SUMMARY

An analysis has been made documenting some of the contradictions, inconsistencies and omissions of the report on "Smoking and Health," which was issued by the Royal College of Physicians, March 7, 1962. Some important facts are as follows:

1. The authors say they are giving a "full summary of the evidence." The fact is they omit scores of pertinent references to many scientific papers that do not support their attitude toward smoking.

2. They naturally recognize there are "gaps and apparent discrepencies" in their own presentation, but say they "must accept the hypothesis" that cigarettes are a major cause of lung cancer -- even though recognizing that it is just "hypothesis."

3. The authors state that substances in tobacco smoke do "not seem likely to be sufficient to account for" the association of smoking with human lung cancer. They say this is a "wide field for further investigation."

4. The committee that wrote the report states that tobacco use is something "most smokers enjoy without injury to health." Yet they advocate a general governmental campaign to discourage everyone from using tobacco.

5. In the United States, it should be noted that the age-adjusted death rates have been declining, rather than increasing, during the past 20 years for most of the diseases which the report attempts to blame on cigarette smoking. Even for the major exception -- lung cancer -- the rate of increase in recorded deaths has been slowing during the past 30 years, according to a 1961 study by National Cancer Institute scientists, who say that if the trend continues, lung cancer will reach a peak in the forseeable future and then start to decline.

6. On one hand, the authors dismiss experiments showing that "exposure of animals to tobacco smoke in inhaled air has failed to produce lung cancers." But they stress much less relevant experiments in which tobacco smoke condensates were painted on the skin of animals.

7. They say it is "not possible to assert" from the evidence that "the association between coronary disease and smoking is causal."

8. The authors say that "smoking does not appear to be a cause of ulcers in the stomach and duodenum" and that "the incidence of gastric ulcers has diminished." Nevertheless they attempt to implicate tobacco use with ulcers.

9. They suggest stamping on cigarette packs the amount of smoke condensates and nicotine of the cigarettes. Yet they admit they cannot identify substances "that may be injurious" and that no claims can be made that one type of cigarette is safer than another.

In short, the report is a review of old and inconclusive data. No new findings are advanced to support the conclusions advanced by the nine-man committee that prepared the report. It relies almost entirely on statistical studies that have been the subject of public and scientific debate for some years. Little or no attention is given in the report to much evidence that shows many factors may be involved in the diseases discussed.

3/7/62

SOME COMMENTS ON THE ROYAL COLLEGE OF PHYSICIANS REPORT*

The report on smoking and health developed by a nine-man committee of the Royal College of Physicians of London, England, relies almost entirely on a number of statistical studies, the validity and interpretation of which have been for many years, and continue to be, in controversy (1-17). The report gives little or no weight to a steadily growing body of evidence that recognizes the possible implication of factors other than tobacco in lung cancer causation (14, 18-24). The report dismisses with brief mention the failure of experimental and laboratory research to demonstrate a lung cancer-causing role of tobacco smoke (25-29).

As to heart disease and other ailments, the report is so ambiguous that it seems obvious there must have been an awareness of the impressive volume of literature that has been published during the past ten years on the complex etiology of these diseases, although only scant mention is given.

There can be raised three major objections to the manner in which this report is presented. These are summarized below. The more important aspects will be discussed later in fuller detail.

First, the report does not present an impartial review of all the data relating to the health conditions discussed. It does not examine the total evidence relating to the various diseases but considers only selected material related to a single aspect of human experience -- smoking.

There is no mention at all of the mounting volume of research pointing to the possible role of viruses in human cancers (30-34) and demonstration of their role in animal lung cancers (35-38). There is no consideration of the studies which show associations between lung cancer and previous chest diseases (39-44). Neither are genetic (45-48), psychological (49-58) and other associations with human cancer considered by the report.

Second, the report purports to have considered and evaluated views that disagree with the conclusions presented:

"The report ... reviews the evidence for and against the hypothesis that smoking causes various kinds of disease..." (para 3). The only "evidence against" this hypothesis cited in the report are three papers by Berkson (3-5) and three by Fisher, which are all included in his book (7). There are no references to other authors who disagree specifically with the hypothesis (2, 8-17, 59).

