Thromboembolism, Oral Contraceptives, and Cigarettes

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THE Medical Research Council of the United Kingdom, in May 1967, released the preliminary results of a study carried out by the Committee on Safety of Drugs, comparing the use of oral contraceptives by women who died in 1966 of pulmonary embolism or infarction, coronary thrombosis, or cerebral thrombosis with that by control women selected from the practices of the same physicians (1).

The council found no relationship between use of oral contraceptives and death from coronary thrombosis. But a relationship was found with death from pulmonary embolism or infarction and possibly also with death from cerebral thrombosis. The estimated number of deaths in the United Kingdom from these conditions that were attributed to the use of oral contraceptives by married women aged 15 to 44 years was about three per 100,000 users per year.

The results of the Medical Research Council study were subsequently amplified by Inman and Vessey (2).

We used an entirely different method to estimate the upper limits of the annual excess mortality from thromboembolism among users of oral contraceptives in the United States. Our purpose was only to estimate the extent of the

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etiologic role—if any—that oral contraceptives played in thromboembolic mortality, not to prove the existence of a causal relationship.

Use of Oral Contraceptives

Our first step was to estimate the number of users of oral contraceptives in the United States in 1966 by age groups. This number was derived from the estimate by Ryder and Westoff (3) of the percentage of married women using oral contraceptives in late 1965 in the age groups 20-34 and 35-44 years. We assumed the same percentage of use by married and unmarried women. Thus, the percentage of married users in late 1965 was applied to the total female population in the respective age groups in 1966.

Using this approach, we estimated the users and nonusers of oral contraceptives in 1966 by age groups. Among women 20-44 years of age, an estimated 4,741,722 were using oral contraceptives, if we assume equal use among the married and unmarried.

If unmarried women used oral contraceptives half as much as married women, then the estimated number of users, both married and unmarried, would have been 4,346,669 in the age group 20-44 years of age; if the unmarried used them twice as much, the number would have been 5,529,681 (table 1).

Since the unmarried women in the age group 20-44 years of age are relatively few, it doesn't make much difference what assumptions are made concerning the use of oral contraceptives

by unmarried women. True, our estimates of the excess mortality rates among users of oral contraceptives vary inversely with our assumptions concerning the use of oral contraceptives by unmarried women. Nevertheless, as will be shown, even the most extreme variations in our assumptions concerning the relative use of oral contraceptives according to marital status result in little variation in the estimates of excess mortality rates among users of oral contraceptives.

Moreover, our estimate of the absolute magnitude of excess mortality due to thromboembolism which is attributable to use of oral contraceptives was not affected by our assumptions concerning the relative use of oral contraceptives by the married and unmarried.

Male Versus Female Mortality

Our second step in estimating the upper limits of the annual excess mortality from thromboembolism possibly attributable to use of oral contraceptives entailed a comparison of the levels of male and female mortality from thromboembolism before and after large-scale use of oral contraceptives began. Using basic data from the National Center for Health Statistics (supplied to us in July 1968 in a personal communication), we computed the deaths per 100,000 from thromboembolism among men and women in the age groups 20-44 years during 1956, 1961—the year large-scale use of oral contraceptives began—and 1966 (table 2).

Next, we computed the percentage change in mortality between the periods 1956-61 and

1961-66, by age and sex (table 3). It is evident that mortality due to thromboembolism in the age groups both in and beyond the reproductive period increased during both periods among both sexes. It may be significant that, with the exception of the group 20-44 years of age, the increase for both periods was about the same for all age groups and for both sexes. In women in the age group 20-44 years, however, mortality due to thromboembolism increased more than twice as much as for men from 1961 to 1966, after oral contraceptives came into use.

Excess Mortality From Thromboembolism

If we heuristically assume that the difference in the increase in mortality due to thromboembolism between men and women between 1961 and 1966 is due solely to the use of oral contraceptives, an etiological assumption which remains to be established, we can estimate the annual excess mortality among 100,000 users of oral contraceptives according to their use and nonuse of oral contraceptives, by age (table 1), the mortality due to thromboembolism among women, by age (table 2), and the increase in thromboembolic mortality, by sex and age (table 3).

