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- I. Studies designed to explore whether constitutional and genetic factors give rise to the statistical associations between smoking and disease indicated by existing epidemiological surveys.
 - II. Studies designed to show the limitations of existing epidemiological surveys.
 - III. Studies designed to test the mechanisms suggested for cigarette causation of lung cancer and the other pertinent diseases.
 - IV. Studies designed to explore the existence and role of various factors other than cigarette smoke suspected in connection with the pertinent diseases.
 - V. Studies designed to test Dr. Auerbach's conclusions concerning "pre-cancerous" changes in human lungs.
 - VI. Studies designed to show limitations of existing animal experimental results.
 - VII. Studies designed to explore beneficial effects of smoking.

I. Studies designed to explore whether constitutional and genetic factors give rise to the statistical associations between smoking and disease indicated by existing epidemiological surveys.

1. Project: Symposium of experts to assist in creating major epidemiological studies designed to explore the genetic and constitutional questions raised by the existing epidemiological studies.

Cross-Reference: II

Purpose: To explore whether the associations indicated between smoking and disease in existing epidemiological surveys are reflections of basic differences between smokers and non-smokers relating to constitutional and genetic factors influencing disease incidence. If this be so, it will demonstrate that the present surveys do not prove a cause and effect relationship between smoking and disease.

Term: Short, with possible long-term results.

Recommended Auspices: C.T.R.

This is a high priority item on the committee's agenda.

2. Project Demonstrate that there has been a change in the population composition in about the last 50 years due to the survival to the chronic disease age of persons with weak lungs, weak hearts, etc.
- a. Document the decline in deaths from respiratory disease, by age.
 - b. Autopsy study showing otherwise damaged lungs in people with lung cancer (Berkheiser type work).
 - c. Demonstration of the fact that animals with previously damaged lungs develop lung cancer.
 - d. Plot therapeutic advances against the changes in death rates for respiratory disease.
 - e. Document the fact that the level of total respiratory morbidity is not declining.

Cross Reference: II

Purpose: To:

- (1) Illustrate that the population composition has changed, and thus support the constitutional hypothesis.
- (2) Show that age-adjusted death rate comparisons cannot demonstrate that

reported increases in various diseases associated with smoking are attributable to smoking.

Term: Long, with possible short-term results.

Recommended Auspices: C.T.R. and Outside.

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3. Project: Determine whether differences can be found in the presmoking experience of smokers as compared with non-smokers and whether these differences can be correlated with differences observed in disease incidence between smokers and non-smokers.

Cross-Reference: II

Purpose: To test the hypothesis that the observed association between smoking and disease is explained by fundamental differences between smokers and non-smokers, and not by a causal connection between smoking and disease.

Term: Long, following short-term pilot studies.

Recommended Auspices: C.T.R. (C.T.R. presently engaged in project in this field). Possibly some pilots outside.

4. Project: Expand and collect more data on the following reported studies:
- a. Harvard Students-----this study compared data on a group of Harvard students taken while they were in college and again

a number of years later and showed, among other things, that there were definite personality differences between those who smoked and those who did not smoke.

b. Twins--these studies (Cavalli-Sforza and Friberg) show a similarity in smoking likes or dislikes among twins.

c. Eysenck showing relationships between extraversion and other personality factors and smoking habits.

d. Yerushalmy showing various "nonsense" correlations between smoking and factors relating to birth experience, menstruation, etc., confirming that an observed correlation is not necessarily causative.

e. LeShan--studies indicating that an unusually high number of cancer victims have experienced prior emotional trauma.

f. Seltzer--studies showing a relationship between morphological characteristics and smoking habits.

g. C. B. Thomas--studies showing a relationship between psycho-physiological characteristics and cardiovascular disease.

h. Friedman, Russek, Wolffe--individual studies showing a relationship of personality factors to heart disease.

i. Kissen--studies showing a relationship of psychological factors to cancer.

j. Sommers--studies showing a relationship at autopsy of specific glandular abnormalities to histological types of lung cancer.

Cross-Reference: II

Purpose: To demonstrate the existence and importance of various constitutional factors in the pertinent diseases.

Term: Long, with possible short term results.

Recommended Auspices: C.T.R., outside and Ad Hoc.

5. Project: A study of differences between smokers and non-smokers and between the pertinent disease victims and controls in the following known or suspected genetically influenced characteristics.
- (a) biochemical (e.g. blood type, endocrine, etc.)
 - (b) neurological
 - (c) sensory (e.g. taste, smell, etc.)
 - (d) use of alcohol
 - (e) use of drugs
- (In this connection check Kinsey data and similar behavior studies.)

Purpose: To support the constitutional hypothesis regarding the pertinent diseases.

Term: Long.

Recommended Auspices: C. T. R.

6. Project: Study utilizing the records of many doctors company clinics and other sources throughout the U.S.A., to develop a checklist of habits of life, heredity, constitutional factors, etc. and to correlate these characteristics in chain smokers, moderate smokers and non-smokers with development of the pertinent diseases.

Cross-Reference: II and VII

Purpose: To develop data supporting the constitutional hypothesis.

Term: Long.

Recommended Auspices: C.T.R. (C.T.R.'s "way of life" project in progress).

7. Project: A survey on chronic lung and other diseases in old people being conducted by the C.T.R. with the Chicago Board of Health. This is a 6 year study now in the pilot stages.

Cross-Reference: IV

Purpose: To find and define significant symptoms which might be used in evaluation of chronic lung and other pertinent diseases.

Term: Long.

Recommended Auspices: C.T.R.

8. Project: Utilizing an organization, such as the Psychological Corporation, to find indicia of differences in addition to those already known and to collect data to demonstrate these in the following comparative groups:
- a. Smokers and non-smokers.
 - b. Cancer victims and controls.
 - c. Lung cancer victims and controls.
 - d. Heart disease victims and controls.
 - e. Emphysema victims and controls.
 - f. Laryngeal cancer victims and controls.
 - g. Chronic bronchitis victims and controls.

Cross-Reference: II

Purpose: To find additional areas of support for the constitutional hypothesis.

Term: Long.

Recommended Auspices: C.T.R. ?

9. Project: Study to determine the factors which cancer families may have in common. Data being collected from G.I. records by Seltzer. Discover sources of genealogy of cancer victims (e.g. life insurance company records).

Cross-Reference: II

Purpose: To show that lung cancer involves familial or hereditary factors.

Term: Long, with possible short-term results.

Recommended Auspices: C.T.R.

- 10. Project: Analysis of Tokuhata's study reporting that some families had an unusually high number of lung cancer cases. If this work is shown to be valid, expand and explore other sources of similar data.

Cross-Reference: II

Purpose: To show that lung cancer involves familial or hereditary factors.

Term: Long, with possible short-term results.

Recommended Auspices: C.T.R.

- 11. Project: Conduct studies of the characteristics of ex-smokers to demonstrate constitutional differences of ex-smokers from both present smokers and non-smokers.

Cross-Reference: II

Purpose: To show that ex-smokers differ constitutionally and psychologically from both non-smokers and present smokers, and to correlate the observed differences with observed differences in disease incidence in these groups.

