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PARENTAL RADIATION EXPOSURE AND DOWN'S SYNDROME WITH PARTICULAR ATTENTION TO IONIZING RADIATION AND RADAR

INTERIM PROGRESS REPORT

BERNICE H. COHEN, Ph. D.

February 28, 1970

Supported by

ADVANCED RESEARCH PROJECTS AGENCY
Department of Defense, Washington, D. C., 20301

Monitored by

U.S. ARMY MEDICAL RESEARCH AND DEVELOPMENT COMMAND
Washington, D. C., 20314

Contract No. DADA-17-69-C-9154

Johns Hopkins University
Baltimore, Maryland
21218

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ABSTRACT

In an epidemiological study of the parents of children with Down's syndrome born from January 1, 1946 to September 30, 1962 and parents of matched control children, a significantly larger percentage of fathers of Down's cases reported radar exposure than control fathers. Moreover, a larger percentage of the fathers of Down's cases reported having been in military service (63.1 percent versus 56.6 percent for control fathers), although this difference was not statistically significant. Because of the possible implications of these findings with regard to the risk of Down's syndrome and possibly other genetic damage to progeny, as well as somatic damage in exposed individuals, a new (CURRENT) series of parents of mongols and matched control children is being studied in an effort to replicate the original study.

Interview information has been obtained in the CURRENT series-Father's Interview Schedule, supplemented with additional questions on radar exposure both in and outside of military service, as well as more detailed questions on military service, service number, duties, etc. Follow-up of all subjects in the ORIGINAL series, irrespective of whether military service was reported, to requestion on military service is being carried out by a combination of telephone, personal visit, mailed questionnaire, etc. Military service records are being validated for both ORIGINAL and CURRENT series by search of U.S. government military records for names of all fathers (whether or not service was reported, whether or not follow-up obtained) for service record dates, MOS classifications and other pertinent data available. Chromosome studies are being carried out on all fathers in the ORIGINAL and CURRENT series who reported exposure to radar and the unexposed fathers matched to them.

Thus far, after ascertainment of over 145 mongols from 27 public and private agencies and hospitals, tracing and interviews have been carried out on 238 mothers and 235 fathers of the mongols and their matched controls in the CURRENT series. Tracing and interviewing is continuing as well as search of hospital records for validation of diagnosis and search of death certificates on deceased index subjects (mongols and their matched controls, their parents and sibs, as they are identified). To date 49 deaths have been searched.

Military service follow-up by phone, mail and personal contact has been carried out on 366 of the 432 fathers of the ORIGINAL series, with similar information obtained by interview on 235 fathers of the CURRENT series. These data are being coded and punched to be forwarded for search of government records, with the remaining to be sent as soon as available. Arrangements have been completed with another agency for search of service records and MOS numbers.

Chromosome studies on radar exposed fathers and unexposed matched fathers are in progress: 92 blood specimens have been collected, including repeats on culture failures and questionable observations. At this date, karyotypes have been completed on 40 and 15 more counted. An attempt will be made to obtain an additional specimen on all culture failures as well as to collect initial specimens from the radar exposed fathers and their matches not yet sampled.

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Completion of coding, punching and analysis of results will be carried out after all the remaining data have been collected.

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Introductory Note

As indicated in the first Quarterly Progress Report, August 29, 1969, this project is jointly funded by the Environmental Control Administration, HEW ($21,885 for 6/69 through 5/70) and the Advanced Research Projects Agency, Office of Secretary of Defense ($64,766 for 6/69 through 5/70). The progress of the total study cannot be fractionated into a segment supported by ECA and another by ARPA, since, except for the chromosome studies which are supported entirely by ARPA funds, the remainder and primary study is organized as a single project to permit the most efficient utilization of personnel, supplies and funds. Therefore, the progress reports constitute summaries of the overall progress of the project with the understanding that each agency will recognize that its funds have contributed in appropriate proportion to the overall accomplishments.

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STATEMENT OF PROBLEM:

Purpose: To determine whether the parents of mongols differ from the parents of matched normal controls with regard to exposure to radar and/or ionizing radiation and to examine the chromosomes of those radar-exposed parents and corresponding parents from the matched series for any discernible differences and/or abnormalities.