Thus, we have estimated the annual excess mortality among 100,000 users of oral contraceptives by age (table 4). This estimate is based on the assumption that married and unmarried women had the same rate of use of contraceptives. Thereby, the excess mortality due to thromboembolism per annum is estimated at 3.6

Table 1. Percent of U.S. married women 20-44 years of age using oral contraceptives in late 1965 and estimated users and nonusers, married and unmarried, of same ages, in 1966

		Married wom	en, late 1965	Married a	omen, 1966	
	Age (years)	Percent of users 1	Percent of nonusers	Estimated users ²	Estimated nonusers	Total U.S. women ³
20-34 35-44		21. 6 6. 3 15. 0	78. 4 93. 7 85. 0	3, 963, 168 778, 554	14, 384, 832 11, 579, 446	18, 348, 000 12, 358, 000
20-44		15. 4	4 84. 6	4, 741, 722	25, 964, 278	30, 706, 000

¹ Reference 3.

² Estimated by applying the percent of married users in late 1965 to the female population in the respective age groups in 1966; the percent of use by the married and unmarried was assumed to be the same.

³ U.S. Bureau of the Census: Statistical abstract of the United States, 1967. Ed. 88. U.S. Government Printing Office, Washington, D.C., 1967; and U.S.

National Center for Health Statistics: Vital statistics of the United States, 1966. Vol. 1, Natality. U.S. Government Printing Office, Washington, D.C., 1968, ⁴ To standardize for differences in age distributions.

the percentage is based on the number of women in the population in 1966 who were 20-34 and 35-44 years of age.

Table 2. Mortality due to thromboembolism ¹ among U.S. residents 20—44 years of age, 1956, 1961, and 1966, by sex

A ma (maa ma)	Nun	nber of deat	ths	Rat	Rate per 100,000	
Age (years)	1956	1961	1966	1956	1961	1966
Men						
20-34	54	80	104	0. 33	0. 49	0. 59
35-44	135	150	245	1. 19	1. 27	2. 09
20–44	189	230	349	. 68	. 81	1. 19
{				2.68	2.80 -	
Women						
20–34	94	129	244	. 54	. 75	1. 33
35–44	127	157	364	1. 08	1. 26	2. 95
20-44	221	286	608	. 76	. 97	1. 98
}.				3.76	3.96 -	

¹ ICD 463-466.

3 To standardize for differences in age distributions,

deaths per 100,000 users of oral contraceptives 20-44 years of age.

The risk from oral contraception, however, increases sharply with age. We estimated the upper limits for the number of excess deaths from thromboembolism attributable in 1966 to the use of oral contraceptives to be 1.9 per 100,000 users 20-34 years old and 13.7 per 100,000 users 35-44 years old (table 4).

If the excess mortality of 3.6 per 100,000 is applied to an estimated total of 4,741,722 users of oral contraceptives 20-44 years of age in 1966, the upper limits of mortality attributable to the use of oral contraceptives in the United States in that year would be 171 deaths.

Our estimate of the absolute magnitude of excess mortality due to thromboembolism attributable to the use of oral contraceptives is not affected by our assumptions concerning the relative use of oral contraceptives by the married and unmarried. If, in the age group 20-44 years, unmarried women used oral contraceptives half as much as married women, the upper limits of the excess mortality due to thromboembolism attributable to oral contraceptives would have been 4.0 deaths per 100,000 users per year. If, on the other hand, unmarried women used them twice as much as married women, the upper limits would have been 3.1 deaths per year per 100,000 users in that age group. In either event,

the rate is based on the number of women in the population in 1966 who were 20-34 and 35-44 years of age.

SOURCE OF BASIC DATA: U.S. National Center for Health Statistics, Public Health Service.

we arrive at the same estimate of the absolute magnitude of mortality attributable to the use of oral contraceptives for women 20-44 years of age in the United States in 1966. The slight difference in the result of one of the computations, namely, 174 rather than 171 deaths, is the result of compounding differences by rounding off the numbers.