Term: Long.

Recommended Auspices: C.T.R.

12. Project: Collection of statistics on lung cancer as a percentage of total deaths in various countries and examination of trends of cancer deaths.

Cross-Reference: II

Purpose: To show variations in percentage of total deaths from lung cancer in various geographic areas not corresponding to variations in smoking habits and also to illustrate that lung cancer is a rare disease.

Term: Short.

Recommended Auspices: Outside.

13. Project: Israel study to determine the impact of a shift in environment and habits of people from various parts of the world who have had different environment and habits and who come to Israel, where they are subject to the same environment and the same habit influences. Consider similar studies in such places as New York City and Hawaii.

Cross-Reference: II

Purpose: To determine whether environmental and habit changes are as important as ethnic background in chronic disease incidence.

Term: Long.

Recommended Auspices: C.T.R.

14. Project: Experiments to show that some strains of mice are more inclined than others to cigarette smoke, comparable to the experiments that have shown that some strains of mice are more inclined than others to drink alcohol.

Purpose: To show that the taste for cigarette smoke is genetically influenced.

Term: Long, with possible short term results.

Recommended Auspices: C.T.R.

15. Project: Demonstrate in animals and people an increased desire to smoke following respiratory damage.

Cross-Reference: II

Purpose: To follow up indications that respiratory damage creates a desire to smoke.

Term: Long, with possible short term results.

Recommended Auspices: C.T.R. (for animal) and outside (for people).

16. Project: Determine whether the decline in infectious heart diseases matches the rise in coronary heart disease, so that total deaths from heart disease are approximately constant.

theoretical forecast

Cross-Reference: II and IV

Purpose: To refute the theory of a real increase in cardiovascular disease and to determine whether there is a basis for the theory that those formerly dying of infectious heart disease survive to die of coronary heart disease.

Term: Short.

Recommended Auspices: C.T.R.

17. Project: Prepare smokers' mortality curves for diseases other than lung cancer and compare such curves with their lung cancer curve.

Purpose: To determine whether there is a distinctive mortality curve for all diseases in the types of persons who smoke and thus support the constitutional hypothesis.

Term: Short.

Recommended Auspices: Outside.

18. Project: Conduct a clinical study to develop tests for determining susceptibility or resistance to respiratory cancer (similar to Lisanti's work: developing saliva and leucocyte characteristics as predictive factors in oral cancer).

Purpose: To support the constitutional hypothesis by showing that certain individuals or types of individuals are more susceptible or more resistant to respiratory cancer.

Term: Long.

Recommended Auspices: C.T.R.

19. Project: Explore with Eysenck the possibility of financing the furtherance of his work, both as to animals and as to humans.

Purpose: To develop Eysenck's theory that lung cancer and other pertinent diseases are related to constitutional and personality factors, and to encourage Eysenck's continued interest in this field.

Term: Long.

Recommended Auspices: Outside.

20. Project: A longevity study on Olympic athletes to record their health histories (collection of data in process by Dr. Wolffe).

Purpose: To demonstrate the relationship of morphological type to the pertinent diseases and to document variables in these health histories that relate to these diseases.

Term: Long.

Recommended Auspices: Outside.

21. Project: Explore the reported correlation between ulcers and lung cancer.

Cross-Reference: IV

Purpose: To determine whether something in the constitutional background of some persons either causes or predisposes them to this combination of diseases.

Term: Long.

Recommended Auspices: C.F.R.

22. Project: Devise studies to explore "habituation" in smoking, including comparisons with coffee, alcohol, chewing gum, Coca-Cola, etc.

Purpose: To demonstrate that the tobacco habit is no different from other habits involving use of other common products.

Term: Long.

Recommended Auspices: C.T.R.

23. Project: Study of adjustment to civilian life of World War II veterans, using World War II induction records and follow-up questionnaires sent out in the early 1950's.

Cross Reference: IV

Purpose: To determine whether susceptibility to the pertinent diseases is connected with stress.

Term: Long.

Recommended Auspices: C.T.R.

24. Project: A study to determine whether the form of smoking (c.s. pipe, cigar, cigarette) and the amount of smoking have a genetic basis.

Purpose: To show a genetic basis for type and amount of smoking.

Term: Long.

Recommended Auspices: I.R.H.

25. Project: Study of the male-female ratio in all respiratory diseases.

Purpose: To determine whether all respiratory diseases are predominant in the male.

Term: Short.

Recommended Auspices: Outside.

26. Project: Review of the literature on constitutional factors relating to the pertinent diseases.

Purpose: To determine what additional work can be done regarding constitutional factors in disease causation.

Term: Short.

Recommended Auspices: Ad Hoc.

II. Studies designed to show the limitations of existing epidemiological surveys.

1. Project: Arrange for a critique by a panel of experts of statistics relied upon by the Surgeon-General's Advisory Committee.

Purpose: To demonstrate that the conclusions based upon apparent statistical associations are not justified.

Term: Short.

Recommended Auspices: Ad Hoc.

2. Project: Specific refutation, possibly by the panel of experts, of misleading statements regarding cigarette smoking, commonly appearing in anti-smoking propaganda:
- a. 250,000-300,000 excess deaths per year from smoking.
 - b. One million school children of today will die from lung cancer before they are 70 years of age.
 - c. 14.4 minutes of life are lost with each cigarette smoked.

d. One in every ten smokers will get lung cancer.

e. Twenty-seven million people living today will die prematurely due to smoking.

Purpose: To refute the statements commonly made in endeavoring to alarm the public about cigarette smoking.

Term: Short.

Recommended Auspices: Ad Hoc.

3. Project: Larger study involving inclusion of many more variables in statistical analyses.

Purpose: To seek to reduce the correlation of smoking and disease by introduction of additional variables.

Term: Long, with possible short-term results.

Recommended Auspices: Ad Hoc.

4. Project Critical re-examination of Hammond matched pair analyses. Depending on results, further check could be done by comparing the twin studies to Hammond's matched pairs.

Purpose: To follow up suggestions that Hammond's matched pair study will fall apart under critical evaluation.

Term: Long, with possible short-term results.

Recommended Auspices: Ad Hoc.

5. Project: A collection to be made of "predictions that have not come true", including:
- a. "After women have been smoking for a longer period of time, the incidence of female lung cancer will equal that of men."
 - b. "The male population will be decimated by lung cancer in ten years."
 - c. "The curve of lung cancer will be like that of other cancers."
 - d. "Benzpyrene and other ingredients of tobacco smoke or condensate act as direct carcinogens."
 - e. "The age of peak incidence will become lower."

Purpose: To demonstrate that the predictions made years ago by the proponents of the cigarette causation theory have not come to pass and many have been abandoned.

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Term: Short.

Recommended Auspices: Ad Hoc.

6. Project: Further studies
- (a) to point out the chain of association which produces a statistical but non-causal association between cigarette smoking and certain diseases such as peptic ulcer, cirrhosis of the liver, etc.
 - (b) collect nonsense associations with smoking, such as accidents, homicides and the associations between smoking and breast and cervical cancer reported by Tokuhata.
 - (c) to demonstrate the inverse relationship between smoking and suicide and attempted suicide.

