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Research and Development

# Estimation of Risk from Carcinogens in Drinking Water

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# Estimation of Risk from Carcinogens in Drinking Water

by

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## ABSTRACT

This report gives the results of a study aimed at developing a means for estimating cancer mortality as a function of carcinogen concentration in drinking water. Cancer risk data for cigarette smokers was treated by the method of standard additions to provide an estimate of ambient carcinogen levels in drinking water. A similar treatment was carried out on lung cancer risk data to give an estimate of carcinogen levels in ambient air.

This report was prepared for the Industrial Environmental Research Laboratory-RTP, Environmental Protection Agency, to present results of the work carried out by RTI under Contract No. 68-02-2612 (Task 16). This work was performed in the Chemistry and Life Sciences Division of the Research Triangle Institute.

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## TABLE OF SYMBOLS AND DEFINITIONS

$A, B, D$ = Correlation constants,

$L_{resp}$ = Respiratory carcinogen intake (μg/yr or ng/day),

$M_{lc}$ = Annual lung cancer mortality/100,000,

$M_{os}$ = Annual cancer mortality/100,000 at all sites excluding lung and bronchus,

$N$ = Number of cigarettes smoked/day,

$r^2$ = Correlation coefficient,

$S_{oral}$ = Systemic carcinogen uptake from the gastrointestinal tract from food and drinking water (ng/day),

$S_{dw}$ = Systemic carcinogen uptake from drinking water (ng/day),

$S_{food}$ = Systemic carcinogen uptake from food (ng/day),

$S_{resp}$ = Systemic carcinogen uptake from respiratory tract (ng/day),

$S_{total}$ = Systemic carcinogen uptake from both the gastrointestinal and respiratory tract, $S_{oral} + S_{resp}$ (ng/day),

$X_{aa}$ = Carcinogen concentration in ambient air (ng/m$^3$),

$X_{dw}$ = Carcinogen concentration in drinking water (ng/l),

$X_e$ = Estimated safe drinking water concentration (ng/l),

$X_{food}$ = Carcinogen concentration in food (ng/kg).

## INTRODUCTION

The purpose of this report is two-fold. (1) Lung cancer risk: Carcinogen exposure data will be evaluated using the method of standard additions to estimate background ambient air carcinogen levels. (2) A means of estimating cancer mortality risk as a function of carcinogen concentration in drinking water will be developed using the same smoker mortality data that served as the basis for the ambient air treatment.

The EPA has set several maximum concentration exposure levels for environmental pollutants in both air and water. However, there are many known toxic materials for which no safe concentration levels have been established. The main objective of an earlier report was to derive pollutant hazard criteria for this group of compounds in order that safe, permissible concentrations in the environment might be estimated.[1]

A means for estimating lung cancer mortality risk as a function of carcinogen concentration in ambient air was developed and presented in Section V of that report.[1] Since lung cancer mortality data for smokers was the best human dose response data available, this information was used to correlate carcinogen exposure and lung cancer death rates.

## SUMMARY AND CONCLUSIONS

A previous report by Handy and Schindler[1] analyzed published lung cancer mortality data for smokers (Kahn Study)[3] and derived an estimate for a carcinogen level in ambient air. The result of this treatment gave a carcinogen concentration to which the nonsmokers of the study group were exposed prior to 1962 (the Kahn study covered cancer deaths from 1954 to 1962). A value of 4.9 ng carcinogens/$m^3$ was obtained using a methodology that did not take into account the ambient air contribution to the smokers' respiratory carcinogen intake.

This report evaluates the same smoker-lung cancer risk data using a treatment analogous to the standard additions method used routinely in the field of analytical chemistry. The result obtained by this approach gives an estimate of 22.9 ng carcinogens/$m^3$, higher than the previous approximation by a factor of approximately five.

From this treatment, it is concluded that the concentration figure of 22.9 ng/$m^3$ more closely approximates the actual carcinogen concentration in ambient air prior to 1962 and that amounts in excess of this level will result in an increased lung cancer risk relative to the pre-1962 base period (see Figure 4). The lung cancer mortality may be estimated by the following equation.

$$M_{1c} = 362.5 \ln \left(\frac{X_{aa}(\text{ng/m}^3)}{350.5} + 1\right);$$

when $X_{aa} = 22.9$, $M_{1c} = 22.9$

A similar treatment of total cancer mortality, excluding lung and bronchus, gave a nonsmoker systemic carcinogen intake of 92.7 ng/day from all sources (air, food, and drinking water). Analyzing this "other site" mortality data within the limitations delineated in the Caveat

Section afforded an expression relating "other site" mortality (total cancer risk excluding lung and bronchus) and carcinogen concentration in drinking water. Since this cancer death rate is a function of both oral and respiratory carcinogen intake, the effect of drinking water carcinogens on cancer risk is depicted graphically (Figure 6) at different ambient air concentrations.

The estimated ambient air concentration of 22.9 ng/$m^3$ corresponds to a systemic uptake of 116 ng/day through the respiratory tract. Since this checks closely with the 92.7 ng/day figure for total systemic uptake from all sources, it must be concluded that the average carcinogen intake through the gastrointestinal tract was negligible prior to 1962.

It is also apparent that any combination of carcinogens in ambient air, food, and water which results in a total systemic carcinogen uptake in excess of 92.7 ng/day will produce an elevated other site mortality relative to the pre-1962 base period. This daily systemic carcinogen uptake corresponds to a maximum ambient air concentration of 18.3 ng/$m^3$ (no contribution from food and drinking water) or a maximum drinking water concentration of 30.9 ng/l (no contribution from ambient air). The total systemic carcinogen uptake ($S_{total}$) is determined by the following equations.

$$S_{total\ (ng/day)} = S_{resp} + S_{oral},$$

where $S_{resp\ (ng/day)} = 5.07\ X_{aa}\ (ng/m^3)$

and $S_{oral\ (ng/day)} = 3X_{dw}$.

The total other site cancer mortality may then be estimated by the following equation.

$$M_{os} = 43.3 \ln \left(\frac{S_{total}}{0.34} + 1\right).$$

Use of Figure 6 allows the estimation of other site cancer mortality at different carcinogen levels in ambient air and drinking water. For example, an increase in the drinking water concentration from 4 to 20 ng/ℓ at a constant carcinogen air concentration of 10 ng/$m^3$ results in an other site cancer mortality increase from 226 to 251/100,000 (11% increase)

Similarly, increasing the air concentration from 10 ng to 25 ng/m$^3$ at a constant drinking water concentration of 4 ng/ℓ gives an other site cancer mortality increase from 226 to 360 (15% increase). Note that examples reflect an increase cancer risk relative to the pre-1962 base period.