The approach we used to estimate the excess mortality from thromboembolism attributable to oral contraceptives was based on the assumption that the difference between male and female mortality was due solely to the women's use of oral contraceptives. Actually, this assumption remains to be established. Therefore, our ap-

Table 3. Percent increase in mortality due to thromboembolism ¹ between the periods 1956–61 and 1961–66 among U.S. men and women

A (1956	3–61	1961–66		
Age (years)	Men Women		Men	Women	
20–34	48	40	22	77	
35–44	6	17	6 5	134	
20–44	20	28	47	105	
45 and over	60	74	42	49	

¹ ICD 463-466.

SOURCE OF BASIC DATA: U.S. National Center for Health Statistics, Public Health Service.

² To standardize for differences in age distributions, the rate is based on the number of men in the population in 1966 who were 20-34 and 35-44 years of age.

proach merely indicates the probable upper limits of excess mortality from thromboembolism attributable to oral contraceptives; it does not establish whether any of this excess mortality due to thromboembolism is in fact attributable to oral contraceptives.

The coding and reporting of deaths from thromboembolism leaves much to be desired. Substantial error is to be expected in reporting and diagnosis. Once use of oral contraceptives became suspect as a possible etiological factor in thromboembolic deaths, this suspicion may well have alerted physicians to the possibility of such a condition and thus may have led to improved reporting of thromboembolism, particularly of deaths from this cause among women in the reproductive age group. Therefore, any etiological role that oral contraceptives have played may have been magnified by our method of estimating the upper limits of excess mortality, since this method is based on the reporting and coding of causes of death.

Other factors might explain the greater increase in mortality from thromboembolism in women compared with men, such as differential trends in smoking.

Cigarette Smoking

A Public Health Service report (4) has indicated that cigarette smoking may cause an acceleration of the thrombus formation of human blood in vitro. The adhesiveness of platelets, as measured by in vitro tests, also appears to be increased by cigarette smoking. Observations that platelet survival time is shortened and that the platelet turnover rate is increased in smokers are cited in the report. Platelets also showed an increased tendency to adhere to the vascular endothelium.

Cigarette smoking may potentiate the possible etiological role of oral contraceptives relative to thromboembolism. Such a potentiating effect is suggested when the data of Vessey and Doll (5) are retabulated to facilitate the evaluation of the possible separate or combined effects of smoking and use of oral contraceptives on thromboembolism (6). The data indicate that smoking plays a possible role in the pathogenesis of thromboembolism in combination with the use of oral contraceptives (table 5). Moreover, Vessey and Doll's data indicate a lack of asso-

ciation between use of oral contraceptives and smoking in the control patients (table 6).

In reply to our letter (6) suggesting that heavy cigarette smoking and use of oral contraceptives might interact in the pathogenesis of thromboembolism, Vessey and Doll (7) stated that it seems more probable that the association of cigarette smoking and use of oral contraceptives among thromboembolic patients was due either to an extreme effect of chance or to a sociological effect no longer present. Vessey and Doll suggested the possibility that oral contraceptives were more likely to be used by women who also smoked cigarettes, but that the association has disappeared as the use of the preparation has become more general.

Table 4. Hypothetical number of deaths in 1966 due to thromboembolism per 100,000 U.S. women 20–44 years of age, by use of oral contraceptives

Age (years)	Users	Nonusers	Annual excess deaths per 100,000 users	
20-34	2. 8	0. 9	1. 9	
35-44	15. 8	2. 1	13. 7	
20-44	5. 0	1. 4	3. 6	

Table 5. Relative distribution of female patients with thromboembolism and of female control patients, by use of oral contraceptives and number of cigarettes smoked per day

Cigarettes smoked per day	Percent of 58 patients with throm- boembo- lism		Ratio of patients with thrombo-embolism to control patients
Users of oral contraceptives smoking— 0-14 15 or more Nonusers of oral		6. 9 1. 7	3.0 to 1 14.2 to 1
contraceptives smoking— 0–14 15 or more		72. 4 19. 0	.6 to 1 .6 to 1

Source of Basic Data: Reference 5.