Specific Aims:

1. To compare the parents of mongols with those of controls with regard to reported radar exposure, occupations involving radar exposure or exposure to any sources of radioactive substances or radiation.
2. To compare mothers and fathers of Down's syndrome cases with mothers and fathers of matched controls with regard to medical radiation exposure (diagnostic and/or therapeutic).
3. To compare the parents of mongols and of controls with regard to other factors (socioeconomic status, religion, menstrual and medical history, marital history etc.) recognized or suspected to be associated with the occurrence of Down's syndrome and to examine their possible interaction with radar and/or ionizing radiation exposure.
4. To examine the chromosomes of the fathers with a history of exposure to radar and the fathers of children matched to them, and to compare them.

BACKGROUND OF STUDY AND UNDERLYING RATIONALE

In an epidemiological study of the parents of children with Down's syndrome born from January 1, 1946 to September 30, 1962 and parents of matched control children, a significantly larger percentage of fathers of Down's cases reported radar exposure than control fathers.[1] Moreover, a larger percentage of the fathers of Down's cases reported having been in military service (63.1 percent versus 56.6 percent for control fathers), although this difference was not statistically significant. Because of the possible implications of these findings with regard to the risk of Down's syndrome and possibly other genetic damage to progeny, as well as somatic damage in exposed individuals. A new (CURRENT) series of parents of mongol and matched control children is being studied in an effort to replicate the original study.

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1 Sigler, A. T., Lilienfeld, A. M., Cohen, B. H., and Westlake, J. E.; Radiation exposure in parents of children with mongolism (Down's syndrome). Bull. Hopkins Hosp., 117 (6): 374-399, 1965 (Dec.).

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The further studies undertaken consist of:

(1) An independent replication of the previous study utilizing families of Down's cases born in 1945 and between 10/1/62 and 12/31/68 called the CURRENT interview series. This involves the collection of the same data as in the ORIGINAL series, with supplementary portions on military service and radar exposure to determine whether the same patterns appear in an independent replication and at a different period in time.

(2) Follow up of the ORIGINAL interview series for more detailed information on military service and radar exposure. Follow up is being carried out by a combination of phone contacts, mailed questionnaires, and personal visits.

(3) Chromosome Study - All fathers in the ORIGINAL and CURRENT interview study series reporting radar exposure and unexposed fathers of children matched to the children of those radar exposed fathers are being followed up and samples of peripheral blood examined for chromosome abnormalities. In addition, the chromosome study group includes radar exposed fathers ascertained for the ORIGINAL and CURRENT series but not in the final interview study series because of unavailability of the complete matched pair for interview. For these unmatched radar exposed fathers (unmatched in the interview series) a new unexposed match is being obtained for chromosome analysis.

In addition, since the initiation of this presently ongoing phase on June 1, 1969, certain opportunities to extend the scope of this investigation have become apparent both in regard to obtaining more objective validation of the military service and radar exposure on all fathers - ORIGINAL and CURRENT series - irrespective of reported service and/or exposure (a fourth phase of the study); and also in regard to increasing the size of the CURRENT study series.

(4) Validation of military service and exposure - Through consultation on procedures for checking military service and radar exposure from government military files a plan has been designed for documentation of military service and radar exposure. This is to be carried out along with supplemental interview information by partial follow-up reinterview of the original series. Moreover, even in the absence of available reinterview data, validation procedures will be applied. Thus the search of government records on fathers in both the ORIGINAL and CURRENT series will be entirely independent of whether or not service or radar exposure was reported.

Increased size of study series: It is now apparent that a larger study series than expected will be available. Whereas it was estimated that the families of approximately 95 cases and 95 controls would be available for the current study, more comprehensive methods of ascertainment, probably improved diagnosis and more complete case-finding by community and private agencies as well practicing physicians, has made it possible to identify over 147 cases for study, thus a 50% larger sample.

The likelihood of attaining more definitive results would be considerably enhanced both by being able (1) to include the total study series available rather than the previously estimated smaller study group, and

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(2) to carry out more intensive search and validation of military service records and radar exposure.

For these purposes, therefore, an extension of the time schedule beyond the original date and additional funds will be required to accomodate the 50% larger sample. A budget for supplementary funds has been submitted. It should be noted also that while the changing circumstances leading to improved ascertainment in the time interval between the original and current investigation has made possible an increased yield of cases, other changes, such as those pertaining to residential patterns of families of children born in metropolitan Baltimore hospitals have increased the travel time and cost per case studied, as explained in the first Quarterly Progress Report (September 30, 1969).

