Chapter 1

Smoking-Related Health Problems Unique to Women

INTRODUCTION

Smoking habits and attitudes among women and teenage girls have differed in the past from the habits and attitudes among men and teenage boys. Women tended to smoke fewer cigarettes, were less likely to inhale, and were more likely to smoke low "tar" and nicotine and filter-tipped brands. Surveys have indicated, however, that the smoking habits of women are becoming more like men's. Women are taking up the habit at an earlier age and have become heavier smokers. This has made them more vulnerable not only to lung cancer and other smoking-related diseases, but also to specific health problems that are unique to their sex. For example, research on the relationship between cigarette smoking and the outcome of pregnancy has established that there are definite risks to both the fetus and the mother associated with cigarette smoking during pregnancy. Moreover, women who use oral contraceptives are at greater risk of cardiovascular disease if they smoke cigarettes. There is also evidence that nicotine is present in the breast milk of lactating mothers who smoke. The following is a review of the current information on these and other health consequences of smoking unique to women.

EFFECTS OF SMOKING ON THE OUTCOME OF PREGNANCY

There are definite health risks associated with smoking and pregnancy, including effects on birth weight, perinatal mortality, and long-term physical and intellectual development of the child. This section reviews each of these subjects and also includes information about the likely mechanism of action of smoke and its contents on the mother and the products of conception.

Smoking and Birth Weight

In 1957, Simpson published her original finding that babies born to women who smoke during their pregnancy weigh on the average 200 grams (g) less than the babies born to women who do not smoke

(34). Since then, more than 100 articles on this relationship have led to the general acceptance that smokers' babies generally weigh 150 to 250 g less than nonsmokers' babies, and twice as many of the former weigh less than 2500 g (13). The 1973 report of *The Health Consequences of Smoking* presented evidence to support a causal association between cigarette smoking and fetal growth retardation (39). A strong dose-response relationship was also established in that report, with differences in weight being in direct proportion to the number of cigarettes smoked.

The following additional points were summarized in the 1973 report to further support the causal association between cigarette smoking during pregnancy and lower birth weight:

1. Results are consistent in all studies, retrospective and prospective, from many different countries, races, cultures, and geographic settings.

2. The relationship between smoking and reduced birth weight is independent of other factors that influence birth weight, such as race, parity, maternal size, socioeconomic status, sex of child, and all others that have been studied.

3. If a woman gives up smoking by the fourth month of pregnancy, her risks of delivering a low-birth-weight baby is similar to that of a nonsmoker.

Subsequent to the 1973 report, additional reports have further discussed and corroborated the association between smoking in pregnancy and low birth weight (19, 25, 33, 35).

Smoking and Perinatal Mortality

A strong, probably causal, association between cigarette smoking and higher late fetal and infant mortality rates among smokers' infants is now well established (38). Retrospective and prospective studies have revealed a statistically significant relationship between cigarette smoking and an elevated mortality risk among the infants of smokers. In three of these studies of sufficient size to permit adjustment for other risk factors, a highly significant independent association between smoking and mortality was established. Part of the discrepancy in results between these studies and those in which a significant association between smoking and infant mortality was not demonstrated may be explained by a lack of adjustment for risk factors other than smoking.

The 1973 report also presented evidence indicating that the higher relative risks occurred among populations with risk factors other than smoking being present, such as socioeconomic status, age, parity, race, and previous pregnancy history.

Since 1973, a series of articles by Meyer, et al. analyzed data from the Ontario Perinatal Mortality Study of all single births in ten Ontario teaching hospitals in 1960-61 (26, 27, 28). The study involved 51,490 births, including 701 fetal deaths and 655 early neonatal deaths, and was supplemented by clinical records with interviews of mothers in the hospital, interviews with anesthetists and attending physicians, and autopsy records (29). Perinatal mortality increased significantly with smoking and was also affected by such factors as maternal age, parity, socioeconomic status, previous pregnancy history, hemoglobin level, and other risk factors (29). Smoking frequencies also varied by many of these characteristics. Smoking and other risk factors were cross-tabulated among 52 data subgroups. In all subgroups, the mortality increase with smoking was dose related, but not in a simple, linear way. The increased risk of perinatal mortality associated with light smoking among young, low-parity, nonanemic mothers was less than 10 percent. At the other extreme, mothers with other risk factors of high parity, public hospital status, with previous low-birth-weight infants, or with hemoglobin less than 11 g had further increased perinatal mortality risks of 70-100 percent when they were smokers. The most significant risk factor (mortality rate of 78 per 1,000 total births) was anemia, defined as a hemoglobin of less than 8.0 g. The failure of some earlier studies to find a significant increase in perinatal mortality with maternal smoking may be due to selection of study populations from the end of the spectrum, where light smoking is associated with only a slight increase in perinatal risk. This evidence points up how population selection could influence study findings and shows that exposure to the effects of smoking during pregnancy is much more dangerous for the babies of some women than for others. These findings are corroborated by a number of studies in which fetal, neonatal, or perinatal mortality rates are compared for smoking and nonsmoking women, controlling for the effects of various risk factors previously mentioned (1, 12, 22, 36).