Moreover, the report fails to elucidate fully certain of its own observations: "Although most smokers suffer no serious impairment of health or shortening of life as the result of their habit..." (para 96), and "There can, of course be no question of prohibiting a habit which most smokers enjoy without injury to their health..." (para 103). These statements could readily suggest the existence of evidence that smoking is not a "necessary and sufficient" factor in the causation of disease (see 17). The possibility of there being a small minority susceptible to exceptional health risk is not even considered.

* "Smoking and Health," publ. by Pitman Medical Publishing Co., Ltd., 1962

Third, the report purports to demonstrate impartiality by reviewing "other possible explanations which must be considered" (para 32), and it presents some of these in the technique generally known as "setting up a straw man" that can be easily knocked down. For instance, the report says: (vi) Since there is generally held to be a correlation between heavy smoking and heavy drinking, it has been suggested that alcohol might be the common factor associated with both smoking and lung cancer."

The only scientific paper on this subject, presented by Dr. J. J. Versluys of the Netherlands at the Seventh International Cancer Congress in London in July 1959 (60) showed higher lung cancer rates for people in a drink-profession than in the total population (stomach cancer was less). He concluded: "Is the high alcohol consumption directly responsible for an increased cancer mortality or does it affect only the earlier appearance of potential cases of carcinoma? I am inclined to accept this latter possibility...." He did not suggest alcohol as the common cause of smoking and lung cancer. The Royal College report does not say who suggests this.

This section (para 32) of the report also omits mention of considerable data that disagree with its rebuttal of alternate hypotheses. For instance, it says: "(iii) The fall in mortality from pulmonary tuberculosis might be related to the rise in mortality from lung cancer.... No one has shown that susceptibility to tuberculosis and lung cancer are related..." The facts are very different. More than 100 papers in the past decade have found lung cancer to have developed in lung scars resulting from tuberculosis. Mention of a few will suffice (39-44, 61-64).

The same section (para 32) also says: "(vii) The possibility that motor vehicle exhausts might be an important cause of the recent increase in incidence of lung cancer can be rejected since there is no increase in lung cancer death rates among road haulage workers...." This reliance on one report is superficial, in view of accumulating evidence to the contrary. Exposure to urban traffic and higher automobile driving mileage has been found significantly associated with lung cancer (65, 66); so have idling motors at red lights (67). There are many studies linking auto exhausts and diesel fumes with lung cancer incidence (a few are referred to here: 68-72).

Also, <u>unlike</u> cigarette smoke, an atmosphere of ozonized gasoline has produced lung cancer of the prevalent human type in laboratory animals at highly significant levels (73-74). This is ample evidence that mice lungs <u>are</u> susceptible to the same form of lung cancer as humans.

SINGLE-TRACK STATISTICS

In the introduction, the report says (para 1): "Several serious illnesses, in particular lung cancer, affect smokers more often than non-smokers..." One important objection to the statistics upon which this statement is based is that, in the epidemiological studies cited, the telescope has been turned around and one single factor in the life of the individual has been subjected to statistical analysis. Many others are not in view. Many factors have been found related to lung cancer incidence: sex, race, origin, residence, constitution, occupation, socio-economic status, previous chest diseases, psychological and other differences -- when they, too, have been the object of study. Some examples:

1. Origin: Ethnic group variations in lung cancer incidence have been found in several special studies of this factor (75-80).

2. Socio-Economic Status: Lung cancer has been found more frequently among the poor than among the well-to-do in many studies, of which a few are cited here (78-87).

3. Residence: There are innumerable studies of urban-rural differences in lung cancer incidence. A random selection from these is presented (88-93).

4. Occupation: Because of the plethora of studies on occupational cancer, the following comprehensive surveys have been selected as references rather than individual papers (94-95).

