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Acute Radiation Syndrome in Russian Nuclear Workers

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Introduction:

The overall objective of this work was to add clinical information concerning a group of occupationally radiation-exposed workers who developed the acute radiation syndrome (ARS) in the Soviet Union in the period from 1948 through 1953 to that obtained from similar cases that have been collected over many decades in the Western world. It was planned to use these new data to test the triage scheme that had been developed by Thoma and Wald in 1959 to provide clinicians lacking any special knowledge about radiation effects with early diagnostic and prognostic information about the severity of such injury as a basis for medical management.

Significant Findings:

1. We found that 23 of the 59 cases had more than one blood count within the first 72 hours after the radiation exposure, a prerequisite of the triage injury classification method to be tested. These included 15 of the 49, or 30% of the males and 8 of the 10, or 80% of the females. Nevertheless, it was decided to prepare all 59 cases for further dissemination and study in view of the rarity of the syndrome.

2. The WHO Fliedner-Baranov data extraction questionnaire was reviewed in detail jointly by the Russian Federation (RF) and United States (US) participants and found to be too unwieldy and detailed to manage for our purposes. A selection was therefore made of 77 clinical and laboratory items that were of most significance and likely to be on record in most cases. In addition, *X* demographic details, prior medical and radiation history and laboratory data were included in the data extraction questionnaire.

3. The data extraction and database entry processes were carried out efficiently and accurately by the RF participants. A quality assurance study by the US participants revealed an error rate of 4% in x items selected at random in a subset of the ARS cases. The 23 cases that met the laboratory data requirements were studied in detail and complete medical descriptions of the clinical evolution of the ARS phenomena were prepared from the database information. These were then reviewed by the RF group and any necessary corrections made. The number of alterations required was minimal and virtually all of these were recording errors.

4. Classification of the 23 cases into one of 5 injury groups was carried out by Dr. Wald using only the hematologic data over the whole time period of 90 days post-exposure collected in the database. The coded identifiers in the database were recoded for this study. The same process was carried out using only the clinical data. Finally the process was repeated a third time using all data, i.e., clinical, laboratory and dosimetric information.

5. The testing of the ability of several radiation-naive physicians to correctly classify the RF cases on the basis of 72 hour data using the Thoma-Wald classification scheme was the final step in the project. Although prognostication was quite good, there were shortcomings that indicated a need for modification of the classification scheme. These were carried out and the improved results warrant additional testing.

Usefulness of Findings:

A major objective of the project was to facilitate computerized preservation, dissemination and use of these important clinical data in male and female patients of the Mayak workforce by the international scientific community. The clinical case summaries in Appendix A should serve this purpose when publication is completed.

Another goal was the testing of the suitability of the Thoma-Wald triage scheme for diagnostic and prognostic assessment of ARS patients., using this newly accessible data set. This was accomplished, leading to modification and improvement of the triage scheme. Additional testing of the modified scheme appears to be warranted.

Abstract:
The main objective of the parent project, Joint Collaborative Committee for Radiation Effects Research (JCCRER) Project 2.3, is the development of a database of Mayak PA workers to use for such purposes as the verification of current dose-effect models for deterministic effects of acute exposure including the acute radiation syndrome or "ARS".

The pilot research was carried out with DOE support (January 1997) to evaluate the possibility of applying primary clinical and dosimetry data available at FIB-1 and Mayak PA to the study of deterministic effects from occupational radiation exposures. During the pilot stage, the clinical- and dosimetry database was created using a stratified random sampling of the Mayak PA workers (1948-1954), and a quality control exercise on the resulting data-base. A report on work at the pilot stage of project 2.3 was submitted for the Nuclear Regulatory Commission on February 29, 1997. The work was accepted, approved of, and funded on January 15, 1998, for the long-term stage of Project 2.3.

The first stage of the long-term phase (1st year of work) was to carry out the descriptive analysis of the pilot project database and to verify the existing models of acute radiation syndrome. The next stage of the work (2nd and 3rd years) was to extend the clinical-dosimetry database from the pilot number of 225 to final database of 600 persons. The work on collecting, copying, and inputting clinical data has been completed. The dosimetry, occupational histories, demographic data and vital status have been obtained for all workers.