Additional data were published in 1976–1977 (26, 27) and revealed that frequencies of low birth weight (under 2500 g), preterm delivery (< 38 weeks), perinatal mortality, abruptio placentae, placenta previa, bleeding during pregnancy, and prolonged and premature rupture of the membranes increased directly and significantly ($p < 0.00001$) as the level of maternal smoking increased (Tables 1 and 2). The 1976 paper used multiple regression analysis to measure the independent effect of smoking on the various risk factors. The probabilities of these complications were also compared (Figure 1). Risks of placenta previa and abruptio placentae were higher for smokers than for nonsmokers at all gestations, with

TABLE 1. Adjusted rates and F ratios for maternal smoking and other important factors affecting birth weight, gestation, placental complications, and perinatal mortality

Factor	*Adjusted Rates of Outcome	†F Ratio
	Birth Weight < 2500 Grams Per 1000 Births	
Maternal Smoking Level		
None	49.4	182.8
< 1 Pack Per Day	75.7	
> 1 Pack Per Day	113.7	
Previous Pregnancy History		
No Previous Pregnancy	70.0	123.5
Previous Pregnancy, 0 Loss	57.8	
Previous Pregnancy, Loss	134.8	
Hospital Pay Status		
Private	60.0	84.0
Public	87.4	
	Gestation < 38 Weeks Per 1000 Births	
Maternal Smoking Level		
None	77.1	50.6
< 1 Pack Per Day	92.2	
> 1 Pack Per Day	115.9	
Previous Pregnancy History		
No Previous Pregnancy	69.1	182.6
Previous Pregnancy, 0 Loss	85.7	
Previous Pregnancy, Loss	193.9	
Hospital Pay Status		
Private	78.9	120.3
Public	116.2	
	Placenta Previa Per 1000 Births	
Maternal Smoking		
None	6.5	11.7
< 1 Pack Per Day	8.1	
> 1 Pack Per Day	12.5	
Previous Pregnancy History		
No Previous Pregnancy	8.8	14.4
Previous Pregnancy, 0 Loss	6.6	
Previous Pregnancy, Loss	15.8	
(Hospital pay status not a significant factor)		

TABLE 1. Adjusted rates and F ratios for maternal smoking and other important factors affecting birth weight, gestation, placental complications, and perinatal mortality *(continued)*

	Abruptio Placentae Per 1000 Births	
Maternal Smoking		
None	16.4	17.1
< 1 Pack Per Day	20.3	
> 1 Pack Per Day	27.6	
Previous Pregnancy History		
No Previous Pregnancy	18.8	25.6
Previous Pregnancy, 0 Loss	17.6	
Previous Pregnancy, Loss	37.4	
Hospital Pay Status		
Private	17.5	20.7
Public	25.0	
	Perinatal Mortality Per 1000 Births	
Maternal Smoking		
None	23.5	8.4
< 1 Pack Per Day	28.2	
> 1 Pack Per Day	31.8	
Previous Pregnancy History		
No Previous Pregnancy	23.1	97.4
Previous Pregnancy, 0 Loss	23.6	
Previous Pregnancy, Loss	68.7	
Hospital Pay Status		
Private	23.3	44.2
Public	36.1	

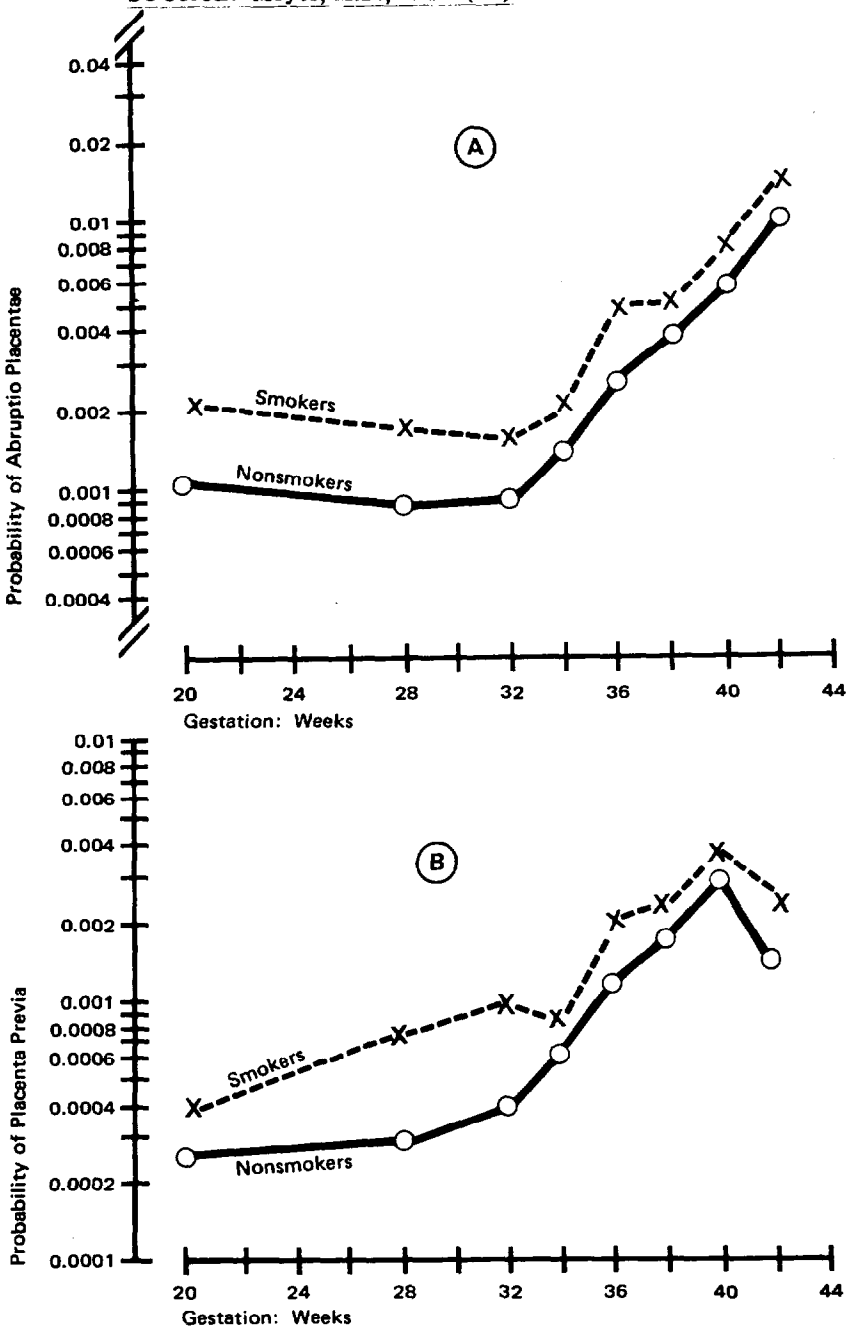
*Adjusted rates show independent effect of the factor given, adjusted for all other factors in regression. They are: maternal smoking, hospital pay status, mothers' birthplace, height, prepregnant weight, sex of child, previous pregnancy history, and age-parity.

