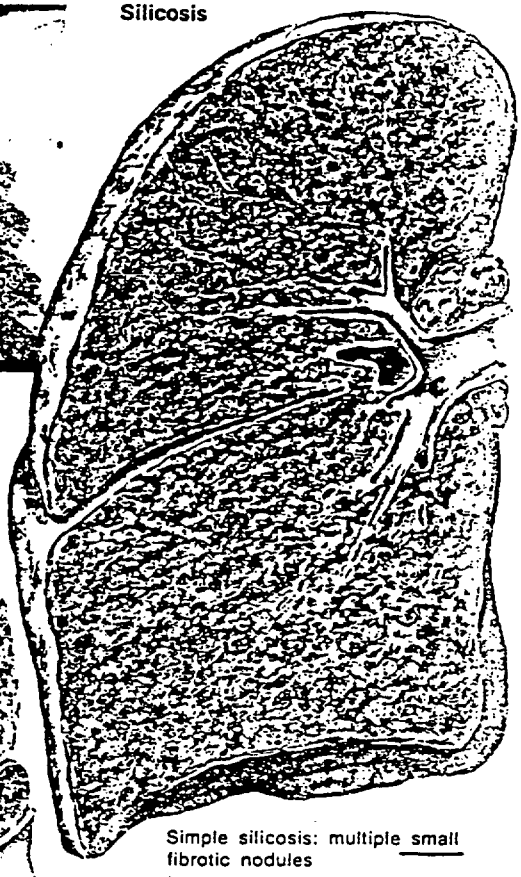


Plate 5

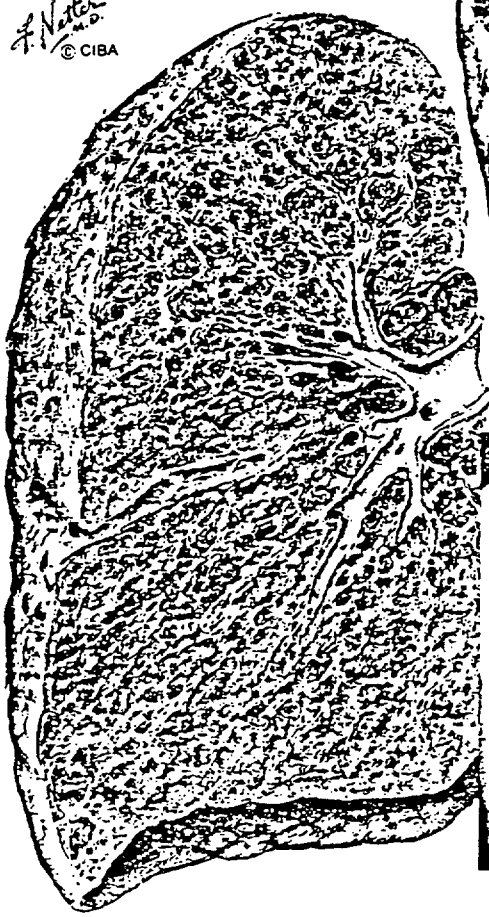
Silicosis



Simple silicosis: nodular fibrosis with calcification of hilar lymph nodes



Simple silicosis: multiple small fibrotic nodules

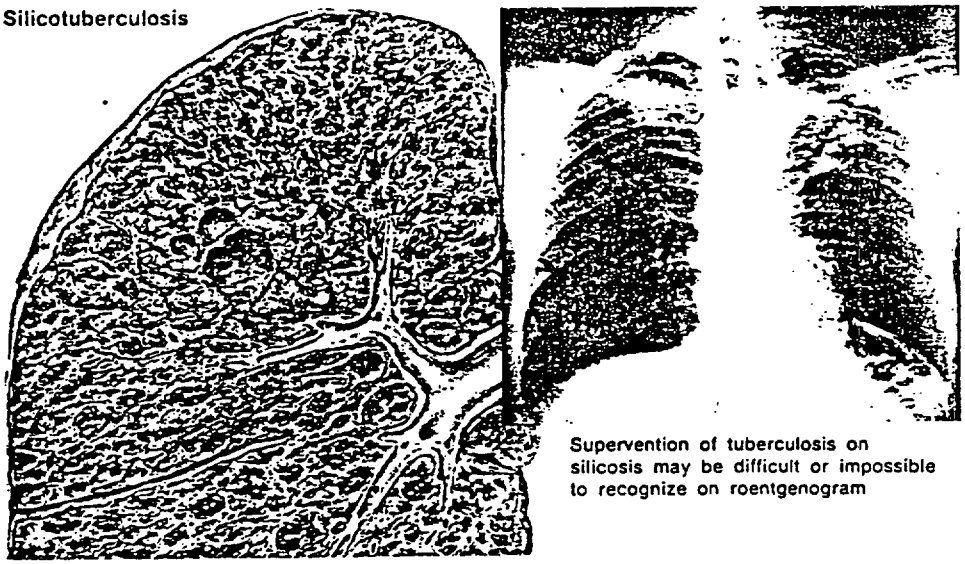


Complicated silicosis: massive fibrosis and conglomerate nodulation. Pleura thickened, nodulated, and adhesive

Complicated silicosis: extensive fibrotic opacification with hyperlucency at bases

Plate 7

Silicotuberculosis

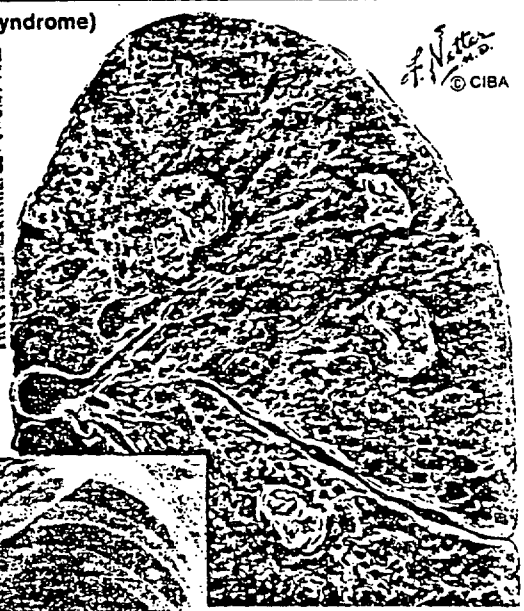


Supervention of tuberculosis on silicosis may be difficult or impossible to recognize on roentgenogram

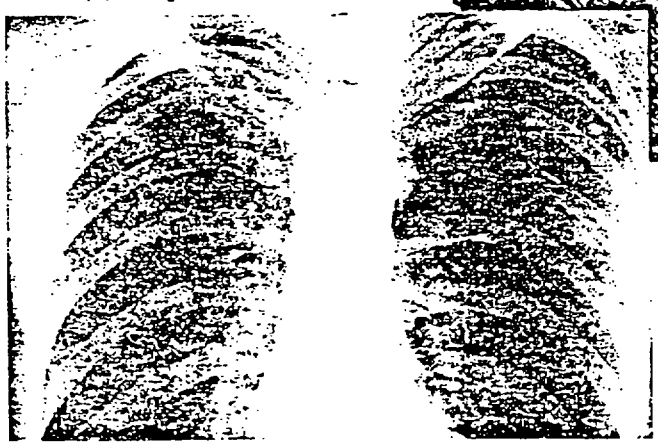
Tuberculosis with cavitation superimposed on silicosis