During the period of the NIOSH study Project 2.3 was carrying out work to complete a

quality control study of the extended database; to prepare standard samples of the data and a library of "clean" data samples for further analysis; to prepare a final Code book; and, to test mathematical and statistical methods of dose-effect assessment for deterministic effects.

Acute Radiation Syndrome. The initial focus of effort on the NIOSH ARS project, a component of Project 2.3, was to add clinical information concerning the 59 accidentally radiation-exposed workers in the former Soviet Union during 1948 through 1958 to a similar number of accident cases collected in the Western world. The work was funded by a National Institute of Occupational Safety and Health (NIOSH) project led by Dr. Nadezhda Okladnikova (FIB-1) and Drs. Niel Wald and Richard Day (University of Pittsburgh). The new data were to be used to test the triage scheme that had been developed by Thoma and Wald in 1959 to provide clinicians without any special knowledge about radiation effects with early diagnostic and prognostic information about the severity of such injury as a basis for medical management.

We found that 22 of the 59 cases had more than one blood count within the first 72 hours after the radiation exposure, a prerequisite for the triage injury classification method to be tested. In view of the rarity of the syndrome, all 59 cases were prepared for further study in Project 2.3 A selection was therefore made of 77 clinical and laboratory items that were of most significance and likely to be on record in most cases. In addition, demographic details, prior medical and radiation history and laboratory data were included in the data extraction questionnaire. A quality assurance study of the data extraction by the US participants revealed a low error rate of 4%.

Classification of the 22 cases into 5 injury groups was performed by Dr. Wald using clinical, laboratory and dosimetric information. A test of the ability of radiation-naive physicians to correctly classify the RF cases on the basis of 72 hours of data was completed and analyzed. This led to modification and preliminary retesting of the triage scheme. The improved results warrant further testing of the modified scheme.

Body of the Report:

Background for the project:

Most of our current knowledge about non-cancer morbidity and mortality, the various nonstochastic or deterministic effects of ionizing radiation in humans, has been derived from:

extrapolations from experimental studies of various animals externally and/or internally exposed to high- and/or low-LET radiations;

studies of the Japanese populations exposed at extremely high dose rates to gamma (or

gamma and neutron) radiation from atomic bombs;

data about medical side effects arising from radiation therapy for cancer, usually given in fractionated, localized doses; or

published data about the relatively rare occurrences of accidentally irradiated radiation workers, predominantly male, as well as some members of the public, who developed deterministic effects.

The exposures have been from incorporation of internal radioactive materials, or by irradiation from external beta and/or gamma as well as from alpha, beta, and gamma sources occurring singly or in combinations, acutely and/or chronically. All of these are situations that might occur in nuclear accidents or intentional incidents.

Although all of these experiences have provided extremely useful radiobiological data, they are limited for the purpose of our general objective, ie., to identify the best clinical and laboratory correlates for prognostication and medical management of the acute radiation syndrome in male and female patients. The value of the first source of data is limited because of the uncertainties of interspecies extrapolations. The second lacks much detailed clinical and laboratory data concerning the ARS because of the devastation of medical resources in the post-bombing period. The third suffers from the confounding manifestations of the patients' primary disease, the generally protracted exposure, and the concurrent use of other forms of treatment.

A major advantage of the fourth source of data described above, despite its relative paucity, is that the worker population is generally in good health at the time of exposure and the medical management of such mishaps often includes detailed dose reconstruction in addition to close clinical observation. Thoma and Wald took advantage of these features in 1959 to promulgate recommendations for the diagnosis and management of acute radiation injury based on a study of seven accidents involving 32 patients about whom there was sufficient detailed clinical information[1]. A triage scheme for clinical diagnostic and prognostic classification according to severity of injury was proposed utilizing the time of appearance and severity of the early prodromal signs and symptoms, and of alterations in the early blood cell counts.