In the extended plan, both the documentation of military service records and addition of the larger series for study are to be incorporated within the framework of the existing project design.

APPROACH TO THE PROBLEM

The approach to the problem constitutes the three aspects described in the initial proposal (1) Follow-up of the ORIGINAL study series, (2) Independent replication in the CURRENT study series, (3) Chromosome study of all radar exposed fathers ascertained in either study series and of unexposed fathers matched to them; and another aspect, (4) Validation of military service and radar exposure (insofar as possible) from government records for all fathers of mongols and of controls in both the ORIGINAL and CURRENT study series. Moreover, the series ascertained is larger than expected and an attempt is being made to extend all phases of the investigation to the larger study series.

The METHOD OF PROCEDURE thus follows the overall design proposed and approved for the project at the awarding of the contract, with the supplementary aspects designated above.

I. Subjects

Selection of cases: Children with a diagnosis of mongolism meeting the criteria already described for the "original" series[1] and born in the greater Baltimore area between 1/1/45 and 12/31/45 and also those born 10/1/62 through 12/31/68 are included. Sources of ascertainment for the ORIGINAL series and for the CURRENT series have been indicated and are described below.

The CURRENT interview sample is being confined to those years for which cases were not ascertained in the ORIGINAL series. In that previous study, 421 cases born from January 1, 1946 to October 1, 1962 were collected, with 288 meeting the study requirements and 216 available for

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1 Sigler, A. T., Lilienfeld, A. M., Cohen, B. H., and Westlake, J. E.; Parental age in Down's syndrome (mongolism). J. Pediat. 67 (4): 631-642, 1965 (Oct.).

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interview. At the same rate of 1.4 per month meeting requirements and 1.07 per month available for interview, it was estimated that approximately 105 additional mongols would be found in the Baltimore area from October 1, 1962 to January 1, 1969, with at least 80 available for final study. If 1945 were added, 13 to 16 more cases would be available, thus approximately 95 cases in all.

Because of the increased number of sources of ascertainment as well as better diagnostic procedures and case finding techniques among physicians, private and public agencies, and possibly also improved searching techniques, it has been possible, as stated above, to obtain a larger study series than previously anticipated, i.e. about 147 cases of Down's syndrome and an equal number of matched controls rather than the 95 of each previously estimated.

Diagnostic criteria for cases

The following physical findings in Down's syndrome, based on previously reported findings are considered "primary" criteria for diagnosis: 1) Brachycephaly, 2) Slanted palpebral fissures, 3) Epicanthic folds, 4) Palmar simian lines, 5) Malformed ears, 6) Broad and/or short neck, 7) Malformed fingers and/or hands, 8) Nasal abnormality, 9) Hypertelorism, 10) Abnormal palate, 11) Brushfield spots, and 12) Broad and/or short trunk.

Each available case of Down's syndrome, or the case record, will have been examined by a qualified pediatrician. Diagnostic verification required for inclusion of the child in the study is as follows:

1. At least seven of the above primary criteria actually listed by a qualified observer on a medical record; or
2. Five primary signs plus chromosomal studies; or five primary signs plus evidence of either congenital heart disease or abnormal hip angles - the heart disease and/or hip angle evidence either documented in medical records or determined by personal inspection by a qualified physician approved by the principal investigator; or
3. Six of the above listed primary signs as indicated by personal inspection of the child by a qualified physician.

Selection of control subjects: Birth certificates of the children with Down's syndrome are being located, and their place of birth and other vital information verified. Control subjects are selected by rigidly matching, in a systematic manner, each case with another certificate for (1) hospital of birth (or at home), (2) sex and race of child, (3) maternal age at time of birth of child and (4) date of birth.

In each case the best control is a child whose birth date was closest to that of the Down's child of the same sex born in the same hospital to a mother of the same age. If the best control on the basis of established criteria either has left the state or cannot be located, the next best control is selected (i.e., with slightly greater difference in birth dates),

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the other criteria remaining the same.

The hospital records as well as birth certificates of all control children are examined to be certain that the "normal" control group contains no cases of Down's syndrome.

II. Data Being Collected

Records. Birth records (certificate and hospital) and other available hospital and medical records are examined for pertinent information.