Cross-Reference: III and IV

Purpose: To demonstrate that many associations are obviously non-causal and that, accordingly, there is no adequate basis for claiming that causation is established by any particular association.

Term: Long.

Recommended Auspices: Outside and Ad Hoc, with C.T.R. assistance.

7. Project: A comparison of reporting sources with respect to apparent incidence and mortality of the pertinent diseases, including
- (a) number of doctors and other facilities available;
 - (b) manner of preparing death certificates;
 - (c) classification system used and when used;
 - (d) cancer registeries and autopsy data;
 - (e) parts of the country or portions of population covered.

Purpose: To show the impact on the results caused by variations among the reporting sources.

Term: Short.

Recommended Auspices: Outside.

8. Project: Collect data for selected areas or countries concerning incidence and mortality with respect to the pertinent diseases:
- (a) by years;
 - (b) by sex;
 - (c) by age;
 - (d) by area; including urban-rural;
 - (e) by race;
 - (f) by country of origin.

Purpose: To establish geographical differences in distribution of lung cancer and other pertinent diseases not corresponding to differences in smoking habits.

Term: Long, with possible short-term results.

Recommended Auspices: Outside.

9. Project: Study of geographic differences in the distribution of lung cancer and the other pertinent diseases among world populations.

Purpose: To demonstrate geographic differences in the incidence of the pertinent diseases.

Term: Short.

Recommended Auspices: Outside.

10. Project:— Collect data for selected areas or countries regarding smoking habits, using available indicia including per capita, male-female, age, etc.

Purpose: To secure data to correlate with cancer incidence and incidence of the other pertinent diseases for use in further studies.

Term: Short.

Recommended Auspices: Outside.

11. Project: Correlate reported increases in lung cancer with the introduction of improved diagnostic techniques and facilities.

Purpose: To demonstrate that some of the apparent increase in incidence is not real but due to improved diagnostic techniques and facilities.

Term: Short.

Recommended Auspices: Outside, with C.T.R. assistance and C.T.R. data.

12. Project: Conduct a study of variables which might correlate with irregular apparent increases in disease. Compare disease increases with such variables as: number of doctors, hospital beds, other facilities and other developments.

Purpose: To demonstrate that these apparent increases in diseases are influenced by many variables and are not necessarily real increases.

Term: Short.

Recommended Auspices: Ad Hoc.

13. Project: Collect Duane Carr, Custer and Rosenblatt type data showing a marked increase in lung cancer and the other pertinent diseases when there is an increase in doctors or improvement in diagnostic facilities.

Purpose: To illustrate that much of the apparent increase in lung cancer and the other pertinent diseases is due to a better ability to diagnose rather than to any real increase.

Term: Short.

Recommended Auspices: Outside.

14. Project: Further study and documentation of the frequency of metastasis to the lung of cancers arising in other primary sites.

Purpose: To demonstrate that a substantial percentage of lung cancer may be primary in other sites.

Term: Short.

Recommended Auspices: Outside.

15. Project: Studies of the type done by Rosenblatt relating to the difficulty in identifying lung cancer as primary or secondary.

Purpose: To demonstrate that much of the claimed incidence of lung cancer may be metastatic.

Term: Short. [?]

Recommended Auspices: Outside.

16. Project: Analyze the accuracy of vital statistics reporting primary and secondary lung cancers.

Purpose: To demonstrate that many cancers of the lung reported under Classification 162-163 of vital statistics arose in other sites and were secondary in the lung. Further purpose to refute Dr. Diehl's letter to the Senate which in substance stated that practically all of the cancers so reported were primary.

Term: Short.

Recommended Auspices: Outside, Ad Hoc.

17. Project: Collect existing data on the declining mortality ratio of smokers (as compared to non-smokers) in the older age groups and explore the implications of the decline.

Purpose: To emphasize that smokers above certain age levels have a greater life expectancy than non-smokers.

Term: Short.

Recommended Auspices: Ad Hoc.

18. Project: Demonstrate in different areas or population groups from those already surveyed that smokers have a death rate below the death rate for the general population.

Purpose: To refute extravagant claims about excess deaths caused by smoking.

Term: Short.

Recommended Auspices: Ad Hoc.

19. Project: Expand Doris Herman's study to show that the increase in lung cancer incidence is primarily adenocarcinoma and not epidermoid at least in certain geographic areas.

Cross-Reference: III

Purpose: To refute the theory that the increase in lung cancer is primarily epidermoid.

Term: Long, with possible short term results.

Recommended Auspices: Outside.

20. Project: Refine the histology of lung cancer to demonstrate that there are many mixed tumors and to show changes in histology with the aging of tumors.

Cross-Reference: IV

Purpose: To permit consideration of possible variables in relation to each newly defined classification.

Term: Long.

Recommended Auspices: C.T.R.

21. Project: Study trends in the incidence of other cancers as compared with lung cancer e.g. compare the alleged decrease in stomach cancers with the alleged increase in lung cancer. Collect theories on reasons for the trends in stomach and other cancers.

Purpose: To demonstrate the lack of knowledge concerning the etiology of cancer and the fallacy of seeking to determine etiology by trends in incidence.

Term: Short.

Recommended Auspices: Outside.

22. Project: Determine whether total cancer incidence in other countries is increasing and whether lung cancer is increasing or decreasing in proportion to other cancers. For this purpose use age-adjusted figures.

Purpose: To investigate whether there is simply a change in site of cancers and not an increase in total cancers.

Term: Short.

Recommended Auspices: Outside.

23. Project: Study, in other countries, along the lines done by Dr. Gilliam in the U.S.A., respecting changes in the rate of increase of lung cancer.

Purpose: To investigate whether the rate of increase of lung cancer is leveling off, as previously indicated in Gilliam's work.

Term: Short.

Recommended Auspices: Outside.

24. Project: A study to demonstrate that, if as little as 5% of other respiratory disease reported about the year 1900 were in fact lung cancer,

there has been no increase in lung cancer
since that time.

Purpose: To demonstrate that the claimed increase in lung cancer can be only an apparent one and not a real increase.

Term: Short.

Recommended Auspices: Outside.

25. Project: A study to document the decrease in mortality from respiratory diseases other than lung cancer (Following this study consider a similar study with regard to all chronic disease deaths.)

Purpose: To support the hypothesis that death from respiratory diseases has been reasonably constant and that the only real change has been in the type of respiratory disease causing death.

Term: Short.

Recommended Auspices: Outside.

26. Project: Prepare a better demonstration of the fact that respiratory cancers other than lung cancer

are not following the reported trends in lung cancer e.g. laryngeal cancer seems to have had only a slight increase.

Purpose: To demonstrate that cancers of other areas of the respiratory tract equally exposed to smoke have not increased in proportion either to the increase in cigarette smoking or to the reported increase in lung cancer.

Term: Short.

Recommended Auspices: Outside.

27. Project: Additional animal studies respecting smoking and longevity along the lines presently contemplated by C.T.R. with Homburger.

Purpose: To investigate whether smoking affects longevity.

Term: Long.

Recommended Auspices: C.T.R.