Rheumatoid Pneumoconiosis (Caplan's Syndrome)

Section through margin of Caplan's nodule: (A) necrotic central area, (B) clefts, (C) zone of fibroblasts and inflammatory cells, (D) collagen



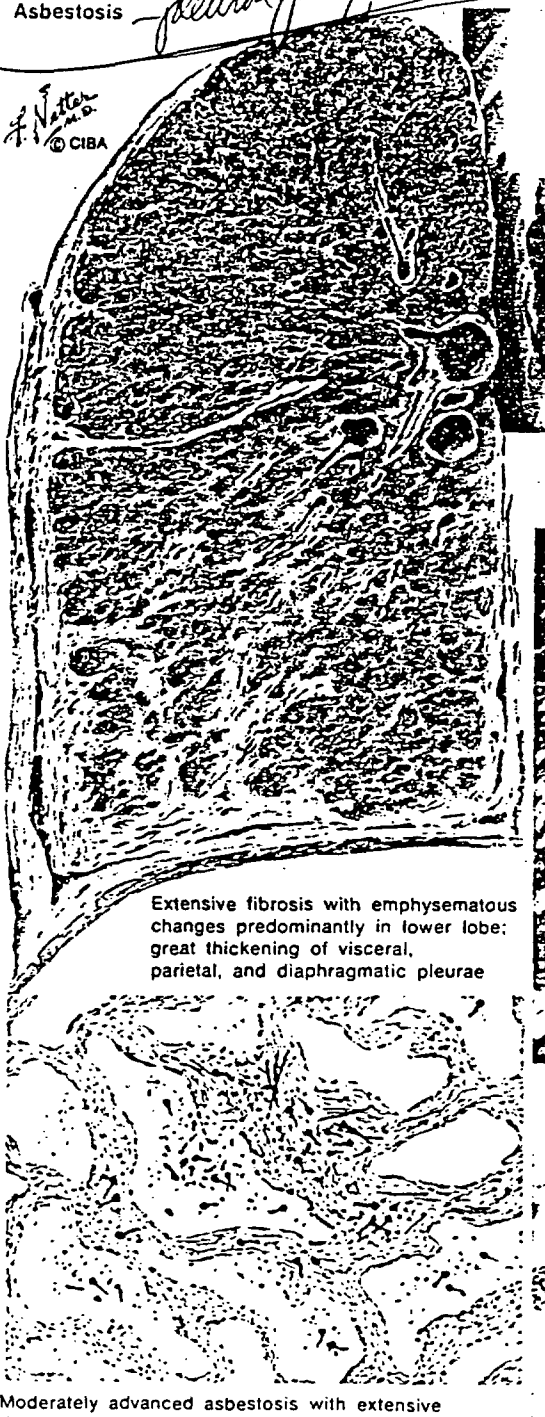
Caplan's nodules of various sizes, silicotic nodules, and deposits of coal dust in lung



Caplan's nodules in both lungs, with some evidence of diffuse fibrosis

Plate 8

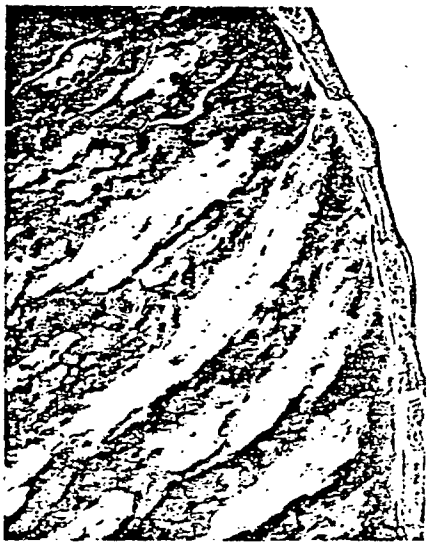
Asbestosis — pleural plaque



Extensive fibrosis with emphysematous changes predominantly in lower lobe; great thickening of visceral, parietal, and diaphragmatic pleurae

Moderately advanced asbestosis with extensive fibrosis and distorted alveoli. Asbestos bodies (some fragmented) and a few asbestos fibers in airspaces and interstitium

Calcified pleural plaques and irregular densities, chiefly in lower lobes, shown on oblique roentgenogram



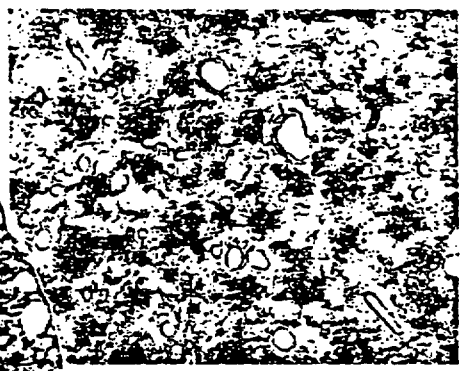
Pleural plaques in pulmonary asbestosis

Asbestos bodies in sputum

Plate 9

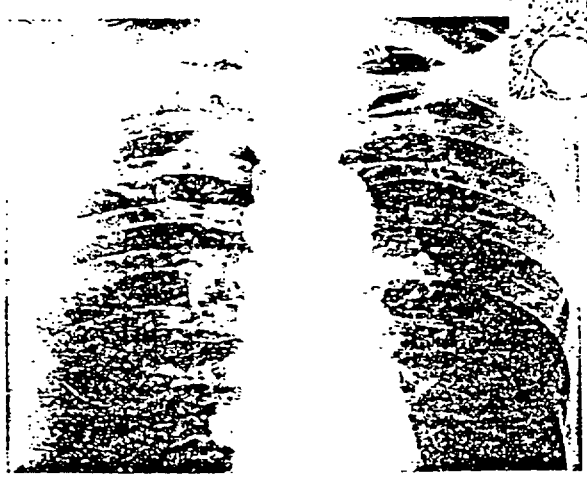
Coal Worker's Pneumoconiosis

Thin section of whole lung showing massive black deposits, smaller nodules, necrotic areas, and emphysematous changes