Interviews. Mothers and fathers are being interviewed to obtain further information. Where mothers or fathers are deceased, information is obtained insofar as possible from the surviving parent. If both parents are deceased, and necessary information is unavailable, the subject is to be excluded from the matched series.

Interview data include:

1. Complete names and addresses of each parent, index child and sibs.
2. Child's sex, place of birth, physician, and history of hospitalizations and medical conditions.
3. Mothers' education; religion; and histories of residence, occupation and marriage. Medical data will include histories of menstruation, pregnancy, hospitalization and details of radiation exposure. The latter will include diagnostic X-ray, radiation therapy, fluoroscopy, and injection or ingestion of radioactive substances.
4. Father's education; religion; residence; occupational history with detailed information about military service; marital history; number of offspring; illnesses; medical and hospitalization histories; and other pertinent data.

The mother and father are usually interviewed independently at home. The approach to both the families of the mongols and controls is uniform; the interviewers are not informed which are cases and controls and recognition of the mongol's family is usually not known until the actual interview is conducted, if then. Questions about radar and radiation exposure, medical conditions, and occupation are phrased without reference to the birth of the index child. Insofar as possible, dates of exposure are obtained, however, so that the time-relationships relative to the index child can be examined in the analysis.

Validation of findings derived from interview data is being attempted by independent and simultaneous examination of several characteristics of the parents of mongols and of controls as well as through independent search of hospital records.

Validation procedures for military service/radar exposure include the above described independent ascertainment of data through search of military files on all fathers, irrespective of whether they reported such

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service/exposure or not.

III. Chromosome Studies:

The chromosomes of fathers who report a history of radar exposure are being examined to determine whether any aberrations, such as aneuploidy, translocations, dicentrics or other aberrations or evidence of breaks, etc., are observed. As a comparison group, the chromosomes of unexposed fathers of the children matched to those whose fathers indicated radar exposure are also being studied.

In the series already published[1] 18 fathers of children with Down's syndrome and seven fathers of control children reported definite radar exposure with several additional fathers (about eight) having questionable exposure. These fathers and the fathers of children matched to those cases and controls are being located and blood drawn for chromosome analysis.

It was estimated that the CURRENT study series (based on cases born Oct. 1, 1962 to Jan. 1, 1969 and 1945 in the Baltimore area) would yield at least 11 additional exposed fathers and 11 matched fathers, making a total of 72-80 fathers on whom chromosome studies would be carried out. That estimate assumed that the rate of Down's syndrome, ascertainment, and radar exposure would be similar for years to be studied with those years already studied. With the larger CURRENT study series available and including those who had worked near radar, it is now estimated that 60 to 70 fathers may be found to be "radar exposed". Thus, with the matched unexposed fathers, the estimated number of persons on whom chromosome studies will be performed has now increased to about 120 to 140. With deaths and refusals, a conservative estimate of 100 to 120 is more plausible.

RESULTS AND DISCUSSION OF RESULTS:

The results necessarily constitute a review of the project progress to date. Because of the larger than expected sample size, ascertainment in the CURRENT series and problems of dispersal of the population to outlying areas, interviewing is not yet complete, nor is the identification of all radar exposed fathers and unexposed matched fathers or the collection of blood specimens from those fathers. Therefore, the cumulative progress to date will be reviewed as such, with analysis of results and conclusions necessarily deferred until completion of data collection.

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1 Sigler, A. T., Lilienfeld, A. M., Cohen, B. H., and Westlake, J. E.; Radiation exposure in parents of children with mongolism (Down's syndrome). Bull. Hopkins Hosp., 117 (6): 374-399, 1965 (Dec.).

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Progress to February, 1970:

Staff recruitment has been completed and is now stabilized to consist of a coordinator, secretary, junior clerk typist, nurse-blood technician, cytogenetics technician, and seven data processors including research technicians, clerk specialists and tracers who are handling various duties involving hospital records, vital statistics, coding, tracing, etc. Whereas there have been up to five part time interviewers in the field simultaneously, there are currently three interviewers on the staff.

The design of basic procedures and forms has been completed including special follow-up letters, and questionnaires on military service-radar exposure, etc., as well as special coding sheets and code forms.

Codes have been established for military service records search as well as for coding of interview data on fathers, mothers, index cases (Down's syndrome and matched controls) and sibs of indices.