†F ratio degrees of freedom: numerator = number of subgroups −1, denominator = infinity. (All differences shown are highly significant. F ratios indicate the relative importance of the factor.)

SOURCE: Personal correspondence, based on data in Meyer, M.B., et al. (26).

FIGURE 1.—Risks of selected pregnancy complications for smoking and nonsmoking mothers, by period of gestational age at delivery for A, abruptio placentae, B, placenta previa, C, premature rupture of membranes (PROM)

SOURCE: Meyer, M.B., et al. (27).



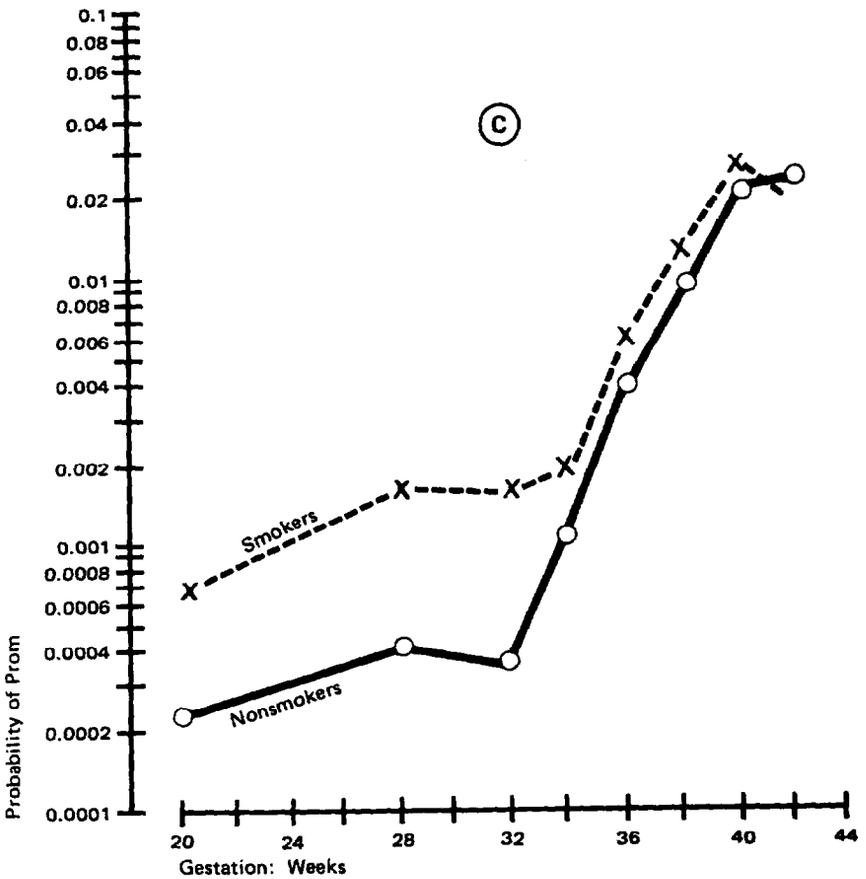


TABLE 2. Perinatal mortality and selected pregnancy complications, by maternal smoking levels

Outcome	Smoking level (packs per day) (rates per 1,000 total births) 0 (23,358 Births)	< 1 (15,328 Births)	> 1 (6,581 Births)	χ^2*
Perinatal Mortality	23.3	28.0	33.4	27.8±
Abruptio Placentae	16.1	20.6	28.9	47.3±
Placenta Previa	6.4	8.2	13.1	28.6±
Bleeding During Pregnancy	116.5	141.6	180.1	201.9±
Rupture of Membranes >48 Hours	15.8	23.3	35.8	109.9±
Rupture of Membranes Only at Admission	30.3	39.3	45.0	45.7±

*Cochran's chi square for trends.

±$p < 0.00001$.

SOURCE: Meyer, M.B., et al. (27).

relatively larger differences in the earlier weeks of pregnancy. The risk of premature rupture of membranes was more than three times greater for smokers than for nonsmokers among deliveries that occurred before 34 weeks gestation and remained higher than the risk for nonsmokers through term (Figure 1C).

A prospective investigation of 9,169 pregnant women was conducted by Goujard, et al. (15), and results showed a substantial increase in stillbirths among smokers. A large proportion of this increase was due to abruptio placentae. There were 100 stillbirths, classified into five categories of causes: vascular, abruptio placentae, mechanical, miscellaneous (syphilis, Rh, malformations, etc.), and unknown (Table 3). The abruptio placentae category exclusively represented cases without toxemia, the one toxemic case being classified with the vascular causes. The higher proportion of smokers is significant for only two of the categories: abruptio placentae ($p = 0.005$) and unknown causes ($p = 0.0005$). Although the numbers were small, the risk of stillbirths by abruptio placentae is six times higher among smokers.

TABLE 3. Stillbirths according to cause in relation to maternal smoking during pregnancy

Stillbirths	Number of Deliveries	Percent Smokers	Comparison With Live Births±
Cause of Death:			
Vascular	8	25	
Abruptio Placentae	13	46	p = 0.005
Mechanical	13	15	
Miscellaneous (Syphilis, Rh, Malformations, . . .)	24	13	
Unknown	37	35	p = 0.0005
Detailed Records Not Available	5	–	
TOTAL	100	26	p = 0.0001
Livebirths	9069	12	

± When p is not given, the difference is not significant.