Table 6. Observed and expected distributions of female control patients by number of cigarettes smoked daily and use of oral contraceptives

Cigarettes smoked per day	Observed patients	Expected patients	
Users of oral contraceptives			
smoking—			
0-14	8	7. 9	
15 or more	2	2. 1	
Nonusers of oral contraceptives smoking—			
0-14	84	¹ 84. 1	
15 or more	22	21. 9	

 $^{^{1}84.1 = \}frac{(84+22)(84+8)}{(84+22+8+2)}$

Source of Basic Data: Reference 5.

Table 7. Relative incidence rates of thromboembolism by history of cigarette smoking and oral contraception

Oral	Number of cigarettes smoked per day					
contraceptives	0	1–14	15 and over	Total		
Nonusers Users	7. 2×I	1. 5×I 3. 9×I	1. 5×I 22. 7×I	1. 2×I 7. 8×I		
Total	1. 7×I	1. 9×I	3. 7×I	2. 1×I		

Note: The table is based on the history of cigarette smoking and oral contraception by 84 patients with thromboembolism and 168 control patients, 1964-67. I=Incidence rate of thromboembolism among those

I=Incidence rate of thromboembolism among those who were not smoking cigarettes nor using oral contraceptives.

Sources of Basic Data: References 5 and 7.

We had already retabulated the original data of Vessey and Doll (5) in order to indicate the lack of association between the use of oral contraceptives and cigarette smoking in the control patients (6). Moreover, a similar retabulation of their more recent data (7) confirms the lack of association between use of oral contraceptives and cigarette smoking in the control patients (8).

In our letter (6), we provided evidence for the possible potentiating effect of smoking on any etiological role of oral contraception in the pathogenesis of thromboembolism. Such potentiating effect is again suggested by merging the data from the two studies by Vessey and Doll (8).

Taking the combined data of Vessey and Doll at face value, we note that users of oral contraceptives who were also heavy smokers had an incidence of thromboembolism 23 times greater than those who neither used oral contraceptives nor smoked cigarettes (table 7). Again, if we combine the data of these authors and compare the proportion of heavy smokers among users of oral contraceptives according to the women's histories of thromboemblism, we find a difference that would occur by chance about once in 15 times (table 8).

Before we draw any firm conclusions concerning the significance of any interactions between cigarette smoking and oral contraception, we would want to observe larger samples of patients with a thromboembolism and control patients. The available data can hardly be used, however, to rule out the possibility of a potentiating effect of cigarettes on the etiological role of oral contraceptives in the pathogenesis of thromboembolism.

Unless, and until, a potentiating effect of cigarette smoking on any etiological role of oral contraceptives can be ruled out, our results suggest that it would be prudent to consider use of oral contraceptives as a contraindication to smoking.

Relative Risks

If our estimates of the upper limits of excess mortality are correct and the etiological role of oral contraceptives is confirmed, then the increased risk of mortality due to thromboembolism attributable to the use of such contraceptives would be less than four deaths per year per 100,000 women 20-44 years of age using oral contraceptives. The risk of death from using oral contraceptives would be about the same as the risk attributed to complications of pregnancy, childbirth, and the puerperium in the United States in 1966, namely, 3.1 deaths per 100,000 women 20-44 years of age.

The number of deaths in the United States attributed to complications of pregnancy, childbirth, and the puerperium among women 20-44 years of age declined from 1,433 per annum in 1961 to 937 in 1966. Deaths attributed

to abortion declined 43 percent and deaths attributed to the remainder of maternal mortality declined 32 percent between 1961 and 1966. During the same period, the number of births declined 19 percent. At least part of these declines are reasonably attributable to the increasing use of oral contraceptives since 1961.

The reduction in maternal mortality in the order of 496 deaths per annum may be compared with the hypothetical excess of 171 deaths due to thromboembolism in 1966. These 171 deaths are the hypothetical and maximum increase in the annual number of deaths that we can attribute to oral contraceptives if we are prepared to assume that the entire difference between the increases in male and female mortality from thromboembolism between 1961 and 1966 is attributable to oral contraceptives. Of course, the etiological role of oral contraceptives remains to be established and, if established, it may not prove to be as great as 171 deaths, since other factors could well explain at least part of the observed differences between the sexes in thromboembolic mortality.

Furthermore, a changeover to oral contraceptives of lesser dosage might reduce the excess mortality from thromboembolism attributable to use of oral contraceptives (9).