Ascertainment of cases of Down's syndrome has been completed with checking out of lists from schools, hospitals, care centers, public and private agencies indicated in the first report. Baltimore City Public Schools from which ascertainment was delayed until opening of the fall semester have been screened, and additional new cases obtained therefrom. Thus far 230 cases have been ascertained, of whom about 140-150 appear to be eligible, according to our current criteria. Ninety of the 230 have been excluded for various reasons: e.g. rejected on basis of current residence out of state (or beyond Baltimore and surrounding metropolitan area), birth certificate check indicated not born in Baltimore, date of birth incorrectly given (outside study period, etc.) , family requested no referral, diagnosis not confirmed from medical records;or thus far cannot be located. The sources of the sample on the CURRENT series are specified in Table 1. Where a case was ascertained from multiple sources, only the initial source is indicated.

Control matching has proceeded and controls have been matched to cases in accordance with the standardized matching procedure of the study previously described.

Tracing and interviewing of mothers and fathers of identified Down's cases and controls have continued. As indicated in previous reports, further follow up and different individual approaches are planned for refusals; and it is hoped that partial or complete interviews may be obtained on some of these subjects. Often several calls are required to complete interviews even on cooperating respondents, both because of the length of the interview and because every effort is made to adjust to the convenience of the respondents. For the readily located respondents, completion of interviews has involved over 17.5 miles per call and well over 50 miles per completed interview at current estimate. This includes hospital record checks and vital records search and also blood collection where indicated. No estimate is yet available for the difficult to locate group, still being traced.

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The completion status of interviewing on the CURRENT series is summarized in Table 2. A total of 473 interviews have been partially or totally completed on parents of mongols and their matched controls. It has not been possible to locate three fathers thus far; 21 fathers and 23 mothers have refused to be interviewed, with a very slightly higher refusal rate among case families than among control families. It should be noted however that whereas mongols were ascertained through agencies with information on them after birth and were thus relatively locatable despite family situation, controls were matched through birth certificates and therefore more difficult to locate, but when located possibly less likely to be in a situation leading to interview refusal. To be noted also is the fact that many of the first matched controls had to be replaced because of inability to locate.

Record validation: As the deaths become known through interview, death certificates are being requested on all deceased index cases, parents and sibs. Validation of medical information and any questionable information is being attempted through search of hospital records and contacts with physicians.

The deaths to indices, parents and sibs of mongols and matched controls in the current series are tabulated in Table 3. Thus far there are 37 deaths reported in the interviews of mongol families and 23 deaths in the control families. For 48 of these, death certificates have been obtained and are being coded; the remainder are being searched.

Follow up - supplementary military service and exposure data on original series: In order to obtain supplementary information for the original series, in particular on military service and radar exposure, a follow up plan has been designed to include a combination of personal visits, phone contacts and direct mailing. This has been initiated, but because of the time interval since last contact and the recent mobility of the Caucasian population from urban to suburban areas, tracing problems have decreased the rate of progress. Table 4 summarizes progress with regard to follow up.

Of the 432 fathers of mongols and of matched controls in the ORIGINAL series, contact has been made and follow up data obtained on 366 fathers. Thus far it has not been possible to locate three fathers - registered letters having been returned by the postal service. Further attempts at search are being made. In addition, 44 mailed questionnaires have not been answered or returned. Some of these may turn out to be refusals or unlocatable.

Validation of military service and exposure

As a result of consultation on procedures for checking military service and radar exposure from government military files, a plan has been designed for documentation of military service and radar exposure. This is to be carried out in conjunction with supplemental partial reinterview of the original series, though the search of government records will be

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entirely independent of whether or not service or radar exposure was reported.

Necessary arrangements have been made between the School of Hygiene and appropriate agencies for this search. For this purpose, the latest military service information available on follow up is being coded and transferred to punch cards to be used as an aid in identification of fathers in the study. Wherever possible military service numbers have been obtained and included. Thus far records for 362 study fathers are ready to be forwarded for government military record search - 269 from the original series and 93 from the current series (Table 5). In addition, 97 more from the original series and 143 more from the current series are being prepared for punching to increase the total by 240 to 602 fathers. The remainder are still being followed up or processed, or, if in the current series, are yet to be interviewed.