5. Sex: There is a considerable lack of concurrence as to the reasons why men are more susceptible to lung cancer than women. Some authorities believe there are definite sex-linked characteristics, hormonal or genetic, applicable to lung cancer and other chest diseases (96-99).

IS LUNG CANCER INCREASING?

An unsettled question is the extent, if any, to which lung cancer has been increasing in incidence in recent years, as some data presented make it appear (para 23). An extensive body of medical literature finds that the increase in lung cancer is more "apparent" than real, for a number of reasons (8, 14-16, 86, 100-105). With increasing longevity, the proportion of the population at cancer-prone ages is rising rapidly (86). Increased knowledge of lung cancer, with better and more kinds of diagnostic facilities available in many more places, have permitted accurate detection of the disease far more frequently than in the past (14-16). This in turn has produced more reliable death registration, so that, today, most lung cancer deaths are so recorded.

However, 10, 20 and more years ago the death certificate of a person dying of lung cancer might have read "pneumonia," "tuberculosis," "heart failure," or something else, including a catch-all item known as "senility and other ill-defined conditions," to cite only a few of the authorities who agree on this point (100, 155-160).

Others who have studied the records of the past and found them wanting in accuracy with respect to lung cancer recording include government and insurance biostatisticians and hospital pathologists (8,9,15,16, 100-110, 154).

TUBERCULOSIS AND LUNG CANCER

The rapid decline in respiratory tuberculosis mortality is almost a reverse image of the rise in recorded lung cancer deaths. Coupled with the evidence showing that respiratory tuberculosis, latent or cured, predisposes to lung cancer (39-44, 62-64) and the evidence of errors in death recording in the past (see preceding paragraph; also 98) is the fact that it is very difficult to tell these conditions apart on X-ray films or even after thorough examination. Tuberculosis bacilli often lurk in the respiratory tracts of persons who do not have the disease.

If the recorded death rates from these two diseases is added together, it will be seen that the human lungs today are less frequently found in the mortality records than 10, 20 and more years ago. A look at age-adjusted death rates of the United States (a country where cigarette smoking has been on the increase), for example, shows the following mortality for several diseases referred to in the Royal College report:

Age-adjusted death rates, all races, both sexes, per 100,000, U.S.

Cause of death	1940	1950	1959
Respiratory tuberculosis	42.2	19.9	5.5
Respiratory cancer	7.2	12.8	18.8
Combined rate	29.4	32.7	24.3
Bronchitis	3.0	1.6	1.8
Gastric & duodenal ulcers	6.8	5.0	5.1
Cardiovascular diseases	485.8	440.1	407.9

DISCREPANCIES ADMITTED

The report acknowledges the inadequacy of the data presented in support of its "hypothesis" -- the word it uses (paras 3 & 33) -- by saying: "There are however several gaps and apparent discrepancies in the evidence which require further consideration" (para 33). One of these discrepancies, the male-female lung cancer ratio (para 36) has been briefly mentioned above (Item 5, page 3). Despite the fact that most observers agree with the report (para 6, last sentence) that per capita smoking among women has risen rapidly for many years, while per capita cigarette smoking among men has risen only moderately, a study of the mortality data in the United States, for instance, shows a widening of the male-female lung cancer ratio, instead of the narrowing which might be expected if cigarette smoking were the factor in rising lung cancer mortality.

In 1925 the ratio of male to female respiratory cancer mortality per capita in the U.S. was 3 to 1; in 1940 it was 3 1/3 to 1; in 1950 it was 4.44 to 1; and in 1959 it was 6 to 1.

In Canada a similar widening of the ratio has been reported. In 1941 the male to female respiratory cancer ratio was slightly less than 3 to 1. In 1950 the ratio was 5 to 1. In 1958 the ratio had risen to nearly 7 to 1. (Phillips, A. J., Brit. J. of Cancer, 15:1, 1961)

This discrepancy has been noted for earlier periods (110) and in England (102) as well. Several authors suggest that hormonal and/or genetic factors may be operative here (96-99). Moreover, war-time losses of the healthiest male specimens may conceivably have left a masculine population more prone to lung cancer, heart disease and other ailments than their female contemporaries, who were not subjected to similar selective elimination by warfare (11, 85).