We do not wish, however, to minimize the possible risks from the use of oral contraceptives. From a public health point of view, it seems prudent to consider that the association between use of oral contraceptives and thromboembolism may be causal. When the excess mortality from thromboembolism possibly caused by oral contraceptives is compared, however, with the mortality from other hazards in the American environment, oral contraceptives are clearly a relatively minor hazard.

Less than 171 of the deaths in the United States in 1966 from thromboembolism in the age groups 20-44 years can be attributed to oral contraceptives, whereas more than 300,000 can reasonably be attributed to cigarette smoking. Fifty thousand of the 300,000 deaths occurred in women (10), many of whom were of reproductive age. (The estimate of 171 is based on tables 1 and 4, which show an estimated 4,741,722 users of oral contraceptives in 1966 and an excess mortality per 100,000 users of 3.6. Our method estimates the upper limits of excess mor-

Table 8. Relative distributions of heavy smokers among users of oral contraceptives according to history of thromboembolism

Users of oral	Number of cigarettes smoked per day			
contraceptives	0–14	15 and over	Total	
Control patientsPatients with thromboem-	20	3	23	
bolism	26	16	42	
Total	46	19	65	

Note: With the Yates correction, the chi-square equals 3.3, indicating a probability of chance occurrence between 0.05 and 0.10.

Sources of Basic Data: References 5 and 7.

tality among users, but does not establish any etiological relationship. Different assumptions concerning the relative use of oral contraceptives according to marital status do not affect our estimate of the absolute magnitude of thromboembolic mortality.)

A total of 937 deaths in the United States in 1966 were attributed to complications of pregnancy, childbirth, and puerperium (11). This total represents 3.1 deaths per 100,000 women 20-44 years of age and 3.6 deaths per 100,000 women 20-44 years of age not using oral contraceptives. A total of 4,457 deaths of women 20-44 years of age were attributed to motor vehicle acidents (11). This total amounts to 14.5 deaths per 100,000 women 20-44 years of age and 19.0 deaths per 100,000 licensed female drivers in this age group. In contrast, the excess mortality from thromboembolism attributable in 1966 to the use of oral contraceptives was less than four deaths per 100,000 users 20-44 years old.

Of course, it would be safer to quit smoking cigarettes and to take oral contraceptives than to quit taking oral contraceptives and smoke cigarettes. As aptly stated by Pott (12), "from the point of view of the health of society it would be more justifiable to have oral contraceptives in slot machines and restrict the sale of cigarettes to a medical prescription."

The possibility remains that the use of oral contraceptives may contribute to other causes of mortality. The causal nature and the magnitude of any suspected relationships, however, remain to be established.

Furthermore, since our method cannot be used to estimate the incidence and severity of any morbidity that might be associated with the use of oral contraceptives, we have not evaluated the magnitude of such risks. Serious disease and severe disability could prove to be a more frequent and, therefore, a more important consequence of the use of oral contraceptives than death. Still, the etiological role of oral contraceptives as a cause of disease remains to be fully and conclusively established.

International Comparisons

Our estimate of the annual excess mortality attributable to oral contraceptives was based on the difference between the increase in male and female mortality attributable to thromboembolism in the reproductive age groups after the large-scale use of oral contraceptives began. Our analysis (13) of British data indicates a similar divergence in the trends of male and female mortality from this disease since 1961 (table 9).

The question has arisen whether the data for men and women in the age group 20-44 years of age from different countries and for different years can be compared without standardization for differences in the distribution of the populations to the age groups 20-34 and 35-44 years. Actually, the proportion of men or of women in England and Wales and in the United States in the age groups 20-34 years, when expressed as a percentage of the total men or women 20-44 years of age, varied at the most between 58 and 60 percent in the years 1956, 1961, and 1966.

Such slight differences in age distribution do not require adjustment of the mortality rates for differences in distributions of the populations to the age groups 20-34 and 35-44 years if our purpose is to compare the levels of mortality in the age group 20-44 years by sex, country, and year. The effect of such standardization was virtually nil for such differences in age distributions (table 2).