28. Project: A study of areas that constitute pockets of high lung cancer incidence without relation to smoking habits (comparing New Orleans, Ten City Survey, El Paso, New York City, Pittsburgh and perhaps Mexican women and Dr. Palmer's project in the southern part of Africa).

Purpose: To illustrate that there are areas which have a high incidence of lung cancer not corresponding to smoking habits.

Term: Long, with possible short-term results.

Recommended Auspices: Outside.

29. Project Target type studies in selected U.S. and other areas, similar to those done in Vienna, Liverpool, Prague, etc., to demonstrate clusters of high incidence of lung cancer and the other pertinent diseases in the immediate area of the suspected cause, such as factory, air pollution, etc.

Purpose: To pinpoint possible environmental factors in lung cancer and the other pertinent diseases.

Term: Long.

Recommended Auspices: Outside.

30. Project: A study of areas which constitute pockets of low lung cancer incidence not corresponding to smoking habits. (Consider survey of desert and mountain state areas, most of which were omitted by Hammond in his study.)

Purpose -> To demonstrate that cancer incidence is not related to smoking habits.

Term: Long, with possible short-term results.

Recommended Auspices: Outside.

31. Project: A study of the incidence of lung cancer and other pertinent diseases in non-smoking populations (compare Amish, Menonites, nuns and Mormons; consider a re-do of the Seventh Day Adventist studies done by Wynder, as to which question has been raised.)

Purpose: To establish the incidence of lung cancer in non-smoking populations.

Term: Long.

Recommended Auspices: Outside.

32. Project: Further document and analyze the Ten City Survey and Prindle's comparative survey on air pollution to show that widespread differences in the incidence of lung cancer and the other pertinent diseases are not explainable by differences in smoking habits.

Purpose: To demonstrate that smoking habits do not account for widespread differences in incidence of the pertinent diseases.

Term: Short.

Recommended Auspices: Outside.

33. Project: Make geographical comparisons of disease rates of immigrating groups with those of native populations, using Dean type analyses (consider Japanese, Mexicans, Yugoslavs, Poles, Irish, Swedes, Puerto Ricans).

Purpose: To demonstrate a different incidence of lung cancer and the other pertinent diseases in ethnic groups not corresponding to their smoking habits.

Term: Long, with possible short-term results.

Recommended Auspices: Outside.

34. Project: Study lung cancer and smoking habits of Italians in Rosedale, Pennsylvania, who have been shown to have a low incidence of heart disease.

Cross-Reference: IV

Purpose: To see if persons in a presumptively stress-free environment have less lung cancer than do people in a more stressful environment.

Term: Short.

Recommended Auspices: Outside.

35. Project: In studies where no relationship between smoking and lung cancer was observed, examine whether there is a similar lack of relationship between smoking and the other pertinent diseases (e.g. Perrone, Poche studies).

Purpose: To see if the same pattern of lack of association appears with regard to both lung cancer and the other pertinent diseases.

Term: Long.

Recommended Auspices: Outside.

36. Project: Investigate possibility of additional statistical studies, such as those made by Perrone and Poche, which showed no association between smoking and lung cancer.

Purpose: To refute the many statistical studies in which an association is shown.

Term: Long.

Recommended Auspices: Outside.

37. Project: A study of cancer cases in city hospitals

by residence of the patients.

Purpose: To show that urban-rural differences are not attributable to rural people going to the city for treatment and thus to refute Hammond's contention that such is the fact.

Term: Short.

Recommended Auspices: Outside.

38. Project: Check whether male-female ratio in lung cancer vital statistics is changing. (Check the preliminary 1962 figures, which suggest a narrowing of the ratio rather than the widening shown by previous figures.)

Purpose: To determine whether the differences in incidence of lung cancer between males and females is changing.

Term: Short.

Recommended Auspices: Ad Hoc.

39. Project: A study of lung cancer in women to test the hypothesis that the incidence is rising and that the increased incidence is in epidermoid lung cancer.

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Purpose: To determine whether any increase in lung cancer among women is in the type of cancer most often associated with cigarette smoking.

Term: Short.

Recommended Auspices: C.T.R. and Outside.

40. Project: A study to determine whether all histological types of lung cancer occur in non-smoking women. Prepare a slide demonstration to illustrate.

Purpose: To establish whether women have the same types of lung cancer that men have.

Term: Short.

Recommended Auspices: C.T.R. and Outside.

41. Project: Study whether, in female lung cancer cases, the sex or other hormonal balances differ from those of females who do not have lung cancer, males who have and males who do not have lung cancer.

Cross-Reference: I, IV

Purpose: To investigate whether hormonal differences have an effect on lung cancer etiology.

Term: Short.

Recommended Auspices: C.T.R.

42. Project: Check cancer registries for evidence of a continued divergence of male-female ratios.

Cross-Reference: IV

Purpose: To further investigate the existence and trend of male-female ratio.

Term: Short.

Recommended Auspices: Outside.

43. Project: Compare sex ratios in cancers other than lung cancer, including those cancers which have been linked with smoking and those which have not, e.g., is bladder cancer sex ratio the same as or different from the lung cancer sex ratio?

Cross-Reference: IV

Purpose: To investigate the sex ratio in the pertinent
and other (e.g. stomach cancer) diseases.

Term: Short.

Recommended Auspices: Outside.

44. Project: Document that, regardless of what latent period is assumed, there has been no parallel increase of lung cancer with cigarette smoking.

Purpose: To illustrate that, even using any latent period suggested by Kreyberg, Ochsner or others, the increase reported in lung cancer has not paralleled the increase in cigarette consumption.

Term: Short.

Recommended Auspices: Outside.

45. Project: Clinical studies to classify various lung complaints, including various types of bronchitis, etc. (Segal's 6 year study now in progress includes an effort to determine whether chronic lung diseases in smokers may be allergic responses to tobacco.)

Purpose: To classify the various types of lung diseases and symptoms so that cigarette smoking can no longer be loosely associated with "chronic lung disease".

Term: Long.

Recommended Auspices: C.T.R.

46. Project: Document that the incidence of emphysema has not paralleled the rise of smoking.

Purpose: To show lack of association between increase of smoking and apparent increase of emphysema.

Term: Short.

Recommended Auspices: Outside.

47. Project: Collect emphysema cases among non-smokers and among young people.

Cross-Reference: IV

Purpose: To demonstrate that both non-smokers and young people who have smoked briefly have emphysema, thus diluting any association between smoking and emphysema.

Term: [REDACTED], with possible short-term results.

Recommended Auspices: Outside.

48. Project: Arrange for a review of the literature with regard to emphysema, particularly to document that the cause or causes of emphysema are unknown.

Purpose: To document how little is known about the cause or causes of emphysema.

Term: Short.

Recommended Auspices: Outside.

49. Project: Explore the work being done by George Wright of Cleveland with regard to emphysema and consider encouraging him to pursue his work with respect to the cause or causes of emphysema.

Cross Reference: IV.

Purpose: To encourage the work of a man whose previous work has been promising.

Term: Long with possible short term results.

Recommended Auspices: Ad Hoc.