Slightly magnified detail of lung showing indurated coal macules

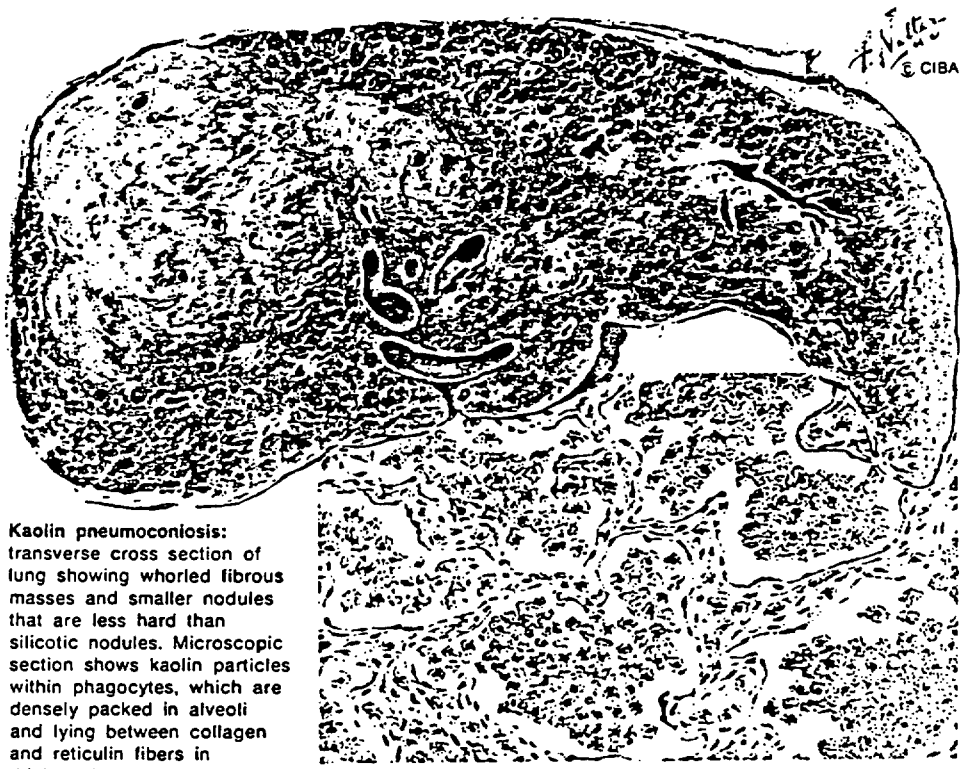
Microscopic section through a coal macule demonstrating large amounts of coal dust, both intracellular and extracellular, with fibrosis near artery



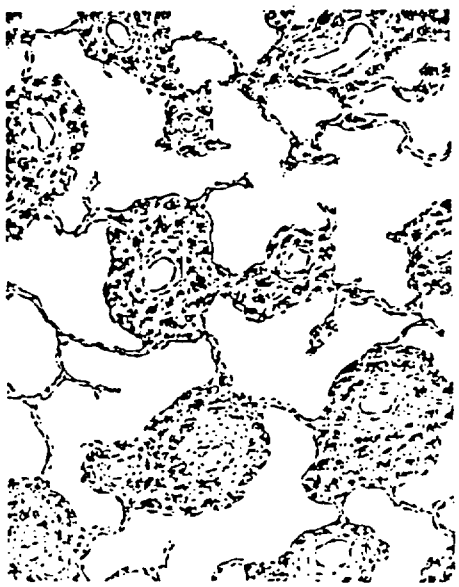
Chest x-ray film of retired coal miner showing massive upper lobe lesions (sometimes called "angel wings") and nodular disease

Plate 10

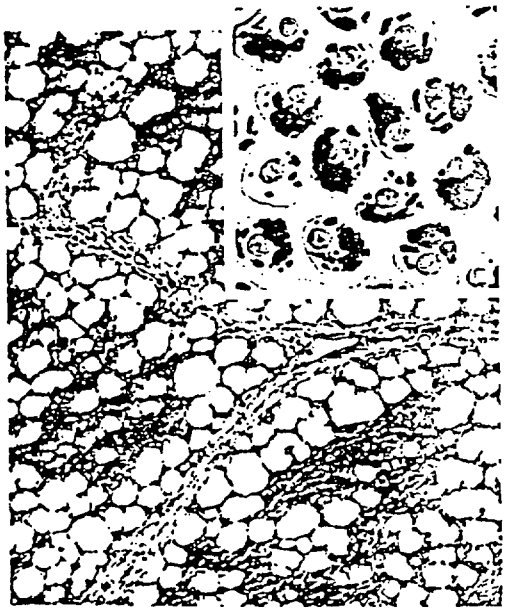
Other Mineral Pneumoconioses



Kaolin pneumoconiosis: transverse cross section of lung showing whorled fibrous masses and smaller nodules that are less hard than silicotic nodules. Microscopic section shows kaolin particles within phagocytes, which are densely packed in alveoli and lying between collagen and reticulin fibers in thickened stroma



Fuller's earth pneumoconiosis: masses of brown pigment within macrophages, chiefly perivascular. Scant tissue reaction

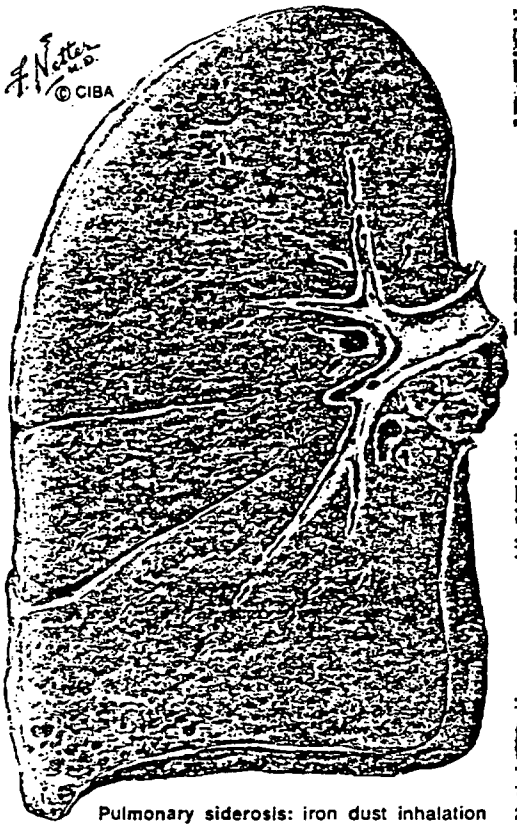


Graphite pneumoconiosis: black deposits and extensive fibrosis. High-power inset shows graphite in alveolar macrophages