# CAVEATS

The reader should be aware of the following limitations of the methodology used in this report.

a) Ambient Air-

- The term carcinogen refers only to agents responsible for the initiation and development of lung and bronchial cancers.
- It is assumed that a major contributing factor in the incidence of lung cancer death of cigarette smokers and nonsmokers alike is the inhalation of carcinogenic compounds.
- The exposure level of eight (8) hydrocarbon carcinogens, identified and quantitated in cigarette smoke, is assumed to be a major contributing factor in lung cancer incidence and a valid measure of lung cancer mortality of smokers and nonsmokers
- The 8-component hydrocarbon mixture, present in cigarette smoke, possesses a total carcinogenic potency equal to a mixture of the same materials in ambient air.
- The presence of other carcinogenic compounds in ambient air is assumed. The quantity (concentration) of these compounds in ambient air may be expressed in terms of an equipotent amount of the eight cigarette carcinogen mixture.
- A number of lung cancer deaths are due to carcinogens in the ambient air and this is reflected in the lung cancer mortality of nonsmokers.
- Any mathematical relationship ($r^2 > .95$) between carcinogen intake by smokers and the lung cancer death rate corresponding to these smokers may be extrapolated to yield valid mortality data for low carcinogen intake values.
- Ambient air concentrations have been calculated assuming a total breathing volume of 3700 $m^3$/year for the average adult.

b) Drinking Water

- The term carcinogen refers only to agents responsible for the initiation and development of cancers at all sites, excluding lung and bronchial tissue.
- The 8-component hydrocarbon mixture, present in cigarette smoke, possesses a total carcinogenic potency equal to a mixture of the same materials in drinking water.
- The presence of other carcinogenic compounds in drinking water and food is assumed. The quantity (concentration) of these compounds in drinking water and food may be expressed in terms of an equipotent amount of the eight cigarette carcinogen mixture.
- A number of cancer deaths are due to carcinogens in drinking water and this is reflected in the cancer mortality of non-smokers.
- Carcinogens ingested orally in the form of food and drinking water exert a negligible effect on the risk of lung cancer, but a major contributing factor in cancers at all other sites.
- Fifty percent of inhaled carcinogens are released from the respiratory tract and into the systemic circulation.
- Food and drinking water contain the same weight percent concentration of carcinogens.
- It is assumed that the average adult consumes two liters of drinking water and one kilogram of food per day.
- Any mathematical relationship ($r^2$>.95) between systemic carcinogen body burden and the cancer mortality rate at all sites, excluding lung, may be extrapolated to yield valid mortality data for low carcinogen burdens.

# METHODOLOGY

## Ambient Air

Cigarette smoke has been analyzed for carcinogens components by several investigators. The amounts of eight (8) hydrocarbon carcinogens present in cigarette smoke have been reported by Wynder and Hoffman and are listed in Table 1 with a ranking of their relative carcinogenicity.[2]

Knowing the carcinogen content in cigarette smoke, a respiratory carcinogen intake rate ($L_{resp}$) is readily determined for individuals smoking a different number of cigarettes/day for varying lengths of time using the following expression:

$$L_{resp} = \frac{10.8(N)365}{100}$$

$$L_{resp} = 39.4N$$

where $L_{resp}$ = respiratory carcinogen intake (μg/yr)

10.8 = carcinogen content (μg) per 100 cigarettes (See Table 1)

N = number of cigarettes smoked/day

Values of $L_{resp}$ for different groups of cigarette smokers are shown in Table 2.

Lung cancer death rates as a function of age and individual smoking patterns have been reported in the Dorn Study of Smoking and Mortality Among U.S. Veterans.[3] This study was conducted over an eight one-half year period with a population of over 293,000 military veterans holding Government life insurance policies. The study group was composed of practically all white males drawn from the middle and upper socioeconomic classes.

The Dorn study gives the cause of death for individuals classified into ten-year age brackets (45-54, 55-64, 65-74 and 75-84). In correlating age and lung cancer mortality (see Figure 1) these groupings are identified

Table 1. CARCINOGENIC HYDROCARBONS ISOLATED FROM CIGARETTE SMOKE

| Hydrocarbon | Relative carcinogenicity* | Micrograms per 100 cigarettes** |
|---|---|---|
| Benzo-a-pyrene | +++ | 2.5 |
| Dibenz-a,h-anthracene | +++ | 0.4 |
| Benzo-b-fluoranthene | ++ | 0.3 |
| Benzo-j-fluoranthene | ++ | 0.6 |
| Benz-a-anthracene | + | 0.3 |
| Chrysene | + | 6.0 |
| Benzo-e-pyrene | + | 0.3 |
| Indeno-1,2,3c,d-pyrene | + | 0.4 |
| | Total µg/100 cigarettes | 10.8 |

* Carcinogenicity determined on mouse skin.

** Isolated from cigarette smoke.

Table 2. RESPIRATORY CARCINOGEN INTAKE FOR SMOKERS AS A FUNCTION OF CIGARETTES SMOKED PER DAY

| Cigarettes smoked/day (N) | Carcinogen intake from cigarettes ($L_{resp}$) μg/yr | ng/day |
|---|---|---|
| 5 | 197 | 540 |
| 15 | 591 | 1620 |
| 30 | 1182 | 3240 |
| 50 | 1970 | 5400 |

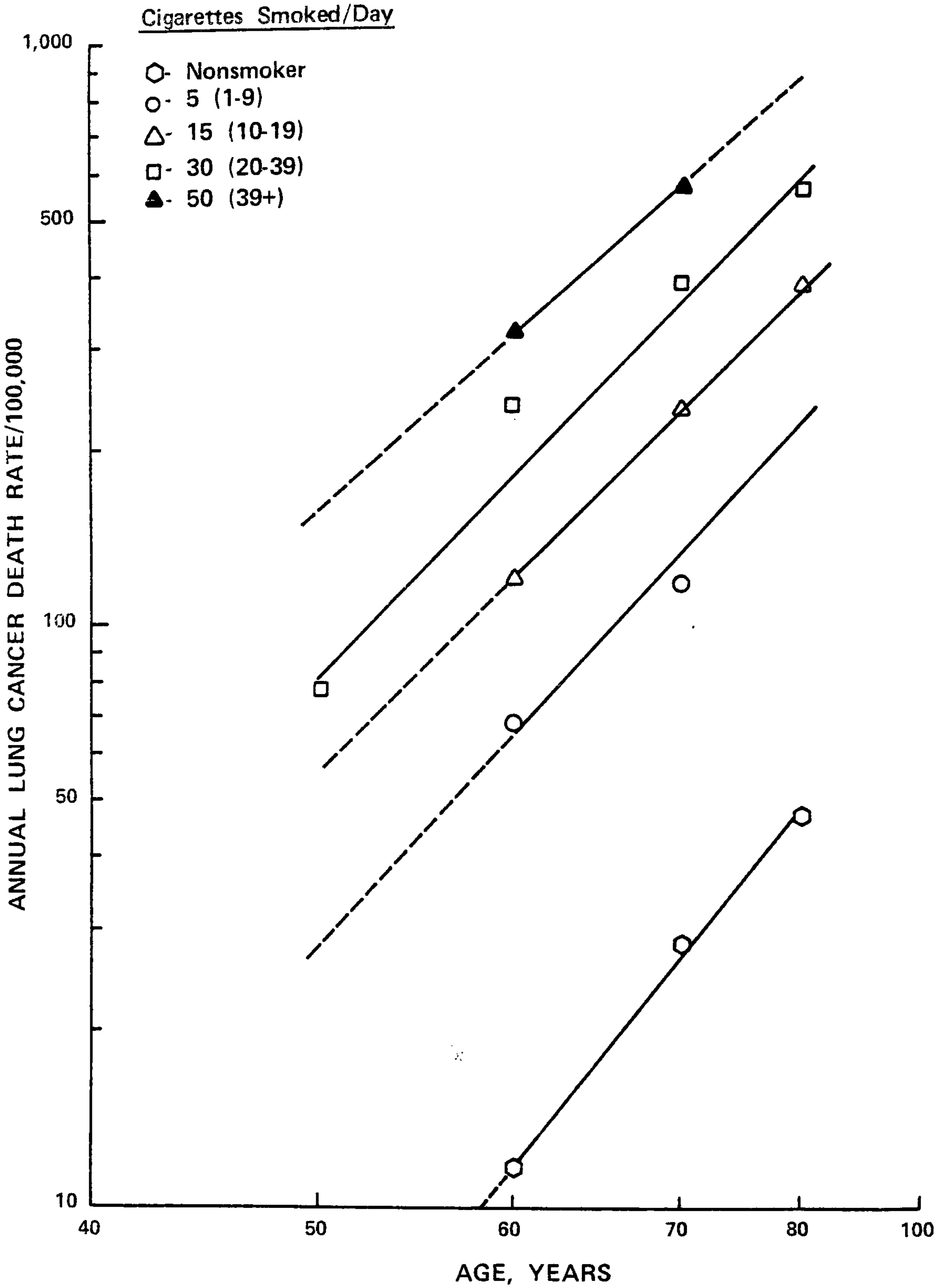


Figure 1. Lung cancer mortality versus age and cigarette use.

by their median age (50, 60, 70, and 80). Dorn classified smoking patterns as never or occasionally smoked, 1-9, 10-20, 21-39 and more than 39 cigarettes/day. These groupings are indicated in the present report as follows: Nonsmokers, 5, 15, 30 and 50 cigarettes/day.