The report says "there is a great deal of evidence" that cigarette smoke is an important cause of lung cancer (para 24). It also says, "exposure of animals to tobacco smoke in inhaled air has failed to produce lung cancers" (para 37), but claims "the causative hypothesis... can still stand without this support (of animal experiments)" (para 38). It further refers to the "infinitesimal amounts" of carcinogenic substances (para 19) in tobacco smoke. It then guesses: "Indeed the action of tobacco might be simply to produce chronic irritation which, as in other tissues, may increase liability of the lung to cancer" (para 39). This is all hypothesis: note "might be" and "may be" in sentence. The paragraph continues: "There is wide field for further investigation here, but no ground for refuting the evidence from human experience." There are solid reasons for questioning the phrase "human experience." The report can only mean "the statistical studies."

The negative results of the animal research have been referred to (25-29). The fallacies in extrapolating the effects of experiments on animal skins to a putative effect on human lungs have been noted by several authorities (15, 16, 103, 110-116). There has been no consistency in results even in animal skin painting tests with tobacco smoke condensates (see British Empire Cancer Campaign Annual Reports 1954-1960 for a series of negative results). Moreover other factors than skin painting with condensates may be involved in the results or failure thereof (117). Most important, it has been shown that the high (60°C-140°F) exit temperatures attained in machine-producing the cigarette smokes used by Wynder and his associates, (who although the most successful in such tests, obtained skin cancers in only a minority of the mice after half a lifetime of frequent painting,) exceeded by far what human smokers encounter or could endure (118).

CARCINOMA IN SITU

The report relies in one place on studies by Auerbach and associates (para 31), and says: "There was a quantitative relationship between cigarette consumption and the frequency of microscopic changes (in human tracheobronchial trees) suggesting chronic irritation. Such changes are possible precursors of some types of cancer and were more frequent in the men with lung cancer." What Auerbach claims is that tracheal and bronchial tissues are subject to progressive changes ranging from normal through hyperplasia, stratification, metaplasia, carcinoma in situ, to cancer, and that cigarette smoking is quantitatively related to this progression.

The report does not refer to numerous similar studies that conflict in whole or in part with Auerbach's findings. Hyperplasia, stratification and metaplasia are known to result from most of the severe chest diseases (119-131), and to result from normal "healing" action of damaged tissues (129, 131, 132). Other scientists found no evidence that these tissue changes lead to cancer (122, 133-137).

Auerbach changed his position on carcinoma in situ radically after his work was criticized (138). Other authorities could find no carcinoma in situ whatsoever in the absence of lung cancer (121-123, 126, 128, 129, 131, 132, 135-137, 139, 161). Several specifically noted their dissent from Auerbach's findings (121, 132, 133, 136, 139). The term carcinoma in situ means "cancer that stays in place" -- has not yet invaded other tissue -- and is considered a misnomer by many authorities (140).

The tissue changes reported by Auerbach in his collection of excised tracheobronchial trees have been noted by others in children and non-smokers (123, 136), and some heavy smokers over a life-time have normal respiratory tissues (136,139). Finally, Auerbach reported all the various tissue changes to be more frequent in the trachea than in the bronchi and in the bronchioles, whereas cancer of the trachea is an extremely rare disease (92 deaths in the U.S. in 1959, compared to 17,042 primary lung and bronchus cancers and to 17,139 lung cancers unspecified as primary or secondary), a point noted by many authorities (123, 131, 132, 134, 139, 140). They raise the question: If indeed these changes lead to cancer, why do they not cause cancer of the trachea at least as frequently as they are supposed to cause cancer of the bronchi? Experimental studies show that similar changes in laboratory animals are reversible, and not precancerous at all (26, 141, 142).