This approach, which does not require the use of physical dosimetric information that is usually difficult to obtain promptly in an accident situation, has been generally accepted and its details disseminated in a variety of publications, e.g., Medical Aspect of Radiation Accidents: A handbook for Physicians, Health Physicists, and Industrial Hygienists, E.S. Saenger, Editor, US Atomic Energy Commission, Washington, D.C., 1963; Principles of Radiation Protection: a textbook of health physics, K.Z. Morgan and J.E. Turner, Editors, John Wiley, New York, 1967; Medical Radiation Biology, G.V. Dalrymple, M.E.Gaulden, G.M. Kollmorgen and H.H.Vogel, Jr., Editors, W.B. Saunders, Philadelphia, 1973; Mettler,

F.A. and Moseley, R.D. Jr., Medical Effects of Ionizing Radiation, Grune & Stratton, Orlando, FL, 1985, and Mettler, F.A. and Upton, A.C., Second Edition, W.B. Saunders, Philadelphia, 1995; T.A. Carder, Handling of radiation accident patients by paramedical and hospital personnel, CRC Press, Boca Raton, FL, 1993; and Textbook of Clinical Occupational and Environmental Medicine, L. Rosenstock and M.R. Cullen, Editors, W.B. Saunders, Philadelphia, 1994.

Since then, additional occupational overexposures have occurred. As of March 1996, the US Department of Energy(DOE)/Radiation Emergency Assistance Center/Training Site (REAC/TS Radiation Accident Registries include 236 U.S. accidents since 1944 involving 781 instances of "medically significant" exposure as defined by DOE and NRC (i.e., > 0.25Gy whole body, >6Gy to skin or extremity area large enough to produce symptoms, 0.75 Gy to other tissues or >half the NCRP occupational maximum internal organ burden[2]) including 30 fatalities. Outside the U.S., 149 accidents led to 2,110 "significant" exposures including 82 fatalities[3].

The large majority of the "significant" exposures in the DOE Registry were not high enough to produce the ARS or radiation burns. This is confirmed by the relatively small number of fatalities. In addition, even in many of the severe cases in the Registry, complete detailed dosimetric, clinical and laboratory information is not available for study. The cases that are reported in the scientific literature are widely scattered as recent compilations by Oliviera[4] and by Anno et al[5] show, and do not necessarily serve for detailed analysis as Baverstock and Ash pointed out in their review[6].

In an effort to facilitate the analysis of clinically significant radiation exposure cases, Fliedner at the University of Ulm, Germany, and Baranov at the Russian Federation Academy of Sciences Institute of Biophysics, Moscow , have collaborated in developing with World Health Organization sponsorship, an international computer database for detailed radiation exposure case histories[7]. In order to provide a uniform format for case reporting, a "Clinical Pre Computer Proforma" or data extraction questionnaire was published in 1994[8].

An important purpose of our project was to make a significant addition to the cases of ARS available for analysis and if suitable, for possible addition to the International Computer Database and to the DOE REAC/TS Registries described above. The unique opportunity to do so is related to the fact that during the past 50 years, defense-related activities in the Russian Federation and in the United States resulted in occasional accidental occupational radiation exposures of nuclear workers as well as in some population exposures. Until recently, however, most of the data related to such exposures were not available for scientific study.

Information has now became available about activities of the first Russian nuclear weapon production facilities, the Mayak Production Association in the South Urals[9] [10]. Several thousands of workers were exposed to relatively high levels of external gamma radiation

and, in many cases, to internal alpha radiation from inhaled plutonium as well. The cumulated doses over 1 to 6 years (1948-1953) were as high as 1 to 10 Gy. A number of these workers developed health impairments that are considered to be forms of radiation injury. More than 1,800 cases of occupational diseases were diagnosed by 1960 and chronic radiation sickness was identified as a major contributor to the total. This syndrome was described by A.K. Guskova and G.D. Baisogolov in 1971[11]. In a recent review[12] Okladnikova also described early deterministic effects including cases of the acute radiation syndromes, local radiation injuries, and cataracts as well as pulmonary pneumosclerosis following large plutonium inhalations.

Systematic medical observations have been carried out by Branch 1 of the Institute of Biophysics of the Russian Ministry of Health on all workers as part of the radiation protection program that began with the start-up of the Mayak facilities. For 48 years these unique data have been collected, now allowing the study of a wide range of deterministic effects, including those involving the hematopoietic, immune, nervous, cardiovascular, visual and, more recently, cytogenetic systems, as well as the key organs of plutonium deposition, i.e., liver, lungs and skeleton.