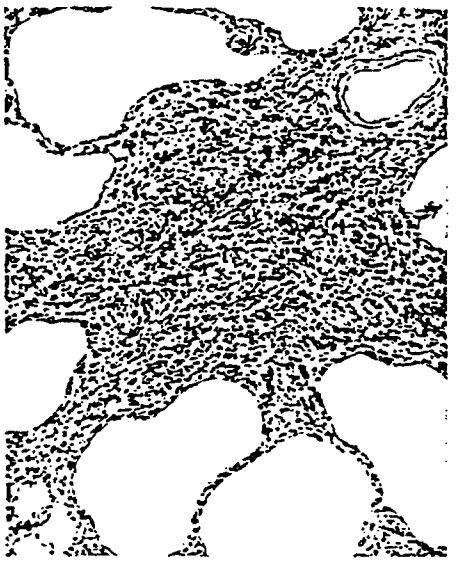
iron oxide — no pulmonary reaction

Plate 11

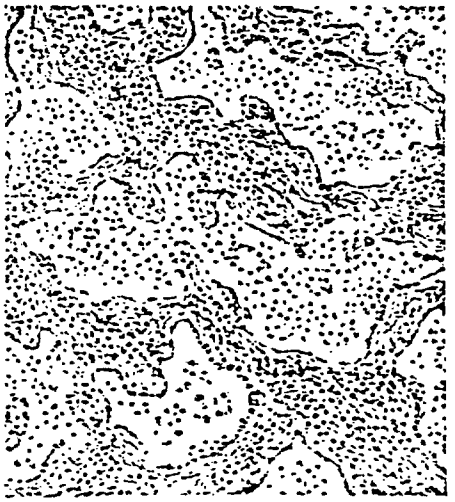
Reactions to Metals and Mixed Dusts



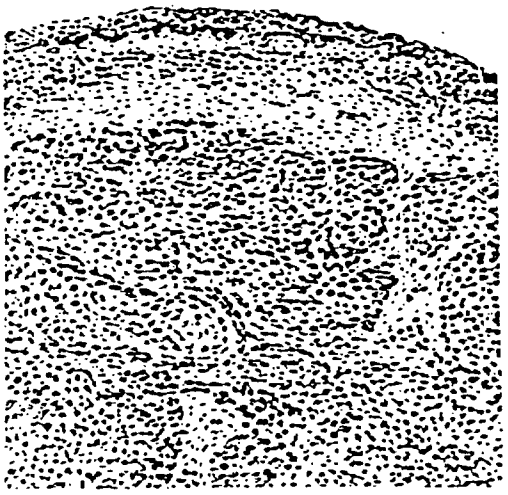
Pulmonary siderosis: iron dust inhalation produces little change in lungs other than brick-red coloration, unless iron is mixed with other dusts, chiefly silica, silicates, and/or carbon. The mild fibrosis, nodulation, and emphysema shown are probably caused by such admixture



Mixed-dust fibrosis: fibrosis surrounding deposits of iron oxide, carbon, and silica. Found in sandblasters, steel dressers, oxyacetylene cutters, and welders having long-term exposure to mixed dusts



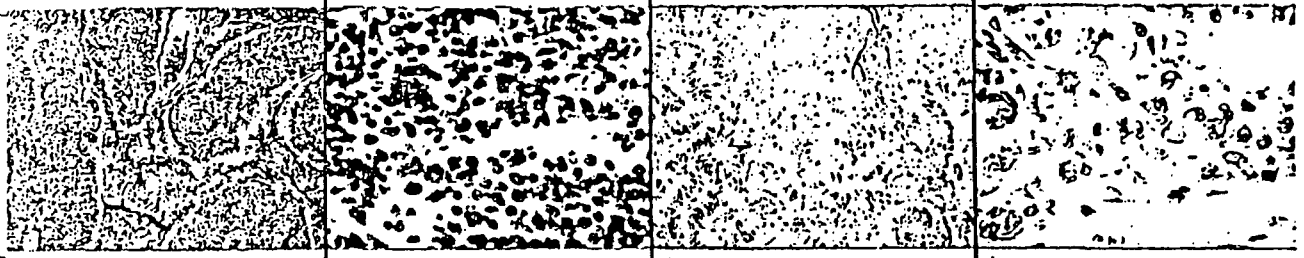
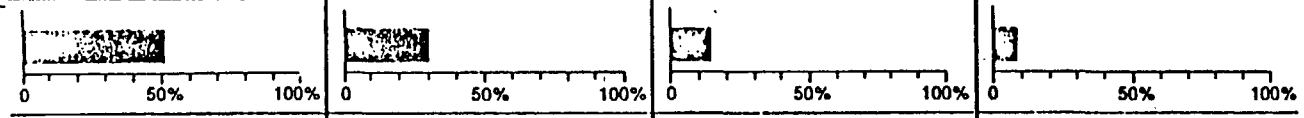
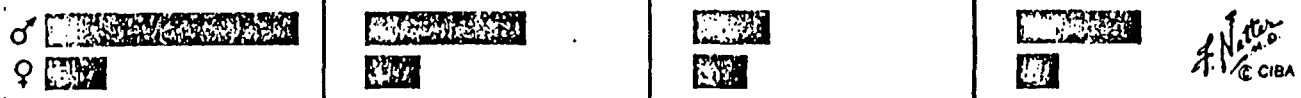
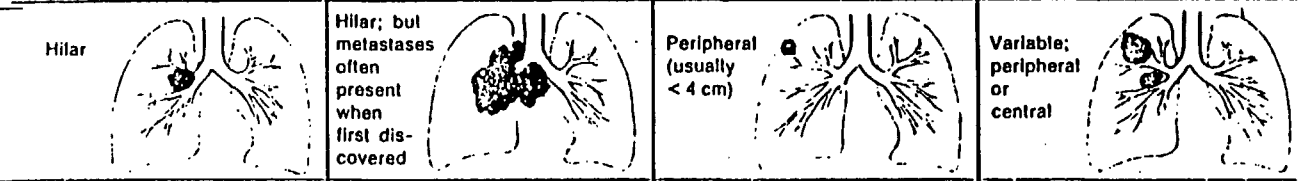
Tungsten inhalation effects: cellular infiltration and increased collagen in lung interstitium. Alveoli show epithelial metaplasia and contain cellular exudate with some multinucleated cells



Nickel inhalation effects: squamous cell carcinoma with overlying metaplastic bronchial mucosa believed attributable to this metal

Classification of Bronchogenic Carcinoma (≈ 95% of All Lung Carcinoma)

as opposed to pulmonary

TYPE	Epidermoid (squamous cell)	Small cell anaplastic (oat cell)	Adenocarcinoma	Large cell anaplastic
HISTOLOGY				
INCIDENCE (% OF ALL LUNG CARCINOMA)	 0 50% 100%	0 50% 100%	0 50% 100%	0 50% 100%
MALE VS. FEMALE	 ♂ ♀			© CIBA
LOCATION TENDENCY	 Hilar	Hilar; but metastases often present when first discovered	Peripheral (usually < 4 cm)	Variable; peripheral or central
SMOKING RELATION	 0 Moderate Great	0 Moderate Great	0 Moderate Great	0 Moderate Great
GROWTH RATE	Relatively slow	Very rapid	Intermediate	Rapid
METASTATIC TENDENCY	Late; then primarily to hilar nodes	Very early; to mediastinum or distally	Intermediate	Early
RESECTABILITY	Fair	0	Poor	Poor

most potent carcinogen known to man

NOTICE OF INTENDED CHANGES
MINERAL DUSTS

Substance	TLV
† Asbestos	
Amosite	0.5 fiber/cc, A1a
Chrysotile	2 fibers/cc, A1a
Crocidolite	0.2 fiber/cc, A1a
Tremolite	0.5 fiber/cc, A1a
Other forms	2 fibers/cc, A1a
Diatomaceous earth, natural	1.5 mg/m³, Respirable dust
Silica, amorphous	5 mg/m³, Total dust (all sampled sizes)
	2 mg/m³, Respirable dust (< 5 μm)
† Talc (fibrous)	0.5 fiber/cc

APPENDIX A
CARCINOGENS

The Committee lists below those substances in industrial use that have proven carcinogenic in man, or have induced cancer in animals under appropriate experimental conditions. Present listing of those substances carcinogenic for man takes three forms: Those for which a TLV has been assigned (1a), those for which environmental conditions have not been sufficiently defined to assign a TLV (1b), and (1c), those whose reassignment of a TLV is awaiting more definitive data, and hence should be treated as a 1b carcinogen.