The data used in this evaluation was taken from the Dorn study as presented in a paper by Kahn on pages 30, 38, 40, 42 and 44 under the cause of death listing of cancer of lung and bronchus.[3] The death rate in each category was determined by dividing the number of deaths by man-years of observation and relating this value to a rate per 100,000.

Supplemental data was taken from a similar study conducted by Hammond.[4] This study was carried out over a 40-year period and consisted of over one million men and women. The study results were reported separately by sex. The male cohort of nonsmokers under age 55 was much larger than the comparable Dorn group and, as a result, provided a more reliable estimate of lung cancer risk for that category.

The lung cancer mortality figures from both studies have dubious significance for age groups under 45 years. The reported number of deaths in these study subgroups was too low (less than 5) to warrant use in this report. Any age-smoking mortality rates derived from less than 5 reported deaths were considered invalid. These values were established by alternative means as described below. Hammond set a similar criterion in evaluating his study results.

The annual death rates used in this treatment for the different age-smoking categories is shown in Table 3.

The operations that lead to the final expression describing the relationship between lung cancer risk and ambient air carcinogen levels are summarized below.

a) construction of log-log plot of lung cancer mortality vs. the number of cigarettes smoked per day (also expressed as μg carcinogen intake/year and annual mean ng carcinogens/$m^3$ air) for the composite age group 45-84.

b) The relationship between lung cancer mortality and carcinogen intake was represented by a straight line, described

Table 3. LUNG CANCER MORTALITY AS A FUNCTION OF SMOKING PATTERN AND AGE (FROM DORN STUDY UNLESS INDICATED OTHERWISE)

| Age | Cigarettes smoked/day | Lung cancer deaths | Person-years of observation | Lung cancer death rate/100,000 |
|---|---|---|---|---|
| 45-54 | NS | 1 | 15,134 | 6.4* |
| | 5 | (1) | 3,129 | 28.0 |
| | 15 | (9) | 16,392 | 57.0 |
| | 30 | 10 | 12,839 | 77.9 |
| | 50 | (3) | 1,928 | 160.0 |
| 55-64 | NS | 25 | 213,858 | 11.7 |
| | 5 | 31 | 45,217 | 68.6 |
| | 15 | 183 | 151,664 | 120.7 |
| | 30 | 245 | 103,020 | 237.8 |
| | 50 | 63 | 19,649 | 320.6 |
| 65-74 | NS | 49 | 171,211 | 28.6 |
| | 5 | 44 | 37,130 | 118.5 |
| | 15 | 239 | 101,731 | 234.9 |
| | 30 | 194 | 50,045 | 387.7 |
| | 50 | 50 | 8,937 | 559.9 |
| 75-84 | NS | 4 | 8,489 | 47.1 |
| | 5 | 5 | 1,923 | 260.0 |
| | 15 | 15 | 3,867 | 387.9 |
| | 30 | 7 | 1,273 | 549.9 |
| | 50 | (2) | 232 | 862.0 |

*From Hammond Study (ref. 4).
Deaths in parenthesis were calculated from a death rate obtained by extrapolation (Fig. 1).

mathematically in the form $M_{lc} = A(L_{resp})^Y$ where $L_{resp}$ = respiratory carcinogen intake, A and Y = constants.

c) $M_{lc}$ was set equal to the value given for nonsmokers and the corresponding carcinogen intake ($L_{resp}$) calculated for this subgroup.

d) Since the Dorn study population consisted only of white males, a correction factor was derived so that the mathematical expressions would apply for the general population,

Since the only source of respiratory carcinogen intake for nonsmokers is ambient air, the value of $L_{resp}$ obtained in (c) was a measure of the cigarette carcinogen concentration in ambient air, $X_{aa} = 4.9$ ng/m$^3$. However this is only an approximation. Since cigarette smokers also inhale ambient air, their carcinogen intake values would have to be increased by this background level. This would result in a new series of data points, a different linear representation and a revised ambient air estimate. A different approach to this problem is described in the following section.

The technique called the method of standard additions is commonly used by the analytical chemist to determine the quantity of a particular component in a complex matrix. The procedure involves the addition of known amounts of the "component of interest" to the complex matrix "original sample" and plotting the changes in instrument response as a function of the amount of added "component of interest". The line that describes the data points is drawn and extrapolated to the negative X-axis. The absolute value of the X-intercept corresponds to the quantity of the "component of interest" in the original sample. The technique is shown graphically in Figure 2.

The estimation of cigarette carcinogens in ambient air is amenable to this kind of treatment. The situation is analogous to the general analytical case described above when making the following substitutions:

Instrumental Response = $M_{lc}$,

Original Sample = Nonsmoker,

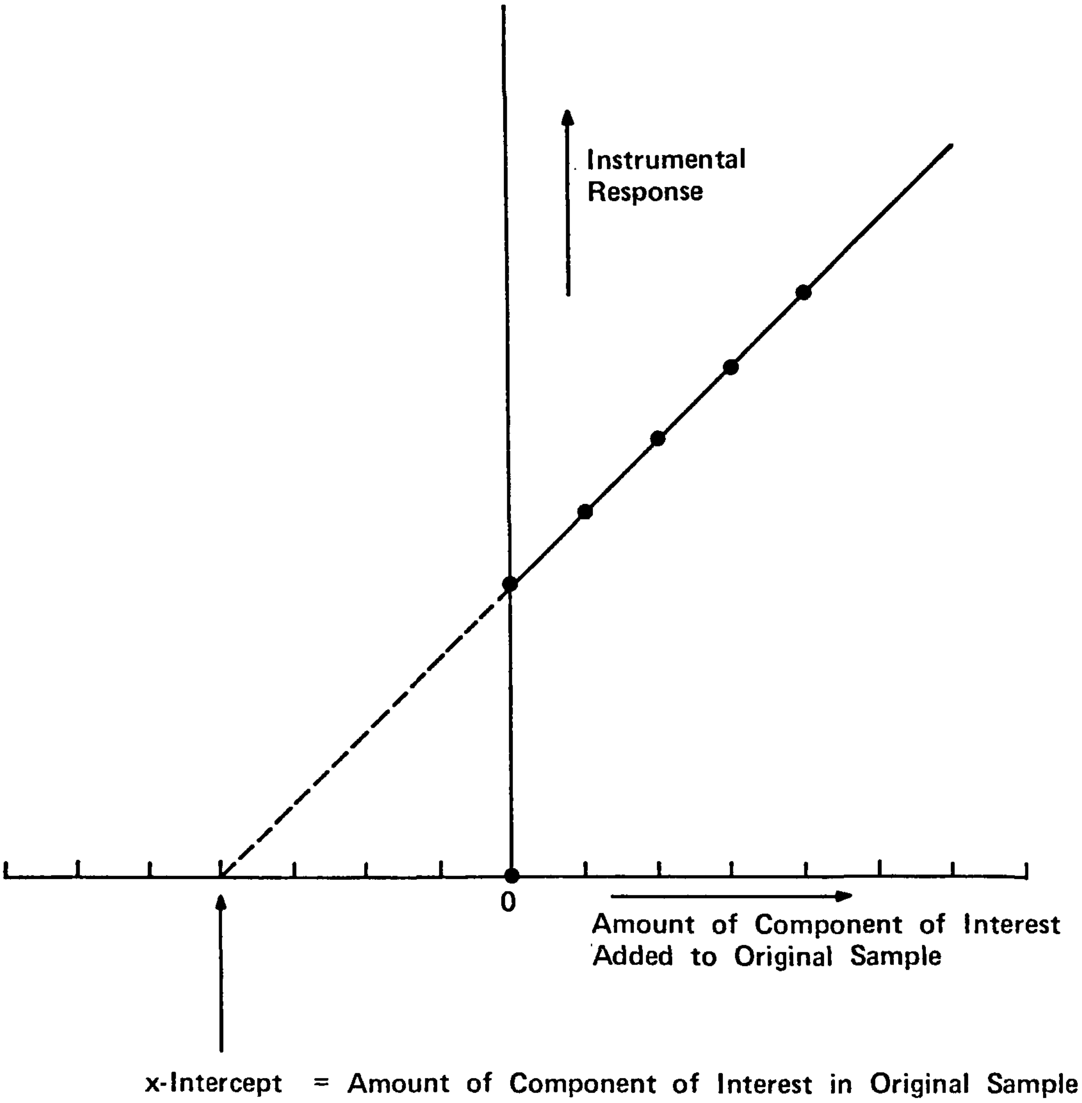


Figure 2. Standard Additions Method

Component of Interest = Cigarette carcinogens,

Standard Additions = Quantity of carcinogen intake by different groups of cigarette smokers,

X-Intercept = Quantity of cigarette carcinogen intake by nonsmoker;

To perform a standard additions treatment it is necessary to replot the Dorn study smokers' carcinogen intake and $M_{1c}$ data on Cartesian coordinates. Several different curve-fitting regression programs were attempts on the data in Table 4. The one which yielded the highest correlation coefficient ($r^2$ = .9968) was an exponential of the following form:

$$L_{resp} = Ae^{BM_{1c}} - D$$

$$M_{1c} = \frac{1}{B} \ln \left(\frac{L_{resp} + D}{A}\right)$$

where A, B, D = constants

The values of the constants were determined to give the following expression:

$$L_{resp} = 3.553\ e^{.0024M_{1c}} - 3.785$$

When $M_{1c}$ = 0, X = 3.553-3.785 = -0.232 (X-intercept)

Nonsmoker carcinogen intake = 232 ng/day

The smooth curve in Figure 3 describes the above equation and shows the agreement with the original data points. The Dorn study nonsmoker carcinogen intake value corresponds to 84.7 μg/year which is approximately 5 times higher than the 17.9 μg/year value previously reported in Section V of reference 1. The former figure is equivalent to an annual mean carcinogen concentration in ambient air of 22.9 ng/$m^3$ (see eqn. 73 in Ref. 1 for conversion calulation). This baseline level is equivalent to 2.15 cigarettes/day.

The graph in Figure 3 may be corrected for the carcinogen level in ambient air by shifting the Y-axis to the X-intercept value of 232 ng/day. The equation describing the curve is modified as follows:

Table 4. LUNG CANCER MORTALITY VERSUS CARCINOGEN INTAKE FOR DORN STUDY GROUP, AGE 45-84

| Cigarettes | Smoker carcinogen intake, ng/day ($L_{resp}$) | Lung Cancer Mortality/100,000 ($M_{lc}$) |
|---|---|---|
| NS | (232)* | 19.1 |
| 5 | 540 | 92.7 |
| 15 | 1,620 | 163 |
| 30 | 3,240 | 273 |
| 50 | 5,400 | 384 |

* Estimated by method of standard additions

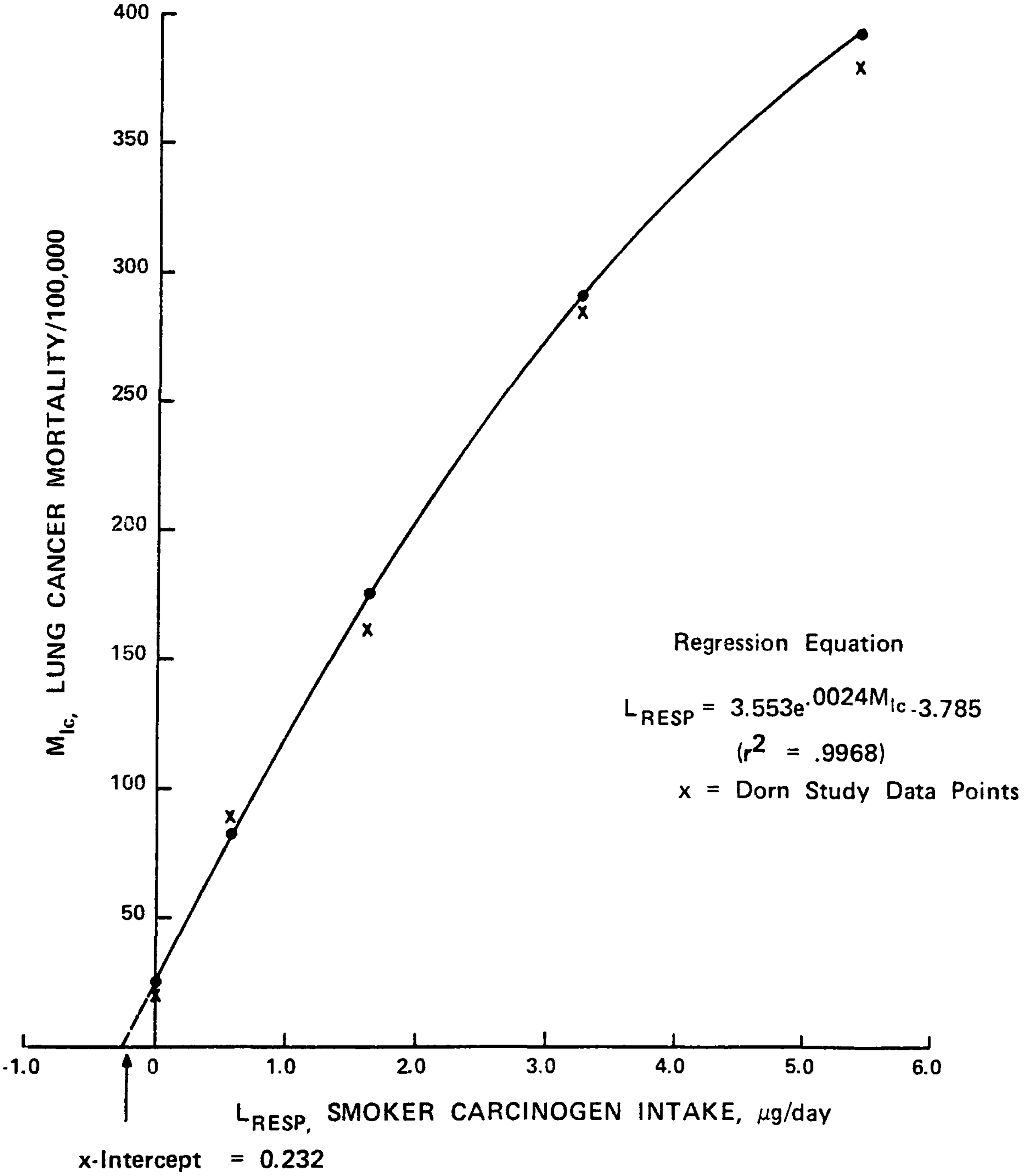


Figure 3. Lung Cancer Mortality Versus Carcinogen Intake of Dorn Study Smokers

$$L_{resp}\ (\mu g/day)\ -0.232 = 3.553e^{.0024M_{1c}}$$

$$L_{resp}\ (ng/day) = 3{,}553(e^{.0024M_{1c}} -1)$$

$$X_{aa}\ (ng/m^3) = 350.5\ (e^{.0024M_{1c}} - 1)$$

$$M_{1c} = 416.7\ \ln\ (\frac{X_{aa}}{350.5} + 1)$$

It was shown in Section V, part G of Ref. 1 that the $M_{1c}$ of the general population was 87% of the Dorn study group. Correcting for this fact results in the following expressions applicable to the general population:

$$L_{resp}\ (ng/day) = 3{,}088(e^{.0024M_{1c}} -1)$$

$$X_{aa}\ (ng/m^3) = 304.6(e^{.0024M_{1c}}-1)$$

$$M_{1c} = 362.5\ \ln\ (\frac{X_{aa}}{350.5} + 1)$$

Table 5 shows estimated lung cancer mortality for the nonsmoker in the general population as a function of the carcinogen concentration in ambient air. The same data is plotted in Figure 4.

<u>Drinking Water</u>

Carcinogens that are present in drinking water (and food) also represent a biological risk to body tissues. Oral ingestion and subsequent transport of these agents increase systemic carcinogen levels. The purpose of this treatment is to establish a correspondence between this body burden and cancer mortality with the view of assessing the risk associated with carcinogens in drinking water.

Carcinogens which are introduced via the respiratory tract come into direct contact with lung tissue and are then potentially available for transport to other tissue sites. It has been shown that approximately 50% of a respiratory carcinogen dose is retained in lung tissue.[5] The

Table 5. ESTIMATED NONSMOKER LUNG CANCER DEATH RATE

VERSUS CARCINOGEN CONCENTRATION IN AMBIENT AIR

Age 45-84

| Carcinogen conc. in ambient air ($X_{aa}$, $ng/m^3$) | Daily carcinogen intake (general population) ($L_{resp}$, ng/day) | Lung Cancer mortality 100,000 ($M_{lc}$) |
|---|---|---|
| 100 | 1,010 | 91.0 |
| 50 | 507 | 48.3 |
| 22.9 | 124 | 22.9 |
| 10 | 101 | 10.2 |
| 5 | 51 | 5.1 |
| 2 | 20 | 2.1 |

* Ambient air baseline level for general population based on Dorn Study data this report

$M_{lc}$ 362.5 ln $\left(\frac{X_{aa}}{350.5} + 1\right)$

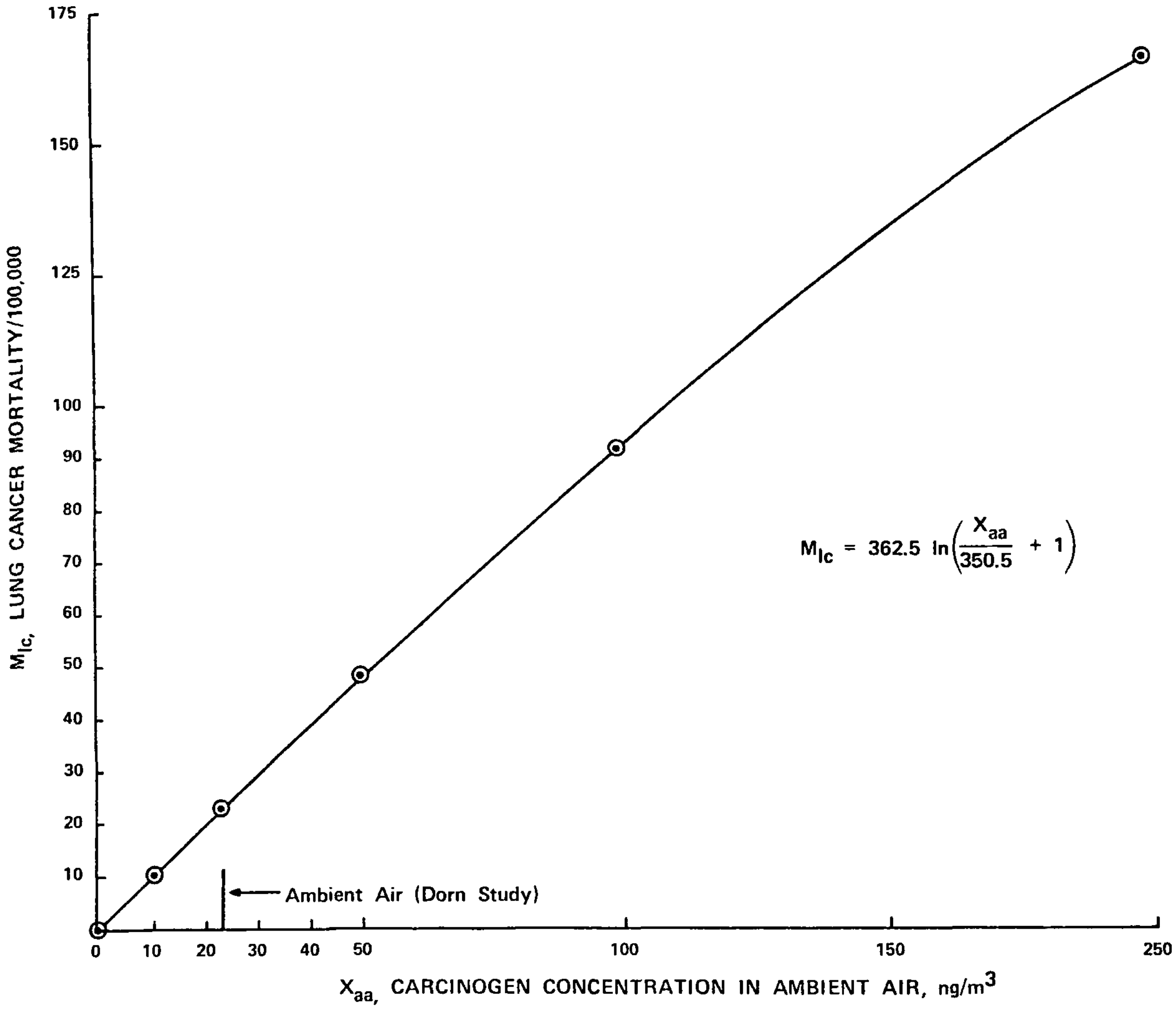


Figure 4. Lung Cancer Mortality Versus Carcinogens In Ambient Air - General Population

remaining portion passes into the systemic circulation and exerts its biological action at other body sites. This 1:1 partition is assumed during this treatment.

Orally ingested carcinogens pass through the gastrointestinal tract and are then presented to other body sites via absorption into the systemic circulation. Complete carcinogen uptake (absorption) is assumed. Several carcinogen distribution studies have shown that amounts ranging from 0.38 to 2-3% of an orally administered dose of polycylic hydrocarbons are found in lung tissue.[6,7] Kotin and coworkers reported a maximum of 2% of the dose in the respiratory tract.[5] The fraction of orally administered carcinogens concentrated by lung tissue is assumed negligible and is not considered further in this report.

The Dorn study report itemizes mortality figures for cancers at all sites. These risk data were compiled for all cancers, other than lung, and categorized by age and smoking history (see Table 6). The same imformation is shown in Table 7 for the combined 45-84 age group.