The ARS subset, which is the focus of this proposal, consists of fifty nine patients, of which forty nine were men and ten were women. Fifty seven of the cases occurred between 1950 and 1958 with two additional cases in 1968. In thirty eight of the patients, follow-up examinations have continued to the present at the FIB-1 clinic. Twenty one others migrated out of the region; however, information about their status is still accumulated at FIB-1. For example, the occurrence and causes of death have been verified in 16 instances.

These detailed clinical data provides a basis for ascertaining the relationships between early effects and the subsequent clinical course. With adequate dosimetry it aids in determination of dose thresholds and dose-response relationships for the production of the deterministic effects of acute occupational radiation overexposure. That information, in turn, makes possible the development and validation of accurate predictive models that can facilitate the early diagnosis and improved treatment of ARS.

This is of particular importance in maintaining preparedness to deal with low probability but high consequence radiation overexposure occurrences whose treatment is most likely to be in the hands of physicians with little or no previous specific professional experience in the recognition of such health problems because of their rarity. The global dissemination of nuclear reactors, materials, and possibly weapons, as well as radiation therapy sources and medical isotopes is still increasing. The number of workers involved in nuclear industries and in the clean-up of former nuclear sites is expanding. For these reasons, radiation emergency preparedness is an essential feature in the modern maintenance of occupational and public health.

Mayak Production Association (MPA):

In view of the unavailability of information until recently about the Mayak facilities, some background material is summarized in this section. It is is based largely on publications by Illyin[9]; Akleyev and Lyubchansky[13]; Okladnikova et al[12] and Shilnikova, N.S. et al[14], as well as a descriptive brochure of the Mayak Production Association, 6 December 1993 and a comprehensive lecture at the Mayak Museum in Ozyorsk in March 1996.

The Mayak Production Association is located near Ozyorsk, a closed city with a population of 85,600 in the Southern Ural Mountains. The city is about 50 miles north of Chelyabinsk, a city with a population of about one million people in the Asian part of Russia. The reactor area is located about 7 miles from Ozyorsk. Construction of MPA began in November 1945, and the first reactor became operational in June 1948.

There used to be six operational reactors at Mayak for the production of weapons plutonium. Of these, five were graphite-moderated while the sixth was originally a heavy water reactor. These reactors have now been shut down. The heavy water reactor was later modified to a light water reactor which remains in operation today. An additional light water reactor produces isotopes for civilian use. There is also a reprocessing facility in use at Mayak, as well as a vitrification facility for liquid waste and storage tanks containing high level radioactive waste.

Reactor types

There were five water-cooled, graphite-moderated reactors at the MPA. The first reactor, the A reactor, was a graphite-moderated production reactor. The reactor was completed in 1948, was operational for 39 years, and was finally shut down in 1987. The second reactor to be started was a heavy water moderated reactor known as "Ruslan". This reactor went into operation around the end of the 1940s and was active until about 1980. Towards the end of the 1980s, it was rebuilt to a light water reactor with a capacity of 1 000 MW. "Ruslan" is used to produce tritium and specific isotopes such as Plutonium-238.

The IR reactor was used for the production of plutonium and to test the fuel of both the A-reactor and the RBMK reactors. It was a small graphite-moderated 65 MWt reactor that became operational in1951 and was shut down after 36 years of operation in 1987. The three large graphite-moderated production reactors AV-1, AV-2, and AV-3 probably all share the same design. They went into operation in the early 1950s and were shut down about 1990. Another type of reactor which is still in use at Mayak is a light water reactor called "Lyudmila". Its power is 1 000 MW and it is also used for the production of tritium and various other isotopes, including Pu-238.

Reprocessing Facilities

Six months after the start-up of the A-reactor in December 1948, the first of at least three reprocessing facilities to be built by Mayak began operation. The facility was in use until 1961 when it was decommissioned.