A1a. *Human Carcinogens*. Substances, or substances associated with industrial processes, recognized to have carcinogenic or cocarcinogenic potential, with an assigned TLV:

	TLV
** Arsenic trioxide production	(As_2O_3, 0.05 mg/m³ as As) (SO_2, C 5.0 ppm)
	(Sb_2O_3, 0.5 mg/m³ (as Sb))
** Asbestos, all forms*	(5 fibers/cc, > 5 μm in length)
bis (Chloromethyl) ether	0.001 ppm
Chromite ore processing (chromate)	0.05 mg/m³ (as Cr)
Nickel sulfide roasting, fume & dust	1.0 mg/m³ (as Ni)
Particulate Polycyclic Aromatic Hydrocarbons (PPAH)	0.2 mg/m³, as benzene solubles
Vinyl Chloride	5 ppm

A1b. *Human Carcinogens*. Substances, or substances associated with industrial processes, recognized to have carcinogenic potential without an assigned TLV:

Chloromethyl methyl ether
4-Aminodiphenyl (p-Xenylamine)
Benzidine production
beta-Naphthylamine
4-Nitrodiphenyl

A1c. *Human Carcinogens*. Substances with recognized carcinogenic potential awaiting reassignment of TLV pending further data acquisition:

Acrylonitrile
1, 2-Dibromoethane (Ethylene dibromide)

For the substances in 1b or 1c, no exposure or contact by any route — respiratory, skin or oral, as detected by the most sensitive methods — shall be permitted.
"No exposure or contact" means hermitizing the process or operation by the best practicable engineering methods. The worker should be properly equipped to insure virtually no contact with the carcinogen.

**See Notice of Intended Changes
†1978 Addition.

*Cigarette smoking can enhance the incidence of respiratory cancers from this and others of these substances or processes.

*From: American Conference of Governmental Industrial Hygienists: P.O. Box 1973, Cincinnati, Ohio

A2. *Industrial Substances Suspect of Carcinogenic Potential for MAN*. Chemical substances or substances associated with industrial processes, which are suspect of inducing cancer, based on either (1) limited epidemiologic evidence, exclusive of clinical reports of single cases, or (2) demonstration of carcinogenesis in one or more animal species by appropriate methods.

3-Amino 1, 2, 4-triazole	
** Antimony trioxide production*	(0.5 mg/m³)
Benzene	10 ppm
Benz(a)pyrene	——
Beryllium	2.0 μg/m³
** Cadmium oxide production	(0.05 mg/m³)
Chloroform	10 ppm
Chromates of lead and zinc (as Cr)	0.05 mg/m³
3, 3'-Dichlorobenzidine	——
Dimethylcarbamyl chloride	——
1, 1-Dimethyl hydrazine	0.5 ppm
Dimethyl sulfate — Skin	0.1 ppm
Epichlorhydrin	5 ppm
Hexachlorobutadiene	——
Hexamethyl phosphoramide — Skin	——
Hydrazine	0.1 ppm
Lead chromate	0.05 mg/m³
4, 4'-Methylene bis (2-chloroaniline) — Skin	0.02 ppm
Monomethyl hydrazine	0.2 ppm
C 2-Nitropropane	25 ppm
Nitrosamines	——
Phenyl-beta-naphthylamine	——
Propane sultone	——
beta-Propiolactone	——
Vinyl cyclohexene dioxide	10 ppm
Zinc chromate (as Cr)	0.05 mg/m³

For the above, worker exposure by all routes should be carefully controlled to levels consistent with the animal and human experience data (see Documentation), including those substances with a listed TLV.

*Cigarette smoking can enhance the incidence of respiratory cancers from this or others of these substances or processes.

A3. *Guidelines for the Classification of Experimental ANIMAL Carcinogens*. The following guidelines are offered in the present state of knowledge as an aid in classifying substances in the occupational environment found to be carcinogenic in experimental animals. A need was felt by the Threshold Limits Committee for such a classification in order to take the first step in developing an appropriate TLV for occupational exposure.

Determination of Approximate Threshold of Response Requirement. In order to determine in which category to classify an experimental carcinogen for the purpose of assigning an industrial air limit (TLV), an approximate threshold of neoplastic response must be determined. Because of practical experimental difficulties, a precisely defined threshold cannot be attained. For the purposes of standard-setting, this is of little moment, as an appropriate risk, or safety, factor can be applied to the approximate threshold, the magnitude of which is dependent on the degree of potency of the carcinogenic response.

To obtain the best 'practical' threshold of neoplastic response, dosage decrements should be less than logarithmic. This becomes particularly important at levels greater than 10 ppm (or corresponding mg/m³). Accordingly, after a range-finding determination has been made by logarithmic decreases, two additional dosage levels are required within the levels of "effect" and "no effect" to approximate the true threshold of neoplastic response.

The second step should attempt to establish a metabolic relationship between animal and man for the particular substance found carcinogenic in animals. If the metabolic pathways are found comparable, the substance should be classed highly suspect as a carcinogen for man. If no such relation is found, the substance should remain listed as an experimental animal carcinogen until evidence to the contrary is found.

Proposed Classification of Experimental Animal Carcinogens. Substances occurring in the occupational environment found carcinogenic for animals

may be grouped into three classes, those of high, intermediate and low potency. In evaluating the incidence of animal cancers, significant incidence of cancer is defined as a neoplastic response which represents, in the judgment of the Committee, a significant excess of cancers above that occurring in negative controls.

EXCEPTIONS: No substance is to be considered an occupational carcinogen of any practical significance which reacts by the respiratory route at or above 1000 mg/m³ for the mouse, 2000 mg/m³ for the rat; by the dermal route, at or above 1500 mg/kg for the mouse, 3000 mg/kg for the rat; by the gastrointestinal route at or above 500 mg/kg/d for a lifetime, equivalent to about 100 g T.D. for the rat, 10g T.D. for the mouse.

These dosage limitations exclude such substances as dioxane and trichlorethylene from consideration as carcinogens.

Examples: Dioxane — rats, hepatocellular and nasal tumors from 1015 mg/kg/d, oral

Trichloroethylene — female mice, tumors (30/98 @ 900 mg/kg/d), oral

A3a. *INDUSTRIAL SUBSTANCES OF HIGH CARCINOGENIC POTENCY IN EXPERIMENTAL ANIMALS*

1. A substance to qualify as a carcinogen of high potency must fulfill one of the three following conditions in two animal species:

1a. *Respiratory*. Elicit cancer from (1) dosages below 1 mg/m³ (or equivalent ppm) via the respiratory tract in 6–7-hour daily repeated inhalation exposures throughout lifetime; or (2) from a single intratracheally administered dose not exceeding 1 mg of particulate, or liquid, per 100 ml or less of animal minute respiratory volume;

Examples: bis-Chloromethyl ether, malignant tumors, rats, @ 0.47 mg/m³ (0.1 ppm) in 2 years;

Hexamethyl phosphoramide, nasal squamous cell carcinoma, rats, @ 0.05 ppm, in 13 months

OR

1b. *Dermal*. Elicit cancer within 20 weeks by skin-painting, twice weekly at 2 mg/kg body weight or less per application for a total dose equal to or less than 1.5 mg, in a biologically inert vehicle;

Examples: 7, 12-Dimethylbenz(a)anthracene — skin tumors @ 0.12-0.8 mg T.D. in four weeks

Benz(a)pyrene, mice 12 μg, 3X/wk for 18 mos. T.D. 2.6 mg, 90.9% skin tumors

OR

1c. *Gastrointestinal*. Elicit cancer by daily intake via the gastrointestinal tract, within six months, with a six-month holding period, at a dosage below 1 mg/kg body weight per day; total dose, rat, ≤ 50 mg; mouse, ≤ 3.5 mg;

Examples: 7, 12-Dimethylbenz(a)anthracene — mammary tumors from 10 mg 1X

3-Methylcholanthrene — Tumors @ 3 sites from 8 mg in 89 weeks

Benz(a)pyrene, mice, 3.9% leukemias, from 30 mg T.D. 198 days

2. Elicit cancer by all three routes in at least two animal species at dose levels prescribed for high or intermediate potency.