50. Project: Study reasons for the sudden unexplained reported rise in incidence of emphysema.

Purpose: To show the extent to which the apparent increase is caused by changes in methods of reporting, diagnosis, definitions, etc.

Term: Short.

Recommended Auspices: Ad Hoc

51. Project: Investigate and document variables noted by Dr. Ogura et al. with regard to laryngeal cancer, including:

- a. Lack of a parallel increase with the increase in cigarette smoking.

- b. The expanding male-female ratio.
- c. The importance of hormonal factors.
- d. Alcohol consumption.
- e. Nutritional deficiencies.
- f. Predisposed families.
- g. Data showing a variation in incidence and association with smoking of cancers in areas immediately adjacent to the larynx and the trends and male-female ratio in regard to these adjacent sites.

Cross-Reference: IV

Purpose: To investigate variables that may be factors in laryngeal cancer.

Term: Long, with possible short-term results.

Recommended Auspices: Outside.

III. Studies designed to test the mechanisms suggested for cigarette causation of lung cancer and the other pertinent diseases.

1. Project: Extensive program of experiments in animals involving production of the pertinent diseases by inhalation techniques and otherwise. This will be a major undertaking involving use of a number of investigators and laboratories. The first objective is the establishment of usable experimental models for production of the pertinent diseases. In each series of experiments, many variations will be systematically imposed upon the model. The program will take many years, but many useful results should be available within two years or so from initiation of the program. Some of this work is under way and much of it can go forward concurrently.

Taking experimental production of lung cancer by inhalation techniques as an example:

1. Develop a basic model by which lung cancer can be reproduced in a given laboratory animal with a particular agent with predictable frequency.
2. Vary the agent--i.e. see what agents, including tobacco smoke, will produce

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lung cancer by the model method.

3. See whether the addition of other agents, including tobacco smoke, increases or decreases the frequency with which the basic model reproduces lung cancer.
4. Alter the animal by such means as scarring, infection, nutrition, systemic damage, to see the effect upon frequency and time of reproduction of lung cancer.
5. Combine variations of agent and alterations of animal - (i.e. paragraphs 2 and 4).
6. Combine with paragraph 5 the addition of other agents singly and in combination.
7. In each instance, vary the dose of the agent or agents used.
8. See if techniques are reproducible in different strains and the higher species of animals and, if so, with what results.

Cross-Reference: II and VI

Purpose: To investigate the experimental production of lung cancer and the other pertinent diseases in animals and the biological mechanisms involved, and to determine what part, if any, smoking plays in these processes.

Term: Long [redacted] with possible short-term pilots and results.

Recommended Auspices: C.T.R., Outside and Ad Hoc.

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2. Project: Collect all of the unpublished negative animal experiments with tobacco (including skin painting and inhalation).

Cross-Reference: VI

Purpose: To bring together the negative results with respect to efforts to produce the pertinent diseases in animals with tobacco.

Term: Short.

Recommended Auspices: Ad Hoc.

3. Project: Examine the organs of Leuchtenberger's mice for any pathological changes, and compare smoking and non-smoking mice.

Purpose: To determine whether smoking resulted in any pathological changes in mouse organs and to give a basis for a long-term study of diseases other than lung cancer by inhalation experimentation.

Term: Short, but possibly resulting in long-term project.

Recommended Auspices: Ad Hoc.

4. Project: Conduct experiments directly on animal lungs to determine whether there is any validity to the theory that tobacco smoke may be a promoter of cancer development, even though something else is the initiator. This could be done with agents which have been shown to have promoter activity in the skin. If such proven promoters act similarly in lung tissues, the possible activity of whole tobacco smoke could then be tested in a realistic manner.

Purpose: To determine whether cigarette smoke acts as a promoter of cancer in the lung.

Term: Long.

Recommended Auspices: C.T.R.

5. Project: Conduct Saffioti type experiment involving the use of hematite dust in putting benzpyrene in the lungs which produce 100% cancer in experimental animals but instead of benzpyrene use whole smoke.

Cross-Reference: IV, V and VI

Purpose: To explore the possibility of showing no production of lung cancer by the use of cigarette smoke in a form most closely resembling the whole smoke, while cancer is produced 100% by the use of known carcinogens such as benzopyrene.

Term: Short-term pilot.

Recommended Auspices: C.T.R. (Saffioti not to be used).

6. Project: Studies

- a. To determine more accurate measurement of actual inhalation by humans of pipe, cigar and cigarette smoke. (E.g. blood and urine tests by McNiven et al.)
- b. To ascertain the difference between the effects of cigarette, pipe and cigar smoke on animals.
- c. To find chemical and physical differences in cigarette, pipe and cigar smoke.

Cross-Reference: II

Purpose: To test the reliability of inhalation data in smoking histories obtained by present methods and to explore the various forms of smoke for differences which may contribute to the epidemiological data.

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Term: Long.

Recommended Auspices: C.T.R.

7. Project: Study to demonstrate by carbon 12 tagged tobacco that the Leuchtenberger index of carbon monoxide intake is more reliable than the Harris index in the measurement of inhalation.

Cross-Reference: VI

Purpose: To develop reliable methods for measurement in future inhalation research and to expose the inadequacy of the Harris inhalation index.

Term: Long.

Recommended Auspices: C.T.R.

8. Project: Pursue an experiment of the type suggested by Prof. Leo Katz, involving the training of laboratory animals to smoke and develop the smoking habit.

Cross-Reference: I and VI

Purpose: To develop experimental animals with an affinity for smoking which can be used in study of the pertinent diseases and to encourage Prof. Katz.

Term: ~~Short~~-term pilot study.

Recommended Auspices: Ad Hoc.

9. Project: Conduct experiments involving the introduction into animals by means other than inhalation of a variety of harmless and harmful substances to show that lung cancer and changes in lung tissue can be produced systemically and are not specific to the inhalation of cigarette smoke.

Cross-Reference: IV and V

Purpose: To demonstrate that lung cancer can be caused by systemic influence and not necessarily by inhalation.

Term: Long, with possible short-term results.

Recommended Auspices: C.T.R.

10. Project: Conduct tests on animals to check the theory that ciliary activity may play a role in the development of lung cancer. This could be done with ciliary stimulation or depression.

Purpose: —To determine whether ciliary activity
 actually plays a part in the occurrence of lung
 cancer.

Term: Long, with possible short-term results.

Recommended Auspices: C.T.R.

11. Project: Studies respecting total lung clearance and smoking and the effect of lung clearance on respiratory disease and infection.

Purpose: To test the effects of variations in lung clearance mechanisms on susceptibility to respiratory disease and to minimize the ciliastasis assertions respecting cancer causation.

Term: Long, with possible short-term results.

Recommended Auspices: C.T.R.

12. Project: Follow-up study of Laurenzi (presently in progress under N.I.H.), to show that secretions of endotoxins have a profound effect on inhibiting lung clearance.

Purpose: To demonstrate that endotoxins have a much greater effect on lung clearance than does cigarette smoking.

Term: [redacted] long, with possible short-term results.

Recommended Auspices: C.T.R.