From this summary it is readily apparent that sites other than lung are responsible for the majority of cancer deaths, particularly among nonsmokers, and that lung cancer risk increases much more rapidly than cancers at other sites with increased frequency of smoking.

As noted above one-half of the carcinogens introduced through the respiratory tract are released into the systemic circulation. Thus, sites other than lung are exposed to 50% of the carcinogens contained in the cigarettes smoked each day. The relationship between cigarettes smoked/ day, the corresponding systemic carcinogen intake ($S_{resp}$), and the resultant other site cancer mortality ($M_{os}$) is given in Table 8.

If one assumes that the carcinogen level in ambient air, drinking water, and food was constant for all Dorn study subjects, the cigarette smoker's increased other site risk must be due to his higher systemic burden ($S_{resp}$) as shown in Table 8. A standard additions treatment of systemic carcinogen uptake ($S_{resp}$) vs. other site mortality ($M_{os}$) values was carried out. A plot of these data is shown in Figure 5. The regression equation which best describes the relationship between $M_{os}$ and $S_{resp}$ is given below.

Table 6. CANCER (OTHER THAN LUNG)

MORTALITY AS A FUNCTION OF SMOKING PATTERNS

AND AGE (from Dorn Study)

| Age | Cigarettes smoked/day | Cancer (other than lung) deaths | Person-years of observation | $M_{os}$ Cancer (other than lung) death rate/100,000 |
|---|---|---|---|---|
| 45-54 | NS (nonsmokers) | 7 | 15,134 | 46.3 |
| | 5 (1-9) | 1 | 3,129 | 32.0 |
| | 15 (10-20) | 8 | 16,392 | 48.8 |
| | 30 (21-39) | 16 | 12,839 | 125 |
| | 50 (> 39) | 0 | 1,928 | - |
| 55-64 | NS | 463 | 213,858 | 217 |
| | 5 | 112 | 45,217 | 248 |
| | 15 | 452 | 151,664 | 298 |
| | 30 | 370 | 103,020 | 359 |
| | 50 | 79 | 19,649 | 402 |
| 65-74 | NS | 589 | 171,211 | 344 |
| | 5 | 183 | 37,130 | 493 |
| | 15 | 518 | 101,731 | 509 |
| | 30 | 250 | 50,045 | 500 |
| | 50 | 59 | 8,937 | 600 |
| 75-84 | NS | 85 | 8,489 | 1,001 |
| | 5 | 19 | 1,923 | 988 |
| | 15 | 42 | 3,867 | 1,086 |
| | 30 | 22 | 1,273 | 1,728 |
| | 50 | 1 | 232 | 431 |

Table 7. CANCER MORTALITY AND RESPIRATORY CARCINOGEN INTAKE

FOR DORN STUDY GROUP AGE 45-84

| Cigarettes smoked/day | Respiratory carcinogen intake µg/yr | Respiratory carcinogen intake ng/day | Cancer (other than lung) deaths | Person-years of observation | $M_{os}$ Cancer (other than lung) death rate/100,000 | $M_{lc}$ Lung Cancer death rate/100,000 |
|---|---|---|---|---|---|---|
| NS | Ambient Air | | 1,144 | 408,692 | 280 | 19.1 |
| 5 | 197 | 540 | 315 | 87,399 | 360 | 92.7 |
| 15 | 591 | 1,620 | 1,020 | 273,554 | 373 | 163 |
| 30 | 1,182 | 3,240 | 709 | 167,177 | 424 | 273 |
| 50 | 1,970 | 5,400 | 139 | 30,746 | 452 | 384 |

Table 8. RELATIONSHIP BETWEEN CANCER (OTHER THAN LUNG) MORTALITY AND SYSTEMIC (ORAL) CARCINOGEN BURDEN

| Cigarettes smoked/day | Systemic carcinogen uptake, no/day ($S_{resp}$) | Cancer (other than lung) mortality/100,000 |
|---|---|---|
| NS | Ambient Air | 280 |
| 5 | 270 | 360 |
| 15 | 810 | 373 |
| 30 | 1620 | 424 |
| 50 | 2700 | 452 |

$S_{resp}$ = 50% of respiratory carcinogen intake

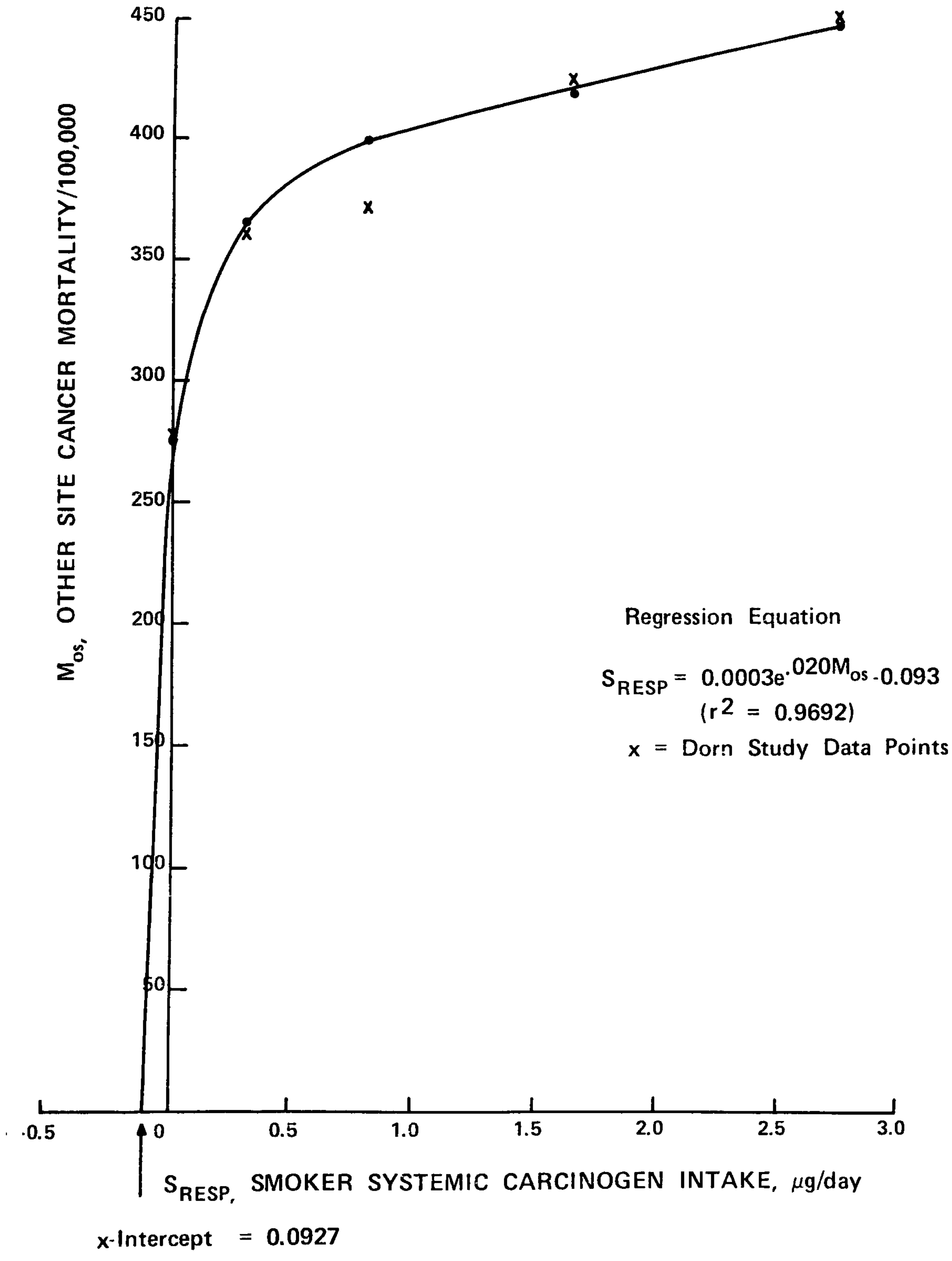


Figure 5. Other Site Cancer Mortality Versus Carcinogen Intake of Dorn Study Smokers

$$S_{resp} = 0.34^{.020M_{os}} - 93.0 \quad (r^2 = .9692)$$

When $M_{os} = 0$, $S_{resp} = -92.66$ (X-intercept)

Thus the Dorn study nonsmoker is subjected to a daily systemic carcinogen dose of 92.7 ng. This value includes carcinogen burden from all sources (air, food, and drinking water).