A3b. *INDUSTRIAL SUBSTANCES OF INTERMEDIATE CARCINOGENIC POTENCY IN EXPERIMENTAL ANIMALS*

To qualify as a carcinogen of intermediate potency, a substance should elicit cancer in two animal spe-

cies at dosages intermediate between those described in A3a and A3c by two routes of administration.

Example: Carbamic acid ethyl ester
Dermal, mammary tumors, mice, 100%, 63 weeks, 500–1400 mg T.D.
Gastrointestinal, various type tumors, mice 42 weeks, 320 mg T.D.

Gastrointestinal, various type tumors, rats, 60 weeks, 110–930 mg T.D.

A3c. *INDUSTRIAL SUBSTANCES OF LOW CARCINOGENIC POTENCY IN EXPERIMENTAL ANIMALS*

To qualify as a carcinogen of low potency, a substance should elicit cancer in one animal species by any *one* of three routes of administration at the following prescribed dosages and conditions:

1a. *Respiratory*. Elicit cancer from (1) dosages greater than 10 mg/m³ (or equivalent ppm) via the respiratory tract in 6- 7-hour, daily repeated inhalation exposures, for 12 months' exposure and 12 months' observation period; or (2) from intratracheally administered dosages totaling more than 10 mg of particulate or liquid per 100 ml or more of animal minute respiratory volume;

Examples: Beryl (beryllium aluminum silicate) malig. lung tumors, rats, @ 15 mg/m³ @ 17 months

Benzidine, var. tumors, rats, 10–20 mg/m³ @ > 13 mos.

OR

1b. *Dermal*. Elicit cancer by skin-painting of mice in twice weekly dosages of > 10 mg/kg body weight in a biologically inert vehicle for at least 75 weeks, i.e., ≥ 1.5g T.D.

Examples: Shale tar, mouse, 0.1 ml × 50 — g T.D. 59/60 skin tumors

Arsenic trioxide, man, dose unknown, but estimated to be high

1c. *Gastrointestinal*. Elicit cancer from daily oral

dosages of 50 mg/kg/day or greater during the lifetime of the animal.

APPENDIX B
SUBSTANCES OF VARIABLE COMPOSITION

B1 *Polytetrafluoroethylene* decomposition products*. Thermal decomposition of the fluorocarbon chain in air leads to the formation of oxidized products containing carbon, fluorine and oxygen. Because these products decompose in part by hydrolysis in alkaline solution, they can be quantitatively determined in air as fluoride to provide an index of exposure. No TLV is recommended pending determination of the toxicity of the products, but air concentrations should be minimal.

B2 *Gasoline*. The composition of gasoline varies greatly and thus a single TLV for all types of these materials is no longer applicable. In general, the aromatic hydrocarbon content will determine what TLV applies. Consequently the content of benzene, other aromatics and additives should be determined to arrive at the appropriate TLV (Elkins, et al. A.I.H.A.J. *24*:99, 1963); Runion, ibid. *36*, 338, 1975).

B3 *Welding Fumes — Total Particulate (NOC)***
TLV, 5 *mg/m³*

Welding fumes cannot be classified simply. The composition and quantity of both are dependent on the alloy being welded and the process and electrodes used. Reliable analysis of fumes cannot be made without considering the nature of the welding process and system being examined; reactive metals and alloys such as aluminum and titanium are arc-welded in a protective, inert atmosphere such as argon. These arcs create relatively little fume, but an intense radiation which can produce ozone. Similar processes are used to arc-weld steels, also creating a relatively low level of fumes. Ferrous alloys also are arc-welded in oxidizing environments which generate considerable fume, and can produce carbon monoxide instead of ozone. Such fumes generally are composed of discreet particles of amorphous slags con-

*Trade Names: Algoflon, Fluon, Halon, Teflon, Tetran.
**Not otherwise classified (NOC).