Chromosome Study:

The methodological approach of the chromosome study is described above. The chromosome study group now comprises 43 radar exposed fathers from the ORIGINAL series - 27 fathers of mongols and 16 fathers of controls - along with 43 unexposed matched fathers - 11 fathers of mongols, 21 fathers of controls, plus 11 fathers who are "new matches"* (five to replace unexposed fathers of mongols of original series and six to replace unexposed fathers of controls). From the CURRENT series there are 16 radar exposed fathers - 8 fathers of mongols and 8 fathers of controls - and 13 unexposed fathers - 6 fathers of mongols, 6 fathers of controls, 1 "new match", and three unexposed father matches to be identified. Other CURRENT series radar exposed father and unexposed fathers matched to them will be added to the chromosome study group as they are identified in the CURRENT series interviews still in progress.

The distribution and the number of specimens of blood collected in the chromosome study are summarized in Table 6. According to the last count, 92 blood samples have been obtained on 75 fathers from the two series. Two of the fathers have been dropped from the study because they were found not to have been radar exposed, leaving 73 study fathers from whom blood has been collected.

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* Replacements are used for unexposed fathers who were initially matched to exposed fathers but who are not available because they are deceased, moved outside the Maryland study area, unable to locate, their matches had refused interview in Original or Current Interview Series and/or are unavailable for other reasons. Replacements are thus unexposed "new matches" to radar exposed fathers.

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On 63 subjects*, only one sample has been obtained; on 8, two samples and on 4, three samples. To date there have been approximately 27 culture failures that required (or still require) a second blood sample or a third blood sample and on one subject, a fourth sample is now required. When an additional specimen is obtained because of culture failure, the same code letters are retained as the failure. However, when an abnormality is suspected a repeat specimen is obtained from the subject with new code letters assigned. This is forwarded to the laboratory along with routine initial specimens, so that the karyotype analysis is carried out independently (blind) by the cytogenetics laboratory.

At the present time, approximately 45 more specimens are to be obtained in order to replace culture failures and to screen subjects not yet sampled, in addition to 28 repeat "blind" samples for checking. In view of the rate of culture failures to this time, it is quite likely that the number of additional specimens to be collected and analyzed is as great or greater than the number already processed.

The latest report from the cytogenetics laboratory is summarized in Table 7, Cytogenetics Laboratory Report Summary. An average of 20 cells per patient (ranging from 7 to 50 cells per patient) is being counted. Among the 55 karyotypes counted thus far, 28 samples will require further study. Every effort is being made to keep the study objective and to make certain that the laboratory on receiving and analyzing blood specimens is not aware of the parental exposure status, etc.

An effort will be made to trace the etiology of abnormal karyotypes in chromosome study fathers insofar as possible in order to provide not only the case-control statistical analysis as planned, but also more specific insight into sources and causes of abnormalities, if and where found.

SUMMARY, CONCLUSIONS AND RECOMMENDATIONS:

A summary of the current status of the project operation has been presented above. It should be noted that at the initiation of the project, it was estimated that approximately 95-105 families of mongols would be available for study, based on the experience of the previous series. However, generally improved methods of diagnosis and ascertainment techniques have made available for study approximately 147 - or about 50% more than expected. Since investigation of a larger group would considerably increase the likelihood of obtaining more definite answers to the questions under study, a renewal of the contract with additional funds has been suggested by this investigator. Accordingly, for maximum efficiency of project operations, interviewing, collection of blood specimens and other field phases of the study were extended into the additional series by reallocating funds previously designated for analysis of the smaller series. Thus, at this point in time, although no completed or near complete summaries of the data content are

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* including 2 fathers later eliminated from the study (Table 7)

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available, numerical counts based on field work, follow up, concurrent coding and blood specimens in various stages of processing have been presented.

Arrangements have already been made for the search of government records on all fathers whether or not reporting service, and whether or not reporting radar exposure, to obtain as much information as possible concerning these matters. In addition, as described above in the chromosome study, when any aberrancies are suspected, additional specimens are being obtained, given new code letters and sent for independent analysis to confirm or reject the initial findings. Every effort is being made to obtain as complete and as accurate information as possible as well as to utilize multiple and varied approaches to discern probable causation, or at least gain as much supplementary informative data as possible.

While this investigation is still in progress, it is most important to extend the observations to as large a sample as is reasonably ascertainable in order to increase the definitiveness of any findings obtained, and, to validate the observations insofar as is possible. Toward these goals, hopefully funds will be made available as requested.