DIFFERENT KINDS OF LUNG CANCER

The report says, "There are three principal pathological types of lung cancer, and precision in microscopical diagnosis shows that smoking is associated specifically with two of these" (para 30). The question of "precision" in lung cancer typing has been the subject of continuous debate and differences of opinion for years. The point of the question is whether or not the "typing" of lung cancers in accordance with the physical appearance and disposition of the cells in cancer tissues can be standardized or is even accurate, because, among other reasons, most cancers contain most of the different cell types in close proximity in varying degrees (143-147).

By histochemical studies combined with histological observation -- determination of the chemical content of the cancer tissue in addition to microscopic determination of cellular appearance -- two American researchers, assisted by several leading pathologists and epidemiologists, recently re-opened to serious reconsideration the problem of precision in lung cancer typing (148).

These authors examined 956 well-preserved lung specimens collected at autopsy in Los Angeles over 31 years and demonstrated that many lung cancers whose appearance was that of epidermoid (surface) cells were actually adenocarcinomas arising from the mucous glands, as proved by the chemistry of the tumors. By methodical classification of all 956 cancers by years of death they showed that the adenocarcinomas had increased in frequency over the 31 year period while the epidermoid cancers had fallen during the same period.

Yet the whole hypothesis of cigarette smoking being involved in lung cancer has rested on the belief that epidermoid lung cancer was on the increase and that this increase was due -- at least in large part -- to increased cigarette smoking.

The Los Angeles findings are precisely opposite to the findings presented in the Royal College report, which was based solely on the views of Dr. Leiv Kreyberg of Norway applied statistically to British data by W. R. Doll and A. B. Hill. Kreyberg's theory was that epidermoid cancers of the lung -- squamous cell and undifferentiated -- were more common in men than in women, were rising year by year, and were due to something new in the environment -- Kreyberg said it was cigarette smoking. He believed adenocarcinomas and certain minor related cancers were of glandular or unknown origin, were not rising in frequency, and were equally common in men and women.

CAUSE AND EFFECT

The report says: "The strong statistical association between smoking, especially of cigarettes, and lung cancer is most simply explained on a causal basis" (para 41). Biostatisticians as a class usually are more rigid in definition of causality than are clinicians, although the statistical studies on which the Royal College relies were the work of biostatisticians and not clinicians. For instance, a standard textbook (149) lists among numerous statistical fallacies the following:

"The assumption of a cause-and-effect relationship between two associated events. Each of the two events may be the result of a third set of antecedent events....

"The fallacy of misplaced concreteness.... For example, analysis may lead to conception of the parts as 'reals' which exist independently, whereas they have been abstracted from the gestalt in which they occur....

"Failure to recognize multiple causes....

"The error of the untested assumption....

"Confusion of the normal with the average."

And so on.

Several authorities have paid special attention to the cause-and-effect fallacies in the cigarette smoking - lung cancer studies (2-6, 9, 10, 13-16, 150-153). Dr. Berkson of the Mayo Clinic recently remarked (6) that "there has developed a fairly vigorous movement to determine the causes of disease by a search for statistical associations of death rates and particular physical factors... It is called the 'New Epidemiology.' I have been following some of the writings of this school and am impressed with:

"1. The courage with which questions of the etiology even of diseases that have defied the best efforts of the greatest biologic investigators for generations are declared to have been solved easily by the study of statistical associations -- and without independent substantiation by biologic investigation.

"2. The practice of attending to the association of particular diseases with particular factors that appear etiologically plausible, while neglecting to note similar associations of the same disease with other factors and the same factors with other diseases -- another variant of the fallacy of misplaced concreteness."

SUMMATION

As to the section of the Royal College report calling for specific actions to be taken against cigarettes by government and physicians (paras 112-121), one may turn to another paragraph (100) for this statement: "It should be realized that since we cannot identify the substances in tobacco smoke that may be injurious to health, no firm claims for the safety of modified cigarette tobaccos or filters can be made."

Would it not have been closer to the facts had this statement read as follows: "It should be realized that since we cannot identify the substances in tobacco smoke that may be injurious to health, no firm claims as to the cause or causes of the diseases herein discussed can be made, and further research is required to ascertain the truth."

March 7, 1962

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