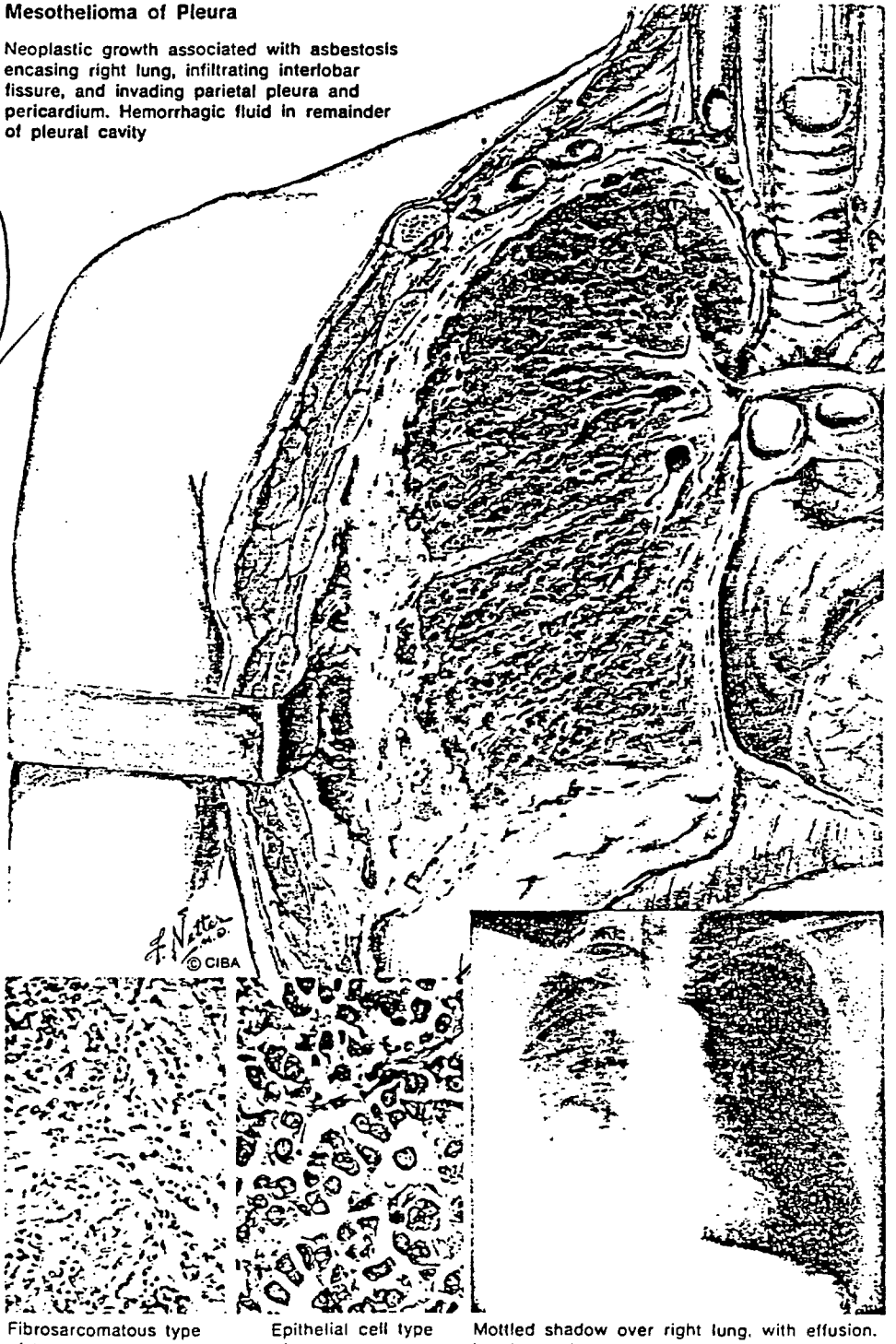
3. MESOTHELIOMA

Plate 14

Mesothelioma of Pleura

Neoplastic growth associated with asbestosis encasing right lung, infiltrating interlobar fissure, and invading parietal pleura and pericardium. Hemorrhagic fluid in remainder of pleural cavity

induced by asbestos



Fibrosarcomatous type of tumor

Epithelial cell type of tumor

Mottled shadow over right lung, with effusion. In advanced cases, lung may be totally obscured

Standards, Definitions, and Promulgating Agencies for Airborne Contaminant Standards

Standard	Responsible Agency	Definition
Threshold Limit Value (TLV)- Time-Weighted Average (TWA)	American Conference of Governmental Industrial Hygienists	"The time-weighted average concentration for a normal 8-hour workday or 40-hour workweek, to which nearly all workers may be repeatedly exposed, day after day, without adverse effect." ** (2)
Threshold Limit Value-Ceiling (TLV-C)	American Conference of Governmental Industrial Hygienists	"The concentration that should not be exceeded even instantaneously." (2)
Short-Term Exposure Limit (STEL)	American Conference of Governmental Industrial Hygienists	"The maximal concentration to which workers can be exposed for a period of up to 15 minutes continuously without suffering from 1) intolerable irritation, 2) chronic or irreversible tissue change, or 3) narcosis...provided that no more than four excursions per day are permitted...The STEL should be considered a maximal allowable concentration, or absolute ceiling, not to be exceeded..." (2)
Permissible Exposure Limit (PEL)	Occupational Safety and Health Administration 1968 TLV's ACGIH were adopted by OSHA	Set in accordance with Sec 6(b)5 of Public Law 91-596 "... standard which most adequately assures to the extent feasible, on the basis of the best available evidence, that no employee will suffer material impairment of health or functional capacity, even if such employee has regular exposure to the hazard dealt with by such standard for the period of his working life." (6)
Emergency Exposure Limit (EEL)	Committee on Toxicology, National Academy of Sciences	"The EEL for short-term exposure to an airborne contaminant is a concentration which, when inhaled for a specified single, brief period, rare in the lifetime of an individual, is believed not to result in a period of disability or interference with the performance of his assigned task." (7)
Air Quality Standard (AQS)	Environmental Protection Agency	"They prescribe pollutant exposures or levels of effect that a political jurisdiction determines should not be exceeded in a specific geographic area..." (8)

** The 1968 TLVs (as 8-hour TWA) have been designated as consensus standards by OSHA until a PEL is established for any given compound.

From: A.I.H.A. Journal 40, 207-229, 1979.

File: Indoor Air Quality

75

TLVs®
Threshold Limit Values
for
Chemical
Substances in
Workroom Air
Adopted by
ACGIH
for 1978

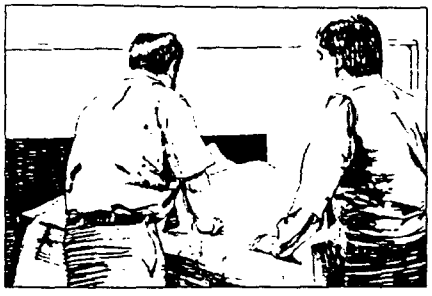
PRICE EACH

1–49	$1.50
50–199	1.25
200–999	1.10
1000–4999	.75
5000 or more	.65

Documentation of the Threshold Limit Values for Substances in Workroom Air.© A separate companion piece to the Chemical TLVs is issued by ACGIH under this title. This publication gives the pertinent scientific information and data with reference to literature sources that were used to base each limit. Each documentation also contains a statement defining the type of response against which the limit is safeguarding the worker. For a better understanding of the TLVs it is essential that the Documentation be consulted when the TLVs are being used.

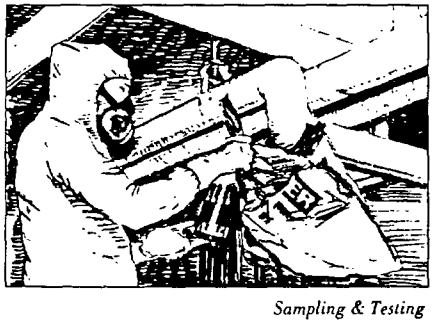
Information concerning the availability of copies of the Documentation of the Threshold Limit Values for Substances in Workroom Air should be directed to the Executive Secretary, ACGIH (third edition, fourth printing, 1978, $20.00).

Asbestos Management

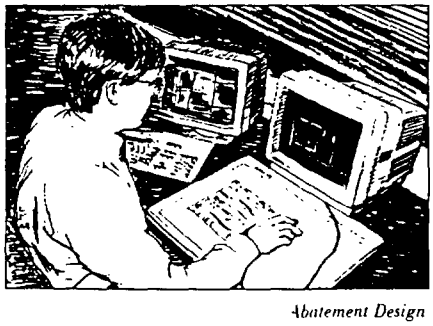


Plan Review

Asbestos Surveys



Sampling & Testing



Abatement Design

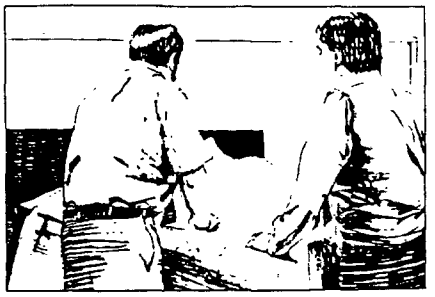
A common material used in many commercial, residential, institutional and industrial facilities built before the late 1970s, asbestos is often found in the form of fireproofing, HVAC insulation, decorative plaster, pipe/boiler insulation, ceiling and floor tiles, and various wallboards. Asbestos has been determined to be a potential health hazard, and many states now have regulations restricting asbestos use and requiring inspections of all structures that are being renovated or demolished to determine the presence of asbestos and ensure that adequate abatement measures are taken. Many government agencies are now completing surveys of publicly owned buildings; and most banks, financial and investment institutions, and insurance companies require similar inspections prior to property transactions.

As a service to our clients, Dewberry & Davis has adopted a technically sound, rational engineering approach to asbestos problems. While the presence of asbestos is cause for reasoned concern, it is not generally cause for panic. In many cases, it is but another technical issue to be addressed and managed in the engineering design, renovation, or operation of a building. Our building systems engineering expertise; appreciation of the complex dynamics and economics of building development, ownership, and management; and years of experience in asbestos management services enable us to provide comprehensive, cost-effective solutions to our clients' needs in this critical area.