SOURCE: Goujard, J., et al. (15).

Long-Term Effects on Physical and Intellectual Development

Three studies (6, 16, 40) report on long-term effects of smoking in pregnancy. Data from two of the studies presented below demonstrate an association between smoking during pregnancy and impaired physical and intellectual development in the offspring. Additional reports further substantiate this association (10, 11).

Butler and Goldstein (6) analyzed the National Child Development Study, a longitudinal study of 17,000 children born in Britain from March 3 to 9, 1958. The test procedures included a reading

test at the age of 7 years, and a mathematics test, a reading test, and a general ability test at the age of 11. At both ages the height of the child was also measured. Analyses at both ages were based on smoking habits of the mother after the fourth month of pregnancy

Statistically significant differences in height and reading ability between smoking categories (0, 1-9, or 10+ cigarettes daily) were found at both 7 and 11 years of age.

When account was taken for such factors as mother's height, age, social class as determined by father's occupation, number of older and younger children in the household, and the sex of the child, there was a deficit of height and reading ability in the offspring of mothers who smoked, the extent of which increased with the amount smoked.

These results establish an association of smoking in pregnancy with later intellectual development, although the gap between children of smokers (at all levels of smoking) and nonsmokers does not appear to change between the ages of 7 and 11 years. Smoking in pregnancy is associated with an impairment of both mental and physical growth, although compared with other social and biological factors, the effects are small.

In the study by Wingerd and Schoen (40), the net effects of various factors on length at birth and height at 5 years were determined in 3,707 single-born, white California children. Children of smoking mothers were found to be shorter ($p < 0.001$) at birth and at 5 years than children of nonsmoking mothers. (Intellectual development was not measured in this study.)

In contrast to these results, Hardy and Mellits (16) found very few significant differences in a number of body measurements and intellectual functions up to the age of 7 years between children of smokers and nonsmokers. A possible explanation for this discrepancy is that their sample was too small, and a weight-matched control group could add a bias. Whereas the British study by Butler and Goldstein involved a sample size of over 5,000 children, Hardy and Mellits based their findings on only 88 matched pairs of children. Calculations by the authors of the British study show that with the small sample used by Hardy and Mellits there was only about a 20 percent probability of detecting statistically significant differences in the heights of children born to smoking and nonsmoking mothers.

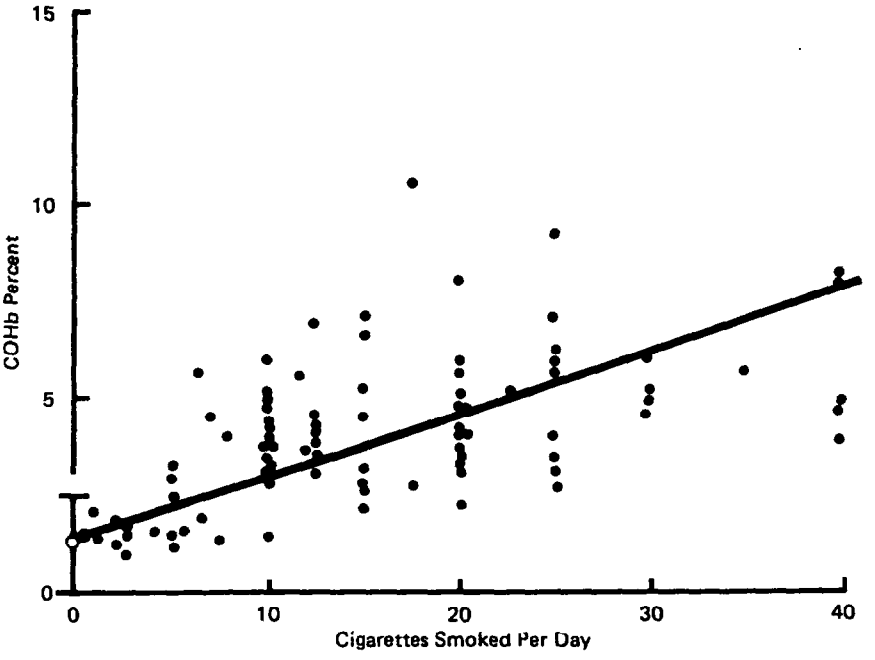
CARBON MONOXIDE AND CARBOXYHEMOGLOBIN LEVELS IN MATERNAL AND FETAL CIRCULATION AND THE POSSIBLE MECHANISMS OF SMOKING EFFECTS ON PREGNANCY

There is evidence to show that carboxyhemoglobin (COHb) levels are substantially elevated in pregnant women who smoke and may result in damage to placental and fetal blood vessels. Higher levels

of COHb in both fetal and maternal blood may also be a factor in the increased incidence of low birth weight of infants born to women who smoke.

Cole, Hawkins, and Roberts (7) studies the smoking habits of a group of pregnant women and related these to the level of COHb in the circulating blood. A group of 222 patients attending antenatal clinics at a London hospital were questioned about their smoking habits. Ninety-three (42 percent) were smokers, and 129 (58 percent) were nonsmokers. Simultaneous maternal and cord blood samples were taken at normal delivery and at Caesarean section from 28 patients, and the COHb and fetal hemoglobin levels of the samples were measured. Results showed that women who smoke during pregnancy have a significantly higher level of COHb in their blood than women who do not smoke ($p < 0.01$). The mean COHb levels were 1.2 percent (range 0 to 2.4 percent) for the nonsmokers and 4.1 percent (range 0.5 to 14 percent) for the smokers. There was a positive correlation betwen the number of cigarettes smoked on the day of sampling and the COHb level (correlation coefficient 0.82) (Figure 2). With the exception of two patients,

FIGURE 2.—Number of cigarettes normally smoked per day compared with COHb level at time of sampling in 93 pregnant women. $\bar{\varphi}$ = Mean range of COHb levels for 129 nonsmokers



SOURCE: Cole, P.V., et al. (7)

all the fetal COHb levels were demonstrably higher than the respective maternal ones. The mean fetal/maternal COHb ratio was 1.84 to 1 (standard deviation ∓0.85). Hemoglobin has a 210 times greater affinity for carbon monoxide (CO) than for oxygen. It is obvious, therefore, that cigarette smoking during pregnancy diminishes the oxygen carrying capacity of both fetal and maternal blood. This affects maternal oxygenation by increased pulmonary venous admixture and diminishes the oxygen available to the fetus at the tissue level by its effect on fetal oxyhemoglobin dissociation.