Although this is one relatively small study to examine possible effects of microwaves, not only its findings per se but also the significance of this whole area of research on radar and microwave effects must not be overlooked. It is, therefore, important to determine whether the previous interview findings of higher frequencies of military service and radar exposure among fathers of children with Down's syndrome are confirmed by an independent replication of the original study, and by record validation of both the ORIGINAL and CURRENT study series. At a time when military and industrial uses of radar and microwaves, and even household exposures to microwaves, are continually expanding, the importance of investigating this problem must not be underestimated.

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SUMMARY

The project plan thus includes the following:

ORIGINAL series

I. To locate the fathers of cases and controls in the original January 1, 1946 to October 1, 1962 series and bring their records up to date, obtaining more detailed information on military service and radar exposure as well as their experience since our last contact.

II. To obtain from the radar exposed fathers of cases and controls and the unexposed fathers matched to the radar exposed subjects blood samples for chromosome studies and to carry out complete chromosome analysis on these fathers in the ORIGINAL series.

CURRENT series

III. To identify and trace parents of children with Down's syndrome born in the Baltimore area from October 1, 1962 to January 1, 1969 as well as from January 1, 1945 to December 31, 1945 and:

A. Verify diagnosis.

B. Search birth certificates on these affected children.

C. Select controls matched to cases on hospital of birth, date of birth, maternal age, race and sex of infant.

IV. To carry out interviews of parents of Down's cases of current series.

V. To trace the matched controls of the current series and interview their parents.

VI. To validate selected portions of the data obtained by interview against medical records in current series.

VII. To obtain blood samples and carry out chromosome analysis on all fathers reporting radar exposure and on the corresponding fathers of children matched to those whose parents were exposed in the current series.

BOTH series:

VIII. To validate paternal military/radar history by independent search of government military files on all fathers irrespective of service/radar report (as well as carry out chromosome studies indicated above under II and VII respectively).

IX. To follow through on any chromosome abnormalities observed in an attempt to trace their etiological bases.

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TABLE 1

Sources of Ascertainment of Mongols in Current Series

Department of Health - Baltimore City	
Handicapped children	21
Biostatistics	5
Baltimore Association for Retarded Children	18
Rosewood State Training School	5
Searchlight School	2
School of Chimes	2
St. Francis	3
Baltimore City Public Schools	
Claremont School (Baltimore City)	1
Baltimore County Public Schools	
Rolling Road School	4
Battle Mt. School	3
Ridge Road School	3
Hospitals	
Johns Hopkins - IBM listing	6
Johns Hopkins Hospital Medical Records	4
St. Josephs	8
St. Agnes	4
Bon Secours	3
Franklin Square	1
Lutheran	1
South Baltimore General	4
Greater Baltimore Medical Center	9
Baltimore City	2
University	3
Maryland General	7
Mercy	10
Church Home and Hospital	3
Union Memorial	6
Sinai	9
	147

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TABLE 2

Status of Interviewing in Current Series (as of February 1970)

	No. Unable to Locate	Inter-viewed	No. Refused	Still being processed	Total
Mothers of mongols	-	118	13	16	147
Fathers of mongols	1	118	12	16	147
Mothers of controls (including new matches when unable to locate)	-	118	10	19	147
Fathers of controls (including new matches when unable to locate)	2	117	9	19	147
Total	3	473	44	68	588

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TABLE 3

Deaths of Index, Parents, and Sibs in Current Series

Deaths (on interviews returned)	
Mongols	
Mothers	4
Fathers	1
Index subjects	17
Sibs (including stillbirths)	15
Total	37
Controls	
Mothers	2
Fathers	3
Index subjects	-
Sibs (including stillbirths)	18
Total	23

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TABLE 4

Military Service Contact Follow Up on Original Series

Total Number of fathers of mongols and controls ascertained	432
Contact made and information obtained	366
Refusals	10
Unable to locate to date	12
Questionnaires still out	44
	432

Deceased 36

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TABLE 5

Processing for Government Record Search of Military Service

	Original Series	Current Series	Total
Punched and to be sent for government record search	269	93	362
Coded and ready to be punched	97	143	240
Total	366	236	602