Our services include:

- *Plan and document review to determine the probable locations and quantities of asbestos that may be present*
- *Inspections and surveys to verify existing conditions*
- *Sampling and testing programs to define the type, condition, and quantity of asbestos material*
- *Preparation of asbestos management plans, abatement strategies, and abatement cost estimates based on site characteristics and testing results*
- *Design of abatement plans and specifications to remove, enclose, or encapsulate asbestos to reduce potential hazards*
- *Abatement contract monitoring and construction management*

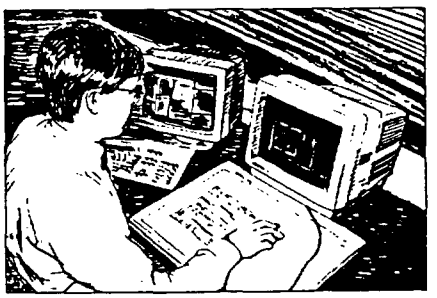
Hazardous Waste Management



Site History Review

Sample Collection

Waste Characterization



Remediation Design

Public concern about environmental damage caused by hazardous wastes continues to grow. Many wastes, including solvents, heavy metals, asbestos, industrial chemicals, radioactive materials, pesticides, herbicides, and waste oil, are commonplace; yet, disposal and clean-up can be complicated and pose a significant operating, economic, and liability concern to facility owners and managers. In addition, the number and complexity of environmental laws facing developers, builders, and facility owners and operators are increasing, as is public awareness of potential environmental problems and demands for proper handling and disposal.

Dewberry & Davis has a long history of responding professionally to the environmental and industrial waste treatment concerns of our clients. Our experience in site development engineering, industrial waste treatment management, and hazard remediation; our EPA-certified laboratory operations; and traditional skills in mapping and ground control provide a unique capability to assist clients in analyzing hazardous waste problems and developing controlled, safe, and economical management programs.

Our services include:

- *Record reviews to determine probable locations and quantities of wastes*
- *Sampling and testing procedures to identify, map, and measure wastes*
- *Waste management plans, designs, and estimates*
- *Contract plans and specifications for clean-up or remediation action*
- *Clean-up or remediation contract monitoring and management*

Conrad A. Carter, Jr., P.E.
Manager - Environmental Protection

ALCOA

Aluminum Company of America
Badin, North Carolina 28009

(704) 422-3621

Bob,
Copy of slides on ODNA.
Thanks.

794960 0161

HIGH RISK OCCUPATIONAL DISEASE NOTIFICATION AND PREVENTION ACT OF 1987 (H.R. 162 & S.79)

I. REQUIREMENTS

II. IMPACT ON ALCOA

III. COSTS TO ALCOA

IV. POSITION ON BILL / STATUS

I. REQUIREMENTS - Identification, Notification, and Prevention of Occupational Disease

A. Identification

1. Risk Chemicals
   a. Occupational Health Hazard
   b. List Undefined
   c. Exposure, Duration
   * d. OSHA Substances (e.g., Carcinogens)

2. Risk Assessment Board (9)
   a. HHS (NIOSH)
   b. 4 Government; 4 non-Government
   c. Political

3. Rule-making Process
   a. Public Comment
   b. Hearing
   c. Variance Procedures

RISK CHEMICALS

A. Dioxin, AIDS - Legislated

B. Anticipated Risk Chemicals (36 substances)

Hazardous Substance	Workers Exposed
Asbestos	4,000,000
Coal tar pitch volatiles	78,764
4-nitrobiphenyl	NA
Alpha-naphthylamine	2,132
4,4-methylenebis	2,094
Methyl chloromethyl ether	NA
3,3-dichlorobenzidine	879
Bischloromethyl ether	11,400
Beta-naphthylamine	5,816
Benzidine	1,650
4-aminodiphenyl	NA
Ethyleneimine	1,712
Beta-propiolactone	38
2-acetylamino-fluorene	896
4-bimethyaminoazo-benzene	4,453
N-nitrosodime-thylamine	7,815
Inorganic arsenic	660,000
Lead	800,000
Coke oven emissions	59,000
Cotton dust	559,700
1,2-dibromo-3-chloro-propane	3,231
Acrylonitrile	55,698
Ethylene oxide	107,450
Vinyl chloride	29,836
Carbon monoxide	1,997,559
Benzene	2,000,000
Beryllium	30,000
Cadmium	1,500,000
Chloroprene	43,712
Talc	527,523
Fibrous glass	200,000
Methyl butyl ketone	220,000
Polychlorinated biphenyls	12,000
Radon daughters	23,000
Silica, silica flour	4,993,655
Formaldehyde	1,600,000
Total Workers Exposed	19,537,013

* R.R. Nathan, Associates, Inc.

I. REQUIREMENTS (cont)

B. Notification

1. Conducted by NIOSH

2. Current Employees at "Risk"

3. Retroactive Employees at Risk (30 years)

4. Contents of Notification

a. Hazard

b. Disease

c. Latency

d. Counseling on Medical Surveillance

e. Plant Postings

I. REQUIREMENTS (cont)

C. Prevention

1. Medical Monitoring and Counseling
   a. Current Employees - Employer Cost
   b. Retroactive - Employee Cost

2. Medical Transfer / Removal Protection
   a. Same Salary
   b. 1-Year Severance Pay

3. Occupational Health Centers (10 --> 50)
   a. Training, Research
   b. Medical Monitoring, if needed

II. IMPACT ON ALCOA

A. Scope Unknown

1. No Defined List
2. Occupational Health Hazard
3. Political

B. Projected Risks (1st 5 Years)

1. Asbestos
2. Coal Tar Pitch Volatiles
3. Silica (Crystalline)
4. Man-made Mineral Fibers
5. PCB's

III. COSTS TO ALCOA

A. Costs Unknown

B. R. R. Nathan Associates

1. Employer's Total Cost -- ≈ $6 billion per year
   a. 475,000 workers identified
   b. 80% notified
   c. 64% responded
   d. 3% job removal ($25,000 per employee)
   e. Medical surveillance ($250 per person)
   f. 25% file liability ($95,000 per claim)

2. Cost per Notified Employee -- ≈ $12,500
   a. Direct (2% -- 10%)
      1. Medical monitoring
      2. Medical removal
   b. Indirect (90% -- 98%)
      1. Litigation expenses
      2. Compensation costs

III. Costs to Alcoa (Cont)

C. Estimated Alcoa Costs

1. Current Employees -- $54 million
   a. 5 Substances covered
   b. 20% Current employees notified
      1. HMS exposures
      2. One or more exposures

2. Additional Costs
   a. Retroactive employees (1:1)
   b. Job rotation

IV. POSITION ON BILL

A. Support Medical Concepts

1. Causal Relationships
2. Prudent Medical Surveillance

B. Oppose Implementation

* 1. Unmeasurable Liability
2. Medical Removal / Job Retention Provisions

C. Status

1. Filibustered successfully
2. Return next session

5/12

1) Please make a copy of this overheads.
Send a copy to Conrad Carter - IH at Berlin Wireless

2) File Hi Risk Disease Notification

Art