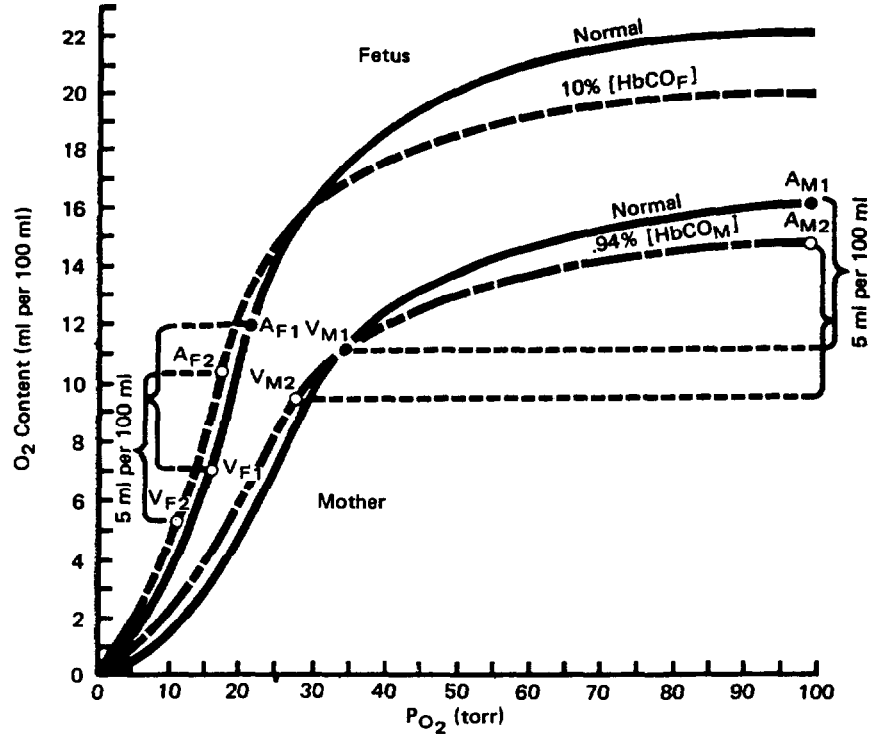
In a 1975 report by Dow, Rooney, and Spence (11), a significantly greater rise in COHb concentration in response to smoking a single cigarette was shown in pregnant women (3.9 percent increase) as opposed to nonpregnant women (2.1 percent increase). This was more pronounced when anemia was present (5.0 percent increase) and appeared to be inversely related to the hemoglobin concentration. Three groups of women, all smokers, were selected for this study. The first group consisted of 10 normal, pregnant women late in the second trimester of pregnancy, with hemoglobin levels of over 11 g per 100 milliliters (ml). The second group consisted of 10 women also late in the second trimester but whose hemoglobin levels were less than 10 g/100 ml. Apart from anemia at the time of admission to the study, these patients were normal. The third group consisted of 10 normal, nonpregnant women with normal hemoglobin levels (over 11 g/100 ml). The change in COHb was estimated spectrophotometrically in response to smoking the first cigarette of the morning, the women having rested for at least 30 minutes. A sample of venous blood was withdrawn before and 2 minutes after smoking the cigarette. The cigarettes were of a standard size and of a "non-mild" (i.e., not low "tar" and nicotine) variety. The women were instructed to take a puff every 40 seconds, inhaling as deeply as possible, to a total of 10 puffs.

In the nonpregnant group, the mean rise in COHb concentration (±standard error of mean) was 2.1±0.2 percent. A significantly greater increase was found in the normal pregnant group (mean rise 3.9±0.4 percent; $t=3.91$; $p<0.005$). The effect was more pronounced in the anemic pregnant women, who had a meaning rise of 5.0±0.2 percent ($t=9.9$; $p<0.0005$).

Longo (21) studied the effects of CO on oxygenation of the fetus in utero. Results showed that the partial pressure of oxygen in fetal blood decreases in proportion to the COHb concentrations in fetal and maternal blood (Figure 3).

This decrease in oxygen tension may be a factor in the low birth weight of infants born to women who smoke or are exposed to severe air pollution. These results suggest that significant increases in maternal and fetal COHb concentrations can significantly reduce oxygen delivery to the fetus.

FIGURE 3.–Oxyhemoglobin saturation curves of human maternal and fetal blood under control and steady-state conditions*



*With 10 percent fetal and 9.4 percent maternal HbCO concentrations. The maternal and fetal hemoglobin contents were assumed to equal 12 and 16.3 per 100 ml of blood, respectively. A normal O_2 consumption of 5 ml per 100 ml of blood was assumed for both the uterus and its contents and the fetus.

SOURCE: Longo, L., (21)

Astrup, et al. (3) carried out experimental studies on animals which may have a correlation with other data based on human studies in this report.

The investigation studied the effect of moderate CO exposure (180p.p.m. and 90p.p.m. CO in atmospheric air) on fetal development in rabbits. Exposure to 180p.p.m. CO (16-18 percent COHb) during pregnancy resulted in a 20 percent decrease in birth weight and a neonatal mortality rate of 35 percent as against 1 percent in the control group. Exposure to 90p.p.m. CO (8-9 percent COHb) had a less pronounced effect. There was a negative correlation between birth weight and maternal COHb concentration ($p<0.05$). The authors conclude that these results indicate that CO in tobacco smoke might be responsible for the reduced birth weight of babies whose mothers smoke during pregnancy.