Adjusting for this background level gives an expression for total systemic burden, a term that includes carcinogen contributions from all sources.

$$S_{total} = S_{resp} + S_{oral}$$

$$S_{total} = 0.5\ L_{resp} + S_{dw} + S_{food}$$

$$S_{total} - 92.66 = 0.34e^{.02M_{os}} - 93.0$$

$$S_{total} = 0.34e\ (e^{.02M_{os}} - 1)$$

$$M_{os} = 50\ \ln\left(\frac{S_{total}}{0.34} + 1\right)$$

As noted in the caveats stated at the beginning of this report a daily consumption of two liters of drinking water and one kilogram of food is assumed. The assumption is also made that drinking water and food contain equal concentrations (wt %) of carcinogens. Thus, two thirds of the carcinogens ingested orally are present in drinking water.

$$X_{dw}\ (ng/1) = X_{food}\ (ng/kg)$$

$$S_{dw}\ (ng/day) = 2(1)X_{dw}\ (ng/1)$$

$$S_{food}\ (ng/day) = 1\ (kg)\ X_{food}\ (ng/kg)$$

$$S_{dw} = 2S_{food}$$

$$S_{oral} = 3S_{food} = 1.5S_{dw}$$

The Dorn study group consisted of adult white males. As a result, data derived from this study group cannot be directly applied to any geographical segment of the general population. The technique used to convert the derived equations to the form necessary for general application is given below. An equal number of males and females is assumed in addition to the following recent mortality figures.[8]

1975 Cancer Death Rates

200 per 100,000 nonwhite male
157 per 100,000 white male
119 per 100,000 nonwhite females
107 per 100,000 white females

Assuming nonwhites make up 15% of the population, the annual cancer mortality for the total population is 136/100,000 or 86.6% of the white male (Dorn study subjects) death rate.

| | |
|---|---|
| 200(.075) | = 15.000 |
| 157(.425) | = 66.725 |
| 119(.075) | = 8.925 |
| 107(.425) | = 45.475 |
| Overall Cancer Death Rate | 136.125 |

Dorn study nonsmoker $M_{os}$ =280 (from Table 8)

Adult population nonsmoker $M_{os}$ =243

The equation that expresses other site cancer mortality as a function of total systemic carcinogen burden and is applicable to the adult general population is shown below.

$$M_{os} = 50.0(.866) \ln \left(\frac{S_{total}}{0.34} + 1\right)$$

$$M_{os} = 43.3 \ln \left(\frac{S_{total}}{0.34} + 1\right)$$

The systemic burdens for various ambient air and drinking water carcinogen concentrations are given in Table 9 and the other site cancer mortality values for different ambient air and drinking water combinations are listed in Table 10. The data from these tables is plotted in Figure 6

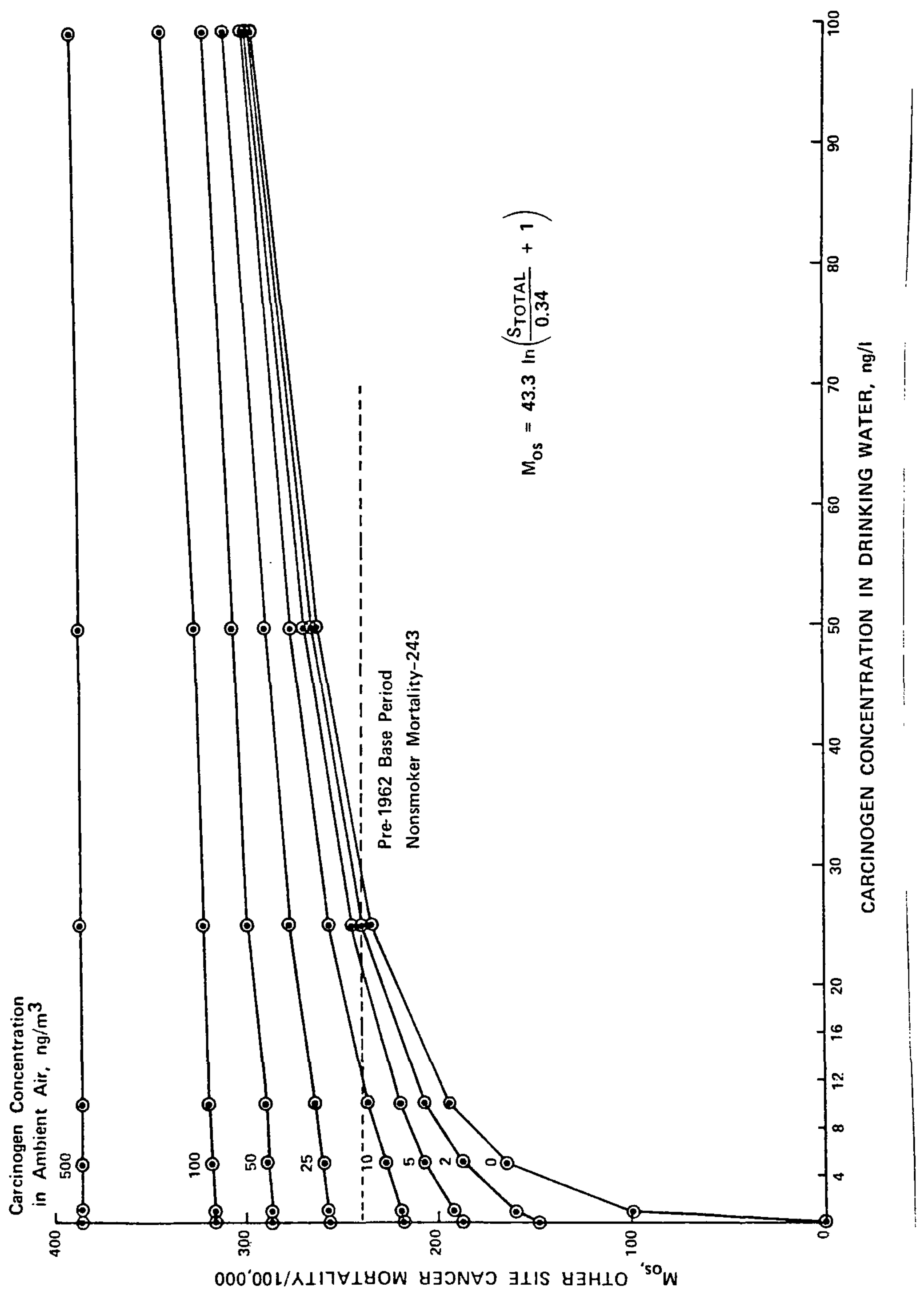


Figure 6. Other Site Cancer Mortality Versus Carcinogens in Drinking Water at Different Ambient Air Concentrations - General Population

Table 9. ORAL AND RESPIRATORY UPTAKE OF CARCINOGENS AS A FUNCTION OF AMBIENT AIR AND DRINKING WATER/FOOD QUALITY

Adult General Population

a) Carcinogens in Drinking Water/Food

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| Concentration in drinking water, $X_{dw}$(ng/l)* | 0 | 1 | 5 | 10 | 25 | 50 | 100 |
| Concentration in food, $X_{food}$(ng/kg) | | | | | | | |
| Total oral (systemic) carcinogen uptake, $S_{oral}$(ng/day)** | 0 | 3 | 15 | 30 | 75 | 150 | 300 |
| Other site cancer mortality, $M_{os}$ | 0 | 99 | 165 | 195 | 234 | 264 | 294 |

* Equal wt.% concentration of carcinogens in drinking water and food.