Markush and Seigel reported that U.S. trends in mortality from thromboembolism are consistent with those in British reports. This consistency suggests that use of oral contraceptives is associated with an increased risk from venous thromboembolism (14). Vessey and Weatherall concluded that in England and Wales the mortality from venous thromboembolism had increased in young women in recent years in a magnitude compatible with the existence of a causal relation between use of oral contraceptives and death from venous thromboembolism (15).

More recently, Seigel and Markush (16) and the Advisory Committee on Obstetrics and Gynecology of the U.S. Food and Drug Admin-

Table 9. Annual death rates from thromboembolism ¹ with ratios of female to male mortality and indices of mortality, for England and Wales and the United States, 1956, 1961, and 1966

	Deaths	per 100,000	Ratio of female to	Indices of mortality	
Year -	Men Women		- male mortality	Men	Women
		England and Wales			
1956 1961 1966	0. 65 . 57 . 81	0. 86 . 61 1. 53	1. 32 1. 07 1. 88	100 88 125	100 71 178
-			United States		
1956 1961 1966	0. 68 . 81 1. 19	0. 76 . 97 1. 98	1. 12 1. 20 1. 66	100 119 175	100 128 261

¹ ICD 463-466.

istration (17) have arrived at similar conclusions concerning the association of increased use of oral contraceptives with increased U.S. mortality attributed to venous thromboembolism.

At the outset we noted that the Medical Research Council of the United Kingdom had estimated the annual mortality from thromboembolism attributable to the use of oral contraceptives by married women 15-44 years of age in the United Kingdom to be about three per 100,000 users. By an entirely different method, we estimated that the upper limit of mortality from thromboembolism in the United States attributable to the use of oral contraceptives by married and unmarried women 20-44 years of age was in the order of three to four deaths per annum per 100,000 users 20-44 years of age.

Summary

The upper limits of the excess mortality from thromboembolism in 1966 that was possibly attributable to use of oral contraceptives by American women 20-44 years of age was estimated to be in the order of three or four deaths per 100,000 users. Less than 171 of the deaths from thromboembolism in the United States in that year could be attributed to use of oral contraceptives by women 20-44 years of age.

These results, obtained by a different method, confirm previous estimates of the levels of mortality due to thromboembolism resulting from use of oral contraceptives in the United Kingdom and the United States.

The annual risk of mortality attributed to thromboembolism from use of oral contraceptives is comparable to the mortality risks due to all causes of death that result from complications of pregnancy, child birth, and the puerperium, namely, 3.1 deaths per 100,000 women 20-44 years of age and 3.6 deaths per 100,000 women 20-44 years of age not using oral contraceptives. The risk of death from thromboembolism resulting from oral contraception increases sharply with age.

Users of oral contraceptives who were heavy smokers had an incidence of thromboembolism 23 times that of women who neither used oral contraceptives nor smoked cigarettes. When the proportion of heavy smokers among users of oral contraceptives having thromboembolism was compared with the proportion of heavy smokers among users of oral contraceptives having no thromboembolism, an association was found between heavy smoking and thromboembolism that would occur by chance about 1 in 15 times.

Firm conclusions concerning the significance of any interactions between cigarette smoking and oral contraception must be based on larger samples. Nevertheless, the available data can hardly be used to rule out the possibility that cigarettes may potentiate the etiological role of oral contraceptives in the pathogenesis of thromboembolism. This possible potentiating effect suggests that oral contraception be considered as another contraindication to cigarette smoking.

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Tearsheet Requests

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Treatment of Scalp Ringworm With X-ray May be Linked to Cancer and Mental Illness

A research program, supported by the Environmental Control Administration's Bureau of Radiological Health, is investigating a possible relationship between X-ray treatments administered to more than 20,000 young people in Israel 10–20 years ago and incidence of mental and nervous diseases and cancer.

The young people were exposed as children to large doses of X-radiation as treatment for ringworm of the scalp (tinea capitis) during an epidemic of ringworm at the time of the 1949–59 wave of immigration into Israel. The treatment was to remove hair temporarily by exposing the scalp to X-radiation from 75 to 100 kilovolt machines. Since the introduction in 1958 of drugs effective against ringworm, X-ray has been used infrequently.