A report from Denmark by Asmussen and Kjeldsen (2) studied the umbilical artery as a possible model for evaluating the vascular injury provoked by tobacco smoking in humans. Cords from newborn children delivered by 15 nonsmoking and 13 smoking mothers were studied in the transmission and the scanning electron microscope. The average weight of children born to smokers was 3,370 g and that of children born to nonsmokers was 3,695 g, a difference of 325 g. A difference of 123 g was found in the weights of the placentas.

Pronounced changes in the intima were found in the umbilical samples from smokers. The most important findings were degenerative changes in the endothelium, such as swelling, bleeding, contraction, and subsequent opening of the endothelial junctions, with formation of subendothelial edema. The basement membranes were considerably thickened. The smooth muscle cells in the ecematous subendothelial space often showed vacuolization. Since similar changes can be induced in arteries of animals by exposure to CO or perfusion with nicotine, the authors conclude that cigarette smoking is harmful to the vascular endothelium and may provide some rationale for the mechanism behind low birth weights and increased perinatal mortality.

SMOKING AND ITS EFFECTS ON CARDIOVASCULAR DISEASE AMONG WOMEN TAKING ORAL CONTRACEPTIVES

Smoking is a major cause of cardiovascular disease among women, and it has been found that the use of oral contraceptives potentiates its effect. Therefore, women who smoke and use oral contraceptives are at a much higher risk for cardiovascular disease and should be encouraged to stop smoking. In a review by Ory (30) of the original scientific data that exists on the association between oral contraceptives and myocardial infarction, cigarette smoking was found to be the most important factor in increasing the probability of women less than 50 years of age having myocardial infarction. Although this increased risk is independent of oral contraceptive use, oral contraceptive use appears to be an added risk factor. The use of these drugs in the absence of other predisposing factors appears to have only a small effect on increasing the risk of dying from myocardial infarction.

Jain (18) studied the risk of mortality associated with the use of oral contraceptives. For women 40-44 who neither use oral contraceptives nor smoke cigarettes, the overall mortality rate from myocardial infarction is 7.4 per 100,000 (Table 4). The comparable annual mortality rate among women of this age group who use oral contraceptives but do not smoke is 10.7 per 100,000. This compares to a rate of 62 per 100,000 for women who take oral contraceptives and smoke.

TABLE 4. Estimated annual mortality rate per 100,000 women from mycardial infarction and thromboembolism, by use of oral contraceptives, smoking habits, and age (in years)

	Myocardial Infarction				Thromboembolism			
	Women Aged 30-39		Women Aged 40-44		Women Aged 20-34		Women Aged 35-44	
Smoking Habits	Users	Nonusers	Users	Nonusers	Users	Nonusers	Users	Nonusers
All Smokers	10.2	2.6	62.0	15.9	1.6	0.2	4.1	0.6
Heavy	13.0	5.1	78.7	31.3	4.4	0.2	11.4	0.6
Light	4.7	0.9	28.6	5.7	0.7	0.2	1.9	0.6
Nonsmokers	1.8	1.2	10.7	7.4	1.4	0.2	3.6	0.4
Smokers and Nonsmokers	5.4	1.9	32.8	11.7	1.5	0.2	3.9	0.5

*Estimated rates for smokers and nonsmokers were 0.24 and 0.16 respectively. Rates appear the same because of rounding.

SOURCE: Jain, A.K. (18).

In a later study, Jain (17) analyzed the synergistic effect of smoking and the use of oral contraceptives on myocardial infarction. The relative risk of nonfatal myocardial infarction among those who use oral contraceptives and smoke is estimated to be 11.7 to 1 (Table 5). The authors suggest that smoking should be considered as another contraindication for the prescription of oral contraceptives.

TABLE 5. Estimated relative risks of nonfatal myocardial infarction, by use of oral contraceptives and cigarette smoking.

	Current User of Oral Contraceptives	
Smoking Data	Yes	No
Smokers		
Total	11.67	2.15
Heavy*	14.81	4.23
Light†	5.38	0.77
Nonsmokers	2.02	1.00

Based on data in Table VII by Mann and associates (25).

*Heavy smokers: at least 15 cigarettes per day.

†Light smokers: less than 15 cigarettes per day.

SOURCE: Jain, A.K. (17).

Results of a study by Beral (4) indicate that oral contraceptive users who smoke have a 10 times greater risk of dying from cardiovascular disease than women who neither smoke nor use the pill. Smoking by itself was responsible for a 4-fold increase in the risk of dying from cardiovascular diseases. Oral contraceptive use in the absence of smoking also appeared to increase one's risk, but the differences were not statistically significant.

Mann and his colleagues also studied the relationships between smoking and myocardial infarction in women (23, 24). Their find-

ings show an apparent but not a statistically significant increase in relative risk of nonfatal myocardial infarction for nonsmokers who use oral contraceptives (2.02, with a 95 percent confidence interval of 0.5 to 8.5). In contrast, for smokers who use oral contraceptives, the relative risk was estimated to be 11.67 compared to that of the nonsmoking, noncontraceptive user. In addition, these authors reported that the risk of nonfatal myocardial infarction was related to the amount smoked. It was found that in comparison with nonsmokers and ex-smokers, the relative risk of myocardial infarction increased significantly to 1.3 in women smoking fewer than 15 cigarettes a day, to 4.4 in women smoking 15 to 24 cigarettes a day, and to 11.9 in women smoking 25 or more cigarettes a day.