** Two liters of drinking water and one kilogram of food consumed per day.

$$M_{os} = 43.3 \ln \left(\frac{S_{oral}}{0.34} + 1\right)$$

b) Carcinogens in Ambient Air

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Concentration in ambient air, $X_{aa}$(ng/m$^3$) | 0 | 2 | 5 | 10 | 25 | 50 | 100 | 500 |
| Respiratory carcinogen uptake, $L_{resp}$(ng/day) | 0 | 20.2 | 50.7 | 101 | 253 | 507 | 1014 | 5070 |
| Release to systemic circulation, $S_{resp}$(ng/day) | 0 | 10.1 | 25.3 | 50.7 | 127 | 253 | 507 | 2535 |
| Other site cancer mortality, $M_{os}$ | 0 | 149 | 187 | 217 | 257 | 287 | 316 | 386 |

* $L_{resp} = 10.14 X_{aa}$

** 50% Lung retention

$$M_{os} = 43.3 \ln \left(\frac{S_{resp}}{0.34} + 1\right)$$

Table 10. OTHER SITE CANCER MORTALITY AS A FUNCTION OF A AMBIENT AIR AND DRINKING WATER/FOOD QUALITY

Adult General Population

| Ambient Air Conc., $X_{aa}$ ($ng/m^3$) | Systemic Uptake from Ambient Air, $S_{resp}$ (ng/day) | Other Site Cancer Mortality, $M_{os}$ | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | | $X_{dw}$ (ng/l) = 0 | 1 | 5 | 10 | 25 | 50 | 100 |
| 0 | 0 | 0 | 99 | 165 | 195 | 234 | 204 | 294 |
| 2 | 10.1 | 149 | 160 | 187 | 207 | 240 | 267 | 295 |
| 5 | 25.3 | 187 | 192 | 207 | 219 | 246 | 271 | 297 |
| 10 | 50.7 | 217 | 219 | 228 | 237 | 257 | 277 | 300 |
| 25 | 127 | 257 | 258 | 261 | 266 | 277 | 290 | 309 |
| 50 | 253 | 287 | 287 | 289 | 291 | 298 | 307 | 321 |
| 100 | 507 | 316 | 317 | 318 | 320 | 323 | 327 | 337 |
| 500 | 2535 | 386 | 386 | 386 | 387 | 387 | 388 | 391 |

$$S_{oral} = 3X_{dw}$$

$$M_{os} = 43.3 \ln \left(\frac{S_{oral} + S_{resp}}{0.34} + 1\right)$$

$$M_{os} = 43.3 \ln \left(\frac{S_{total}}{0.34} + 1\right)$$

as risk of other site cancers per 100,000 versus drinking water carcinogen concentration (ng/l) at various ambient air carcinogen levels.

In 1971 the World Health Organization established a maximum permissible concentration for six polycyclic aromatic hydrocarbons, taken collectively, at 200 ng/l.[9] Four of the six compounds used in this estimation are known carcinogens.

Harrison and co-workers have prepared a comprehensive review on the concentrations of carcinogenic polycylic aromatic compounds found in different types of water streams.[10] Ground water levels ranged from 1 to 81 ng/l (average 60 ng/l). Several studies have been carried out on the effectiveness of polycylic carcinogen removal by conventional sewage treatment processes.[10,11] Treated effluents contained from 7 to 54 ng/l (in most cases less than 30 ng). Untreated river water may contain ten times this amount and if polluted by nearby petroleum-related activities, will probably exceed that concentration.

For the sake of comparison, the permissible concentration of carcinogenic polycyclic hydrocarbons was determined using Method IIIC (see Section V, page 62 of reference 1). The TLV of the benzene soluble coal tar pitch volatiles is 0.2 $mg/m^3$.[12] Since approximately 10% of this material consists of polycyclic hydrocarbons (assumed carcinogenic), the TLV for this fraction may be estimated at 0.02 $mg/m^3$.[13]

METHOD III C ($\tau$=365 days)

$$X_e = 1.14 \times 10^{-3} \text{ TLV}$$

$$X_e = 1.14 \times 10^{-3} \ (.02)$$

$$X_e = 0.0228 \ \mu g/l \ (22.8 \ ng/l)$$

$X_e$ = Estimated safe drinking water concentration

A summary of these different water carcinogen levels ($X_{dw}$) and the calculated other site mortality values ($M_{os}$) is shown in Table 11.

Table 11. SUMMARY OF CARCINOGEN CONCENTRATION IN DRINKING WATER AND CORRESPONSING CANCER RISK

| | Basis for Estimation | Carcinogen Concentration in Drinking Water, $X_{dw}$ (ng/l) | Other Site Cancer Mortality per 100,000 $M_{os}$ | | |
|---|---|---|---|---|---|
| | | | $X_{aa}$ = 2 | 10 | 50 ng/m$^3$ |
| 1. | General adult population based on Dorn Study nonsmoker cancer mortality | 27.2 | 243 | - | - |
| | | 13.6 | - | 243 | - |
| 2. | Method III C - TLV for coal tar pitch volatiles (0.2 mg/m$^3$) and assuming 10% carcinogen polycylic hydrocarbon content | 22.8 | 236 | 254 | 297 |
| 3. | WHO - maximum permissible concentration; based on six polycylics, four of which are known carcinogens | 200 | 324 | 327 | 339 |
| 4. | Method III C - TLV for coal tar pitch volatiles (0.2 mg/m$^3$), assume 100% carcinogen content | 228 | 330 | 332 | 343 |
| 5. | Typical effluents as reported in Reference 7 | | | | |
| | a) Average groundwater levels | 60 | 274 | 282 | 310 |
| | b) typical maximum treated river water levels | 30 | 246 | 261 | 300 |
| | c) minimum treated river water levels | 7 | 196 | 232 | 290 |

$$M_{os} = 43.3 \ln \left(\frac{0.5 L_{resp} + S_{oral}}{0.34} + 1\right)$$

$$M_{os} = 43.3 \ln \left(\frac{5.07X_{aa} + 3X_{dw}}{0.34} + 1\right)$$

$$M_{os} = 43.3 \ln \left(\frac{S_{total}}{0.34} + 1\right)$$

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TECHNICAL REPORT DATA
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16. ABSTRACT
The report gives results of a study aimed at developing a means for estimating cancer mortality as a function of carcinogen concentration in drinking water. Cancer risk data for cigarette smokers was treated by the method of standard additions to provide an estimate of ambient carcinogen levels in drinking water. A similar treatment was carried out on lung cancer risk data to give an estimate of carcinogen levels in ambient air.

17. KEY WORDS AND DOCUMENT ANALYSIS

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|---|---|---|---|---|
| Pollution | Estimating | Pollution Control | 13B | 14B |
| Potable Water | Tobacco | | 08H | 06C |
| Carcinogens | | | 06E | |
| Malignant Neoplasms | | | | |
| Pulmonary Neoplasms | | | | |
| Mortality | | | 05K | |

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