The Israeli experience provides a unique opportunity to investigate the late effects of relatively high radiation exposures among a large population. Such research, by increasing knowledge of relationships between radiation levels and human health effects, will enhance the Bureau's ability to weigh benefits against risks in the use of radiation.

The epidemiologic study is designed as a

3-year project. The work is being conducted under a research agreement with the Tel Hashomer Hospital in Israel.

During the study, investigators will (a) contact young people who were treated with X-rays for ringworm of the scalp to obtain medical histories, (b) study hospital records of the irradiated group for detailed information on the occurrence of cancer and mental and nervous diseases, and (c) compare disease incidence for the study group with a non-irradiated control group.

The study follows research on the subject of scalp irradiation by both the Bureau of Radiological Health and the Institute of Environmental Medicine of the New York University Medical Center. Bureau laboratory investigations have correlated the doses to brain, eye, and thyroid for a variety of skull sizes and X-ray techniques for treating ringworm of the scalp and have shown that similar exposures to animals produce detectable chemical alterations in the brain. Research at New York University showed an increased incidence of cancer and mental illness in a sample of approximately 2,000 patients in New York City treated with X-rays for scalp ringworm.

Survey of Postdoctoral Education in the United States

Postdoctoral education in the United States has grown to institutional status without study or planning, according to a special committee of the National Research Council's Office of Scientific Personnel. The committee, after surveying more than 700 institutions, estimated that there are about 16,000 postdoctorals, persons at the doctorate level who hold temporary appointments to continue their education and conduct research.

The committee's report, "The Invisible University: Postdoctoral Education in the United States," is available from NRC's Printing and Publishing Office, 2101 Constitution Ave. NW., Washington, D.C. 20418 (Publication No. 1730-0, \$10).

This study, the most comprehensive of its kind to date, was directed by Richard B. Curtis, associate dean of the Office of Research and Advanced Studies at Indiana University. Sanborn C. Brown, professor of physics and associate dean of the graduate school at the Massachusetts Institute of Technology, was chairman of the study committee. Staff leadership during the first-half year was provided by Robert A. Alberty of the Massachusetts Institute of Technology, and for the remainder by Dr. Curtis, who was on leave from Indiana University.

Postdoctoral activity at the intermediate and senior levels often has the greatest impact on the quality of teaching; therefore the committee recommends that more postdoctoral opportunities be made available at these levels. Currently about 60 percent of the postdoctorals have recently received Ph.D.'s or M.D.'s.

According to the committee, 45 percent of the postdoctoral population in this country is foreign, and a steady flow of foreign postdoctorals should be maintained so long as the essentially American atmosphere is not sacrificed. The United States should encourage foreign post-

doctorals to return to their countries after completing their research activities. It is also important that more American Ph.D.'s have the opportunity to work and study abroad.

Postdoctoral education should have bettercoordinated programs of training and support. The committee suggests that postdoctorals be considered when existing space in institutions is being allocated or new facilities are being planned, and they should have their own source of support so that they are not dependent on the senior scientist for their research activities.

This 2½-year study was supported by the Alfred P. Sloan Foundation, the National Institute of General Medical Sciences, the National Endowment for the Humanities, the National Science Foundation, the National Aeronautics and Space Administration, and the U.S. Office of Education.

Number of postdoctorals, by field and percent foreign

Field	Num- ber	Per- cent	Per- cent foreign
Astronomy	108	1. 0	56
Mathematics	240	2, 2	40
Physics	1, 267	11. 8	50
Chemistry	1, 660	15. 5	63
Earth sciences	189	1. 8	54
Engineering	274	2. 6	64
Biochemistry	1, 322	12. 3	51
Other basic life sciences	1, 030	9. 6	40
Other biosciences	907	8. 4	44
Agricultural sciences	55	. 5	62
Internal medicine	1, 059	9. 9	36
Other medical sciences	1, 166	10. 8	35
Allied medical sciences	425	4. 0	37
Psychology	246	2. 3	11
Social sciences	196	1. 8	36
Arts and humanities	228	2. 1	23
Other fields	368	3. 4	36
Total	10, 740	100. 0	45

Source: NRC, OSP, postdoctoral census questionnaire.