Among nonsmokers, oral contraceptive users have 2.0 (95 percent confidence interval, 0.5 to 8.5) times the risk of having a myocardial infarction. (Because the confidence interval includes 1.0, chance variation is a possible explanation for this finding.) Among smokers, if a woman uses oral contraceptives, she has 5.4 (95 percent confidence interval, 2.0 to 14.7) times the risk of having a myocardial infarction than if she is a nonuser. This result is highly statistically significant ($p = 0.001$).

EFFECTS OF CIGARETTE SMOKING ON LACTATION

Studies by Richer and Giudicelli (31), Rowan (32), and Vorherr (39), further document the effects of nicotine in breast milk on infants of smoking mothers. Since nicotine has been shown to cause nausea, vomiting, diarrhea, and tachycardia (38), it is recommended by the authors that lactating mothers refrain from smoking.

Bradt and Herrenkohl (5) studied the relationship between cigarette smoking and DDT in human milk. A total of 55 human milk samples from eastern Pennsylvania were studied. Ten of the donors were cigarette smokers, and they donated 13 of the milk samples. Results of the study showed that smoking was one of four variables which contributed to the increase in DDT. Mean total for the nonsmoker was .101 units versus .146 units for smokers. Four factors were identified statistically as accounting for 54 percent of the variance on total DDT levels in human milk. These factors are: (1) number of children nursed; (2) number of cigarettes smoked daily; (3) use of nonpersistent pesticides; and (4) diet in calories. The relationship between the number of cigarettes smoked per day and the total amount of DDT in human milk suggests either that cigarette smoke may be a source of the human body burden of DDT or that cigarette smoke may cause more DDT to be excreted in the milk.

WHAT WOMEN KNOW ABOUT SMOKING AND PREGNANCY

There is much information circulating in the scientific community

regarding the effects of smoking on health in general and, specifically, on the outcome of pregnancy. In a survey conducted by the National Clearinghouse for Smoking and Health (37), an attempt was made to find out how successfully this information had been disseminated to the general population and particularly to women.

To what extent was the average woman informed about the consequences of her smoking on her own health and the health of her unborn child? The questions were designed to find out what women knew at the time of their last pregnancy (which in some cases was many years ago) and what they knew at the time of the survey.

At the time of their last pregnancy, 24 percent said they believed smoking was hazardous to the health of a pregnant woman, and 31 percent said they believed it harmed the developing fetus.

At the time of the survey in 1975, however, 53 percent reported that they knew smoking was harmful to a pregnant woman, and 60 percent believed it harmed the fetus.

It is clear that the level of knowledge among women about the effects of smoking on pregnancy is appreciably lower than that in the scientific community.

SUMMARY OF SMOKING-RELATED PROBLEMS UNIQUE TO WOMEN

1. A strong, probably causal, association exists between cigarette smoking and higher late fetal and infant mortality among smokers' infants.
2. Perinatal mortality increases significantly with smoking as well as with other risk factors such as maternal age, parity, socioeconomic status, previous pregnancy history, and hemoglobin level.
3. A dose-response relationship exists between smoking and the incidence of low birth weight, preterm delivery, perinatal mortality, abruptio placentae, placenta previa, bleeding during pregnancy, and prolonged and premature rupture of the membranes.
4. In one study, the risk of premature rupture of membranes was more than three times greater for smokers than for nonsmokers among deliveries that occurred before 34 weeks gestation.
5. In another study, the risk of stillbirths by abruptio placentae was six times higher among smokers.
6. There is an association between smoking during pregnancy and impaired physical and intellectual development in the offspring.
7. COHb levels are substantially elevated in pregnant women who smoke and may result in damage to placental and fetal blood vessels.
8. Higher levels of COHb in both fetal and maternal blood may be a factor in the increased incidence of low-birth-weight babies among smokers.
9. The use of oral contraceptives potentiates the harmful effects of smoking on the cardiovascular system.
10. Results from one study showed that the relative risk of nonfatal myocardial infarction among women who use oral contraceptives and smoke is approximately 11.7 to 1.
11. Nicotine is present in the breast milk of lactating mothers who smoke and has been shown to cause nausea, vomiting, diarrhea, and tachycardia.
12. In one study, smoking was one of four variables which contributed to the increase of DDT in breast milk.
13. As recently as 1975, 40 percent of the women in the United States were not aware of the hazards to the developing fetus if they smoked during pregnancy.

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Chapter 2

Smoking and Overall Mortality

Contents

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INTRODUCTION

In 1964, the subject of smoking and overall mortality was examined in the Report of the Advisory Committee to the Surgeon General of the Public Health Service (9). This subject was reviewed in 1967 and 1968 in *The Health Consequences of Smoking* (6,7). Since then, the updated results of three prospective, epidemiologic studies concerned with tobacco use and overall mortality have been published (1, 3, 5). The following is a review of work previously reported as well as an analysis of the three more recent studies.

Summary of the 1964 Report (9):

1. The death rate for male cigarette smokers was about 70 percent higher than that for nonsmokers.*
2. The death rates increased with the amount smoked.*
3. The ratio of the death rate of smokers to that of nonsmokers was highest at the earlier ages (40-50) and declined with increasing age.*
4. The mortality ratio was substantially higher for men who started smoking before the age of 20 than for men who started after 25.
5. The mortality ratio increased as the number of years of smoking increased.
6. In two studies which recorded the degree of inhalation, the mortality ratio for a given amount of cigarettes smoked was greater for inhalers than for noninhalers.
7. Cigarette smokers who had stopped smoking had mortality ratios of 1.4, compared to 1.7 for current cigarette smokers.
8. The mortality ratio declined as the number of years of cessation increased.
9. Death rates for men smoking less than five cigars daily were about the same as those of nonsmokers. For men smoking five or more cigars daily, death rates were slightly higher (9 to 27 percent) than those for nonsmokers. Death rates for ex-cigar smokers were higher than for current smokers in all four studies in which this comparison could be made. One possible explana-

*Data are derived from seven major prospective studies of male smokers and nonsmokers. The rate is for smokers of cigarettes only at the time of entry into the study. These are obtained by subtracting the yearly death rate for nonsmokers from the death rate of a comparable group of smokers. This measure reflects the added probability of death in a 1-year period for the smoker over that for the nonsmoker.

tion may be that a substantial number of cigar smokers quit smoking due to illness.