13. Project: Studies of lung surfactant (which is essential for the proper elastic function of the lungs) including:
- (a) Origin of surfactant in lung tissues;
 - (b) Methods of simulating surfactant;
 - (c) Influences of smoking on the secretion of surfactant.

Purpose: Basic research with regard to surfactant as a suspect in the etiology of emphysema.

Term: Long.

Recommended Auspices: C.T.R.

14. Project: Studies to determine whether there are cancers without so-called "pre-cancerous" changes and to demonstrate that there are so-called "pre-cancerous" changes which do not progress to cancer. Collection of slides showing these. A slide and history demonstration of so-called "pre-cancer" in areas other than lung

(e.g. uterine cervix, oral cavity, leukoplakia, skin, etc.), which have regressed or remained the same throughout a period of years following their diagnosis.

Cross-Reference: V

Purpose: To demonstrate that the so-called "pre-cancerous" changes referred to by Auerbach and others are not in fact precursors of cancer.

Term: Long, with possible short-term results.

Recommended Auspices: Outside.

15. Project: Seek to devise experiments to see if "pre-cancerous" changes can be followed in animals while the animal is still alive.

Cross-Reference: IV and V

Purpose: To observe the progression or regression or other developments with regard to the so-called "pre-cancerous" changes in a living animal and thus demonstrate that such changes do not inevitably progress to cancer.

Term: Long.

Recommended Auspices: C.T.R.

16. Project: Expand the work of Garland, Tuttle and Rigler on the peripheral origin of most lung cancers.

Purpose: To demonstrate that many lung cancers originate in the periphery of the lung, which is reached by little or no smoke.

Term: Long.

Recommended Auspices: Outside.

17. Project: Clinical studies to be conducted by Langston and others to show that duration and amount of smoking have no relation to the age of peak incidence of lung cancer.

Cross-Reference: II

Purpose: To fortify Passey's observations that the amount and duration of smoking do not affect the time when lung cancer appears and thus to cast doubt on any causal hypothesis.

Term: Long, with possible short-term results.

Recommended Auspices: Outside and Ad Hoc (Langston study now in progress).

18. Project→ Collect cases of persons surviving more than five years after treatment of lung cancer, and develop as much data as possible concerning potential variables.

Cross-Reference: I and II

Purpose: To explore the reasons why lung cancer so rarely reoccurs in victims who do survive and to determine ways in which these persons differ from those who do not survive.

Term: Long, with possible short-term results.

Recommended Auspices: Outside and Ad Hoc.

19. Project: Conduct experiments to check the accuracy of Radford's identification and measurement of polonium. Examine human lungs in smokers and non-smokers duplicating Radford's experiment. Measure polonium in pipe and cigar smoke. Check oral cavity tissues for polonium, possible polonium dose response studies in mice. Secure relevant data of human dose response to polonium from the Atomic Energy Commission (from mines in the Western United States of America). Investigate the source of polonium in human existence and where tobacco gets polonium.

Compare sources in the atmosphere and otherwise and check geographical differences in polonium content of tobacco; compare with lung cancer incidence. Explore possibility of checking polonium count in grazing animals.

Purpose: To do basic research on the presence and importance of polonium in the environment, including tobacco.

Term: Long, with possible short-term results.

Recommended Auspices: C.T.R. (SAB will consider part of this next week).

20. Project: Investigate Nitrosamines.

Purpose: Basic research to investigate whether nitrosamines in cigarette smoke play any important role in the causation of disease.

Term: Long.

Recommended Auspices: C.T.R.

21. Project: Investigate free radicals.

Purpose: Basic research to test theory that free radicals in smoke cause disease.

Term: Long.

Recommended Auspices: C.T.R.

22. Project: Studies with respect to oral cavity cancer and its relationship to liver damage. (Presently to be investigated by C.T.R.). Should be further pursued with respect to respiratory cancers and liver damage. (Compare Kotin work).

Cross-Reference: IV

Purpose: To investigate possible causation of oral and respiratory cancer by endogenous factors rather than environmental exposure.

Term: Long.

Recommended Auspices: C.T.R.

23. Project: Develop further investigation respecting anti-carcinogens in tobacco smoke.

Purpose: To increase knowledge concerning anti-carcinogens that may be found in tobacco smoke.

Term: Long.

Recommended Auspices: C.T.R. (Previously proposed project).

24. Project: Investigate bladder cancer enzyme block.

Purpose: To test the theory that cigarette smoking causes an enzyme block which in turn causes bladder cancer.

Term: Long.

Recommended Auspices: C.T.R. (Proposed by Dr. Hockett).

25. Project: Expand Wilens' autopsy work showing no correlation between smoking and heart damage.

Cross-Reference: V

Purpose: To demonstrate that smoking does not damage the heart and coronary arteries, as claimed by Auerbach, Hammond and others.

Term: Long, with possible short-term results.

Recommended Auspices: C.T.R. (part of this is a current project).

26. Project: [REDACTED]umentation of the discrepant data in the Albany and Framingham studies concerning cardiovascular disease (expansion of observations of Dr. Wolffe.) Correlate Albany and Framingham findings with Russek findings that there is more heart disease in non-smokers than in ex-smokers.

Purpose: To demonstrate the inadequacy of existing epidemiological data indicating smoking as a cause of heart disease.

Term: Short.

Recommended Auspices: Outside.

27. Project: Study of primates on special atherogenic diets in which nicotine is administered to determine whether there is an accelerating or aggravating effect on arterial degeneration. (Consider expanding this type of study by administering [REDACTED] nicotine to primates on ordinary diets to see if nicotine produces arteriosclerosis.)

Purpose: To investigate whether nicotine plays any part in the initiation or aggravation of cardiovascular disease.

Term: Long.

Recommended Auspices: C.T.R. (presently proposed project).

28. Project: Study to measure the mechanisms of blood clotting to see if smoking has any effect on such mechanisms in already diseased arteries, (see Murphy's work), or whether it has any effect on blood clotting time in normal arteries. (See work of Engelberg).

Purpose: To determine whether cigarette smoking has any effect on causing or aggravating cardiovascular disease.

Term: Long.

Recommended Auspices: C.T.R.

29. Project: Expand C.T.R. continuation of the work of Holman presently being done by Doctors Strong and McGill with regard to accident victims to include a broader field than accidents. Explore the possible expansion of this work through the world wide study of arterial diseases in which Strong and McGill are participants.

Purpose: To review autopsy material in conjunction with smoking histories to show no relationship between smoking and evidence of cardiovascular disease.

Term: Long.

Recommended Auspices: C.T.R.

30. Project: Conduct a study to pursue Dr. Soloff's findings that peripheral vascular effects of smoking are minimized by physical activity.

Purpose: To refute the theory that peripheral vascular disease is caused by smoking.

Term: Long, with possible short-term results.

Recommended Auspices: C.T.R.

31. Project: Expand the Kasparian type experiments which measure the effect on an artery size, of cigarettes, alcohol, etc., and determine whether an investigator can measure the effect of stress and other factors besides smoke and alcohol on the coronary arteries.

Cross-Reference: IV

Purpose: develop a means for measuring the effect of stress on the coronary arteries as a suspect in the causation of cardiovascular disease and to show no effect on the coronary arteries of the inhalation of cigarette smoke.