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TABLE 6

BLOOD SPECIMENS ON RADAR EXPOSED AND UNEXPOSED FATHERS

ORIGINAL SERIES	Number Fathers	Number of specimens obtained 1st	2nd	3rd	4th	Number of fathers: Deceased	Living out of Baltimore	Unable to locate	Refusals
Exposed fathers of:									
Mongols	27	14	2	1	-	2	3	2	6
Controls	16	14	5	1	-	-	1	-	1
Total exposed	43	28	7	2	-	2	4	2	7
Unexposed fathers of:									
Mongols	11	4	1	1	-	1	3	-	2
Controls	21	19	4	2	-	2	-	-	2
New matches	11	5	-	-	-	2	-	-	3
Total unexposed	43	28	5	2	-	5	3	-	7
NEW SERIES (thus far)									
Exposed fathers of:									
Mongols	8	5	-	-	-	1	-	-	-
Controls	8	6	-	-	-	-	-	-	-
Total exposed	16	11	-	-	-	1	-	-	-
Unexposed fathers of:									
Mongols	6	4	-	-	-	-	-	-	-
Controls	6	2	-	-	-	-	-	-	-
New matches	1	-	-	-	-	-	-	-	-
Unidentified (to be obtained)	3	-	-	-	-	-	-	-	-
Total unexposed	16	6	-	-	-	-	-	-	-
Total Chromosome Study	118	73	12	4	-	8	7	2	14

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TABLE 7

Cytogenetics Laboratory Report Summary - February 1970

Blood specimens received:	92 including repeats on failures
Different code numbers:	78*

Status of Chromosome analyses:

Completed with karyotype	40
Additional counted# and photographed	14
Additional counted# not photographed	1
Total counted	55
Samples received but still to be counted	12
Specimens successfully cultured	67

7 to 50 cells per patiented counted, average 20 cells per patient.

* This involves 75 fathers, 3 fathers having been given new code numbers for blind checking of duplicate samples. Of the 75, 2 listed as radar exposed were subsequently dropped from the study because of lack of confirmation of radar exposure.

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13. ABSTRACT

In an epidemiological study of the parents of children with Down's syndrome born from January 1, 1946 to September 30, 1962 and parents of matched control children, a significantly larger percentage of fathers of Down's cases reported radar exposure than control fathers. Moreover, a larger percentage of the fathers of Down's cases reported having been in military service (63.1 percent versus 56.6 percent for control fathers), although this difference was not statistically significant. Because of the possible implications of these findings, a new (CURRENT) series of parents of mongols and matched control children is being studied in an effort to replicate the original study.

Interview information has been obtained in the CURRENT series with Father's Interview Schedule supplemented by additional questions on radar exposure both in and outside of military service, as well as more detailed questions on military service, service number, duties, etc. Follow-up of all subjects in the ORIGINAL series irrespective of whether military service was reported - to requestion on military service - is being carried out by a combination of telephone, personal visit, mailed questionnaire, etc. Military service records are being validated for both ORIGINAL and CURRENT series by search of U.S. government military records for names of all fathers (whether or not service was reported, whether or not follow-up obtained) to obtain service record dates, MOS classifications and any other pertinent data available. Chromosome studies are being carried

(Continued)

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ABSTRACT (Continued)

out on all fathers in the ORIGINAL and CURRENT series who reported exposure to radar and the unexposed fathers matched to them.

Thus far, after ascertainment of over 145 mongols from 27 public and private agencies and hospitals, tracing and interviews have been carried out on 238 mothers and 235 fathers of the mongols and their matched controls in the CURRENT series. Tracing and interviewing is continuing as well as search of hospital records for validation of diagnosis and search of death certificates on deceased index subjects (mongols and their matched controls, their parents and sibs, as they are identified). To date 49 deaths have been searched.

Military service follow-up by phone, mail and personal contact has been carried out on 366 of the 432 fathers of the ORIGINAL series, with similar information obtained by interview on 235 fathers of the CURRENT series. These data are being coded and punched to be forwarded for search of government records, with the remaining to be sent as soon as available. Arrangements have been completed with another agency for search of service records and MOS numbers.

Chromosome studies on radar exposed fathers and unexposed matched fathers are in progress: 92 blood specimens have been collected, including repeats on culture failures and questionable findings. At this date, karyotypes have been completed on 40 and 15 more counted. An attempt will be made to obtain an additional specimen on all culture failures as well as to collect initial specimens from the radar exposed fathers and their matches not yet sampled.

Completion of coding, punching and analysis of results will be carried out after all the remaining data have been collected.

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