10. Death rates for current pipe smokers were little if at all higher than for nonsmokers, even for those smoking 10 or more pipefuls per day and for those who had smoked for more than 30 years. Ex-pipe smokers, on the other hand, showed higher death rates than both nonsmokers and current smokers in four our of five studies. As similarly noted above, one possible explanation may be that a substantial number of cigar and pipe smokers quit smoking because of illness.

In the 1967 report of *The Health Consequences of Smoking*, additional conclusions were made relative to the effect of smoking on overall mortality (6). The highlights of that report are presented below:

1. The previous conclusions with respect to the association between smoking and mortality were both confirmed and strengthened.

2. With respect to effects of smoking on specific age groups, men 45 to 54 years of age were at greatest risk, both in terms of mortality ratios and excess deaths expressed as a percentage of total deaths. Nevertheless, although both of these measures declined with advancing age, the increment added to the death rate, which reflects one's personal chances of being affected, continued to increase with age.

3. Women who smoked cigarettes had significantly higher death rates than those who had never smoked regularly. The magnitude of the relationship varied with several measures of dosage. The same overall relationships between smoking and mortality were observed for women as for men, but at a lower level.

4. Previous findings on the lower death rates among those who had discontinued cigarette smoking were confirmed and strengthened by the additional data reviewed.

In 1968 report of *The Health Consequences of Smoking* (7) reported that the life expectancy for a two-pack-a-day or more smoker at age 25 is 8.3 years less than that for the corresponding nonsmoker. Even light smokers (those smoking less than 10 cigarettes per day) had 2.8 to 4.6 fewer years of life expectancy than corresponding nonsmokers.

MEASURING MORTALITY

Overall mortality is a term familiar to epidemiologists and statisticians but one which is not commonly used or appreciated by many who are concerned with the health of the public. To many physicians, dentists, nurses, and other health professionals who have a primarily clinical orientation, the concept of overall mortality is often not clearly understood, since it has no immediate application to their practice. Individuals die of specific diseases. Disease-specific mortality rates are of more immediate interest to many in the health care field. Overall mortality rates are particularly useful in measuring the effect of agents which affect multiple organ systems and which are capable of causing or contributing to the cause of several diseases. In contrast, disease-specific mortality rates measure the effect of an agent on a specific cause of death but fail to measure the total impact of an agent on the public health. Overall mortality is, therefore, a good measure of the cumulative or total effect of an agent on health. The problem of how best to measure the relationship between smoking and mortality has been discussed in previous reports, as well as in some of the prospective study reports. A brief discussion of some of the measures of comparison available and their utility is presented below.

Mortality Ratios: These are obtained by dividing the death rate for a classification of smokers by the death rate of a comparable group of nonsmokers. A mortality ratio has been considered to reflect the degree to which a classification variable (e.g., smoking) identifies or may account for variations in death rates. As such, it is a measure of risk which indicates the relative effect of that variable on mortality, given that other important factors affecting mortality (e.g., age) are comparable in the numerator and denominator groups.

Differences In Mortality Rates: These are obtained by subtracting the yearly death rate for nonsmokers from the death rate of a comparable group of smokers. This measure reflects the added probability of death in a 1-year period for the smoker over that for the nonsmoker. As such, it is a measure of personal health significance, a means for the individual to estimate the added risk to which he is exposed.

Excess Deaths: These are obtained by subtracting from the number of deaths occurring in a group of smokers the number of deaths which would have occurred if that group of smokers had experienced the same mortality rates as a comparable group of nonsmokers. This measure is an indicator of the public health significance of the differences found, since it measures the number of people affected and therefore quantifies the magnitude of the

problem for society as a whole.

Life Expectancy: This is a concept which is easier to understand than it is to calculate. At a given age, it represents the average number of years one might be expected to live. It identifies the point in time at which half the population in question theoretically will be dead and the other half will be alive.

DESCRIPTION OF THE STUDIES

The following is a brief description of the design and methods used in each of the three studies which are reported in this chapter. Some comments are made concerning the relative strengths and weaknesses of each study.

The American Cancer Society

The largest of the three studies discussed here is the American Cancer Society (ACS) Study (4, 8). In late 1959 and early 1960, volunteer workers of the ACS enrolled 1,078,894 men and women in a prospective study. Information was solicited on age, sex, race, education, place of residence, family history, past diseases, present physical complaints, occupation, occupational exposures, various smoking habits, and other factors. Information concerning smoking habits included: type of tobacco used, number of cigarettes smoked per day, inhalation practices, age at initiation of smoking, and the brand of cigarettes smoked from which the "tar" and nicotine content of the cigarette could be calculated. All segments of the population were included except migrant workers and similar groups that could not have been traced easily. Also excluded were mental patients and those receiving long-term medical care in institutions. Enrollment was by households, with the specification that there be at least one person over age 45 in each household enrolled. The study area covered 25 states. At the time of enrollment, each person completed a lengthy questionnaire. At 2-year intervals, for a period of 6 years, brief repeat questionnaires were administered to each surviving subject. In the follow-up questionnaires, information was obtained concerning current cigarette usage, hospitalization, diseases acquired in the interval between questionnaires, and several other items. Almost 95 percent of survivors were successfully traced the first 6 years, (that is, through June of 1966). In October 1971 and September 1972, further follow-up questionnaires were distributed to the nearly 900,000 individuals who had been last contacted in September 1965. Nearly 93 percent of the survivors were successfully followed for the entire 12 years. The time period from July 1, 1960, to June 30, 1966, is referred to as Period 1 and that from July 1, 1966, to June 30, 1972, is referred to as Period 2.