Term: Short.

Recommended Auspices: Ad Hoc.

32. Project: Experimental studies of smoking and prematurity.

Purpose: Confirm Yerustalmy's and Hester's work on the non-effect of mothers' smoking on the well-being and health of their babies.

Term: Long.

Recommended Auspices: C.F.R.

IV. Studies designed to explore the existence and role of various factors other than cigarette smoke suspected in connection with the pertinent diseases.

1. Project: Collect cases of epidermoid lung cancer in non-smokers. Prepare a slide demonstration.

Cross-Reference: III and V

Purpose: To demonstrate that epidermoid lung cancers do occur in non-smokers and thus refute assertions that these cancers only occur in smokers.

Term: Short.

Recommended Auspices: Ad Hoc.

2. Project: Further studies to establish the existence of lung cancer and a trend of apparently increasing lung cancer incidence before cigarette smoking became prevalent. (Expand the work of Rosenblatt, Willis and the German autopsy studies).

Purpose: To demonstrate that lung cancer was in existence and apparently increasing in incidence at a time when cigarette smoking could not have been a factor.

Term: [REDACTED] Short.

Recommended Auspices: Outside.

3. Project: Explore and expand the work of Helen Toolin of Memorial Hospital to look for virus-like particles in human cancer. The expansion of her work should focus on demonstrating virus-like particles in lung cancer.

Purpose: To support the viral theory of lung cancer causation.

Term: Long with possible short-term results.

Recommended Auspices: C.T.R.

4. Project: Study in the United States of the relationship between occupation, environment and lung cancer (e.g. Pennsylvania perhaps, using Perrone data [REDACTED] as a starting point and possibly applying Poche's [REDACTED] techniques. Both Perrone and Poche have found no association with smoking.)

Cross-Reference: 1I

Purpose: [redacted] show possible importance of occupation in relationship to lung cancer incidence.

Term: Long.

Recommended Auspices: Inside.

- 5. Project: Conduct a study to compare the age of peak incidence of lung cancer in different geographical areas. Endeavor to tie this information to the peak age of starting smoking, if possible, and also to the average age at death in the particular area.

Cross-Reference: II

Purpose: To determine whether the peak age of lung cancer incidence is affected by variables and, if so, to demonstrate what variables affect it. Also to refute Kreyberg's theory of a 40-year latent period.

Term: Short.

Recommended Auspices: Outside.

6. Project: Expand the existing data on comparative smoking habits which show inverse relationships between socio-economic status and lung cancer and between socio-economic status and smoking. (Check the Calumet, Michigan study).

Cross-Reference: I and II.

Purpose: To investigate socio-economic status as a factor in lung cancer.

Term: Short.

Recommended Auspices: Outside.

7. Project: Develop a project to test Dijkstra's hypothesis that winter babies have more lung cancer than summer babies, possibly due to a deficiency in vitamin A.

Purpose: To investigate the possible effect of nutritional deficiencies in lung cancer causation.

Term: Short.

Recommended Auspices: C.T.R.

8. Project: Collect autopsy data for comparison of and detection of any differences in lung changes as among:

- (a) Geographic areas;
- (b) Ethnic groups;
- (c) Men and women;
- (d) Young and old;
- (e) Secondary and primary lung cancers.

Particular attention should be paid to the question whether the lung picture described by Auerbach is the same in metastatic lung cancer as in primary lung cancer.

Cross-Reference: V

Purpose: To investigate possible significant differences in lung tissue regardless of smoking habits.

Term: Long.

Recommended Auspices: C.T.R.

9. Project: Collect autopsy data showing so-called "pre-cancerous" changes in non-smokers occurring as a result of systemic causes, e.g., substances such as corticosteroids or some vitamin deficiency, etc.

Cross-Reference: III and V

Purpose: demonstrate that so-called "pre-cancerous" changes occur from systemic conditions brought about by medicines in common use, as well as other systemic factors, and not necessarily through direct contact with inhalants.

Term: Long-term, with possible short-term results.

Recommended Auspices: Outside.

10. Project: Collect colored photographs of gross lung tissue of smokers and non-smokers from a variety of geographical areas, including cities of varying population density.

Cross-Reference: V

Purpose: To refute the popular misconception that smoking cigarettes changes the gross appearance of human lungs.

Term: Short.

Recommended Auspices: Ad Hoc.

11. Project: Study of relationship of many factors, including cigarette smoking, to symptoms, prognosis, age at diagnosis and histological type in lung cancer patients.

Purpose: To demonstrate whether these factors affect the symptoms, prognosis or age at diagnosis. Also may refute the hypothesis that existing lung cancer is accelerated or aggravated by smoking.

Term: Long.

Recommended Auspices: C.T.R. and Ad Hoc.

12. Project: Conduct histo-chemical study of the difference between human male and female lungs. Test on an animal model.

Cross-Reference: I and II

Purpose: Basic research into possible sex factor in lung cancer.

Term: Long.

Recommended Auspices: C.T.R.

13. Project: Expand the Sprunt-type experiment involving the damaging of animal lungs with various agents, including viruses, to produce lung cancer.

Purpose: To determine the effect of previous lung damage and virus in the production of lung cancer.

Term: Long.

Recommended Auspices: C.T.R.

14. Project: Continue experiments to induce lung cancer by the injection of common viruses, by common viruses plus smoking, or viruses plus pollution, or viruses plus bacteria.

Cross-Reference: III

Purpose: To investigate the role of viruses in lung cancer causation.

Term: Long.

Recommended Auspices: C.T.R. (Presently proposed project)

15. Subject: Study possible carcinogenicity of X-ray
(in both diagnostic and therapeutic
doses) and drugs, by adding these factors
in experiments involving damaged lungs,
viruses and other suspected carcinogenic
factors.

Purpose: To investigate X-rays and drugs as possible
factors in lung cancer causation.

Term: Long.

Recommended Agencies: C.T.R.

16. Project: Studies and experiments to test various hypotheses of cancer immunization by previous diseases (e.g. polio, bacterial infection, etc.).

Purpose: To determine whether or not the victims of various diseases may thereby be immunized to cancer and thus show that there is some unknown mechanism in the body, responsible for cancer, which is affected by certain diseases.

Term: Long.

Recommended Auspices: C. T. R.

17. Project: Experiments to investigate possible carcinogenic effects of polio vaccines (Dmochowski), flu vaccines, etc. (See also work of Trentin, Huebner, Toolin, Sarah Stewart, etc.)

Purpose: To explore the possibility that various vaccines may be factors in the causation of cancer.

Term: Long.

Recommended Auspices: C.T.R.

13. Project: Analysis within occupational groups of various factors, including smoking, that may be related to the pertinent diseases, in a country with nationalized power, railroads, etc., (e.g. Sweden) where the data is more likely to be available than in the United States.

Cross-Reference: II

Purpose: To investigate occupation and other variables as possible factors in the causation of the pertinent diseases.

Term: Long.

Recommended Auspices: Outside.

14. Project: A study of obesity and cardiovascular disease, to be conducted with the Framingham data (see Seltzer definition of obesity). Consider any relationships to smoking.

Cross-Reference: I and II.

Purpose: To demonstrate the association of obesity with cardiovascular disease and to investigate smoking as a factor.

Term: Long

Recommended Auspices: C.T.R.

20. Project: Using the heart catheter technique of Dr. Barger, study the effects of nicotine and stress on the development of arteriosclerosis in dogs and possibly other experimental animals.

Purpose: To determine whether stress or nicotine are factors in arteriosclerosis and whether nicotine may serve as an alleviating factor.

Term: Short-term pilot project.

Recommended Auspices: C.T.R. (C.T.R. has expressed interest.)

21. Project: Conduct experiments to show increased cardiovascular diseases in frustrated male rabbits. The possibility that cigarette smoking is an alleviating factor should be explored.

Cross-Reference: VII.

Purpose: To establish stress as an important factor in cardiovascular disease with possible establishment of cigarette smoking as an alleviating factor.

Term: Long, with possible short term-results.

Recommended Auspices: C.T.R.

22. Project: Conduct animal experiments regarding the effect on longevity of over-crowding. Investigate tobacco as an alleviating factor.

Cross-Reference: VII.

Purpose: To document the effect of stress on longevity and the possible effect of tobacco, as an alleviating factor.

Term: Long.

Recommended Auspices: C.T.R.

V. Studies designed to test Dr. Auerbach's conclusions concerning "pre-cancerous" changes in human lungs.

1. Project: Combined review by pathologists and a statistician of all Auerbach-type data, including a rearrangement of the data for a multi-variable analysis. Also a review of problems in classifying cancer and "pre-cancer".

Cross-Reference: IV

Purpose: To question Auerbach's conclusions by showing the existence of relevant variables and that his total cases were too few to permit analysis of these variables. To document the extent of disagreement among pathologists about histological classifications.

Term: Long.

Recommended Auspices: Outside

2. Project: Collect and prepare visual demonstrations of slides showing Auerbach-type changes in the lungs of a large number of non-smokers.

Cross Reference: /

Purpose: To demonstrate the so-called pre-cancerous changes are found in the lungs of non-smokers.

Term: Short.

Recommended Auspices: Outside.

3. Project: Electron microscopy study by Dr. Brinkman to see, among other things, if normal cilia exist next to invasive cancer of the lungs.

Cross-Reference: III

Purpose: To question the theory that the destruction of cilia is a factor in the development of lung cancer.

Term: Short.

Recommended Auspices: Ad Hoc.

4. Project: Time and motion study of the Auerbach work to determine the approximate time necessary for him to have devoted to the examination of slides he states he has personally examined.

Purpose: To determine whether it would have been possible for Dr. Auerbach in the time available to have personally examined all of the slides (note that his slides came from comparatively few cases).

Term: Short.

Recommended Auspices: Ad Hoc.

VI. Studies designed to show limitations of existing animal experimental results.

1. Project: Devise methods to measure inhalation and exhalation of smoke in people and in animals. Establish the differences between animals and men and between different men with regard to both inhalation and exhalation, including pipe and cigar smoking in this study. Also compare in animals the amount of smoke brought into the lungs in smoke chambers with that which may be forced into their lungs through other means.

Purpose: To investigate a method or methods by which human smoking habits can best be approximated for experimental purposes.

Term: Long.

Recommended Auspices: C.T.R.

2. Project: Compare the whole smoke used by C.T.R. with the whole smoke used by others, including Harris, to see if chemical or physical differences in the smoke can be shown. Compare the various methods with human smoking.

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Cross-Reference: III

Purpose: To determine which experimental smoking techniques best approximate the smoke inhaled by the human smoker and to investigate the degree of difference between the smoke Harris used and that inhaled by the human smoker.

Term: Long, with possible short-term results.

Recommended Auspices: C.T.R.

3. Project: Determine and document the occurrence of human types of lung cancer in animals.

Purpose: To establish that animals can develop human types of lung cancer, and that, therefore, mouse adenomas are not an appropriate index of carcinogenic activity. This will fortify our position that only the production of human type lung cancer in animals is relevant.

Term: Long.

Recommended Auspices: C.T.R. and Outside.

4. Project: Comprehensive studies of lung adenomas in various strains of mice, including both susceptible and resistant strains.

Purpose: To show that lung adenomas are not an appropriate index of carcinogenicity.

Term: Long, with possible short-term pilots.

Recommended Auspices: C.T.R., Outside and Ad Hoc.

5. Project: Consider skin-painting tests with believed harmless substances in every-day use such as tomato juice, egg yolk, skin salves, coffee, etc.

Purpose: To investigate whether skin cancers can be produced by painting with a variety of so-called harmless substances as was done with tobacco smoke condensate.

Term: Long.

Recommended Auspices: Outside. (C.T.R. would like to work in this field, but Ad Hoc questions the advisability of C.T.R. participation.)

6. Project: Skin painting type experiments, using
whole smoke instead of smoke condensate.

Cross-Reference: III.

Purpose: To demonstrate that the biological activity
of whole smoke is different from that of
condensate.

Term: Long.

Recommended Auspices: Ad Hoc, if at all. (Already
planned by C.T.R.)

VII. Studies designed to explore beneficial effects of smoking

1. Project: Survey smoking population to learn of the beneficial results which the smokers believe their smoking has and to determine why people smoke.

Purpose: To document benefits of smoking.

Term: Short-term pilot.

Recommended Auspices: Ad Hoc.

2. Project: Various experiments showing effects of stress (including particularly those already done) superimposing smoking.

Purpose: To investigate the possible alleviating effects of smoking on stress.

Term: Long, with possible short-term results.

Recommended Auspices: C.T.R., Outside and Ad Hoc.

3. Project: Consider experiments involving stress and fatigue due to altitude and time zone changes and the effects of cigarette smoking in alleviating stress.

Cross-Reference: IV.

Purpose: To investigate the effects of smoking in relieving stress.

Term: Long, with possible short-term results.

Recommended Auspices: C.T.R.

4. Project: Collect the available data on human beings (e.g. from the submarine experiments) to determine the effect of stress and the stress-alleviating effect of smoking. Consider possible additional experiments.

Purpose: To demonstrate that smoking alleviates stress.

Term: Short.

Recommended Auspices: Outside.

5. Project: Conduct a stress experiment involving Dr. Wolffe's "Nutmacker Syndrome". Determine whether cigarette smoking alleviates the stress created by the "Nutmacker Syndrome".

Cross-Reference: IV.

Purpose: To test the possible alleviating effects of smoking on stress.

Term: Short.

Recommended Auspices: Outside.

6. Project: Conduct experiments involving behavioral pattern differences between smoking and non-smoking animals. (Compare Bovet and Domino studies and check Harrogate).

Purpose: To determine the effects of smoking on learning time, personality, etc.

Term: Short-term pilot.

Recommended Auspices: C.T.R.

7. Project: Set up experiments involving the creation of stress from the deprivation of affection or other stimuli, testing possible alleviating effects of smoking.

Cross-Reference: IV.

Purpose: To investigate the effect of smoking on the relief of stress.

Term: Long.

Recommended Auspices: C.T.R.

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