A second plant, the radiochemical facility RT-1, became operational in 1956 and is still in use. It was originally intended to reprocess weapons grade plutonium generated by the spent nuclear fuel from the five production reactors. In 1976 the facility was modified to reprocess civilian plutonium based on spent nuclear fuel from reactors on board submarines and icebreakers, research reactors, liquid metal-cooled fast breeder reactors and from the first and second generation Soviet pressurized water reactors. Also, countries in Eastern Europe and Finland send spent nuclear fuel from their own Soviet Russian-built pressurized water reactors to this facility.

Accidents

There have been a number of accidents of varying severity at the facilities. Most were limited to on-site workers and facilities, but some had environmental consequences as well. Some examples of both types that involved workers overexposures are summarized briefly here.

In two major accidents, large amounts of radioactivity were released. The most serious accident was the September 29, 1957 Kyshtym accident, in which an on-site storage tank containing 20 MCi of high level liquid radioactive waste exploded. Up to 90% of the release deposited in the local area but about 2 Mci formed a radioactive cloud that contaminated an area of 300 km. This led to the evacuation of over 10,000 people as the significance of the accident became clear.

An example of an on-site problem took place on April 21, 1957, approximately six months prior to the Kyshtym accident. A self-sustaining chain reaction occurred in a highly enriched uranium-nitrate solution. Six people were injured, but no areas outside the immediate compound were contaminated. The incident was rated 4 on the INES scale, a nuclear accident rating scale defined by the International Atomic Energy Agency that goes from 1 to 7 in order of increasing severity.

On October 2, 1958, another self-sustaining chain reaction occurred at the reprocessing facility, this time during experimental work to determine the critical parameters of the dissolution of highly concentrated uranium nitrates. The accident resulted in exposure of the researchers to radiation. The accident rated 4 on the INES scale.

Ten years later, a self-sustaining chain reaction occurred at the reprocessing area for metallic plutonium. The accident resulted in injury to two people. This accident also ranked 4 on the INES scale.

It was hypothesized in our original proposal that enough useful clinical prognostic information to facilitate the medical management of radiation overexposure can be derived relatively early, within 72 to 96 hours after exposure using biological indicators that can be observed readily in individual patients as well as in mass casualties. This was based on our previous work suggesting that the early clinical and laboratory features of ARS are reasonably consistent and correlate well enough with the subsequent expression of clinical injury in a variety of occupational radiation exposure situations. It was further hypothesized that the study of newly available data from the medical and dosimetric records of 59 cases of ARS among the Russian nuclear workers who worked at the Mayak PA nuclear weapons facility, including 10 women, could facilitate validation and refinement of the models and methodology currently recommended for such prognostic evaluation, if the clinical course of each patient could be reconstructed from the existing clinical and laboratory records.

To test these hypotheses, our specific aims were to do the following:

1. Collect and examine dosimetric, clinical and laboratory data of the 59 workers, including 10 women, who developed the acute radiation syndrome (ARS) following accidental radiation exposure at the Mayak nuclear facilities in Ozersk, Russian Federation.

2. Test applicability of the WHO Fliedner-Baranov data extraction questionnaire for the Mayak worker cases and modify as needed.

3. Extract clinical, laboratory and dosimetric data and details of the exposure circumstances for further analysis and potential entry into ARS databases accessible to project collaborators and eventually to the international scientific community.

4. Classify each of the Mayak ARS patients into one of the five Thoma-Wald radiation injury groups based on clinical features and determine the median and range of the dose estimates within each group to evaluate dosimetry.

5. Determine whether the Thoma-Wald diagnostic model recommended in the literature for prompt diagnosis of ARS provides reliable prognostic information when applied to the female as well as to the male Mayak ARS patients.

Procedures and Methodology:

The research design and methodology to achieve these specific aims has involved sequential tasks. We will now present each aim-related task, reviewing the work accomplished and the conclusions drawn.

Task 1: The US clinical investigators (including a Russian speaking physician) visited Ozersk in March, 1996 in order to gain assurance that the patient records preserved at FIB-1 contained sufficient detail to justify the project and to prepare for data extraction. Three to five cases were randomly selected (including at least one female) for abstraction over a seven day period. These were test/learning cases in which the US and RF investigators could develop agreements on handling difficult or ambiguous data and other data collection issues.

Task 2 : In the initial mid-December 1996 joint work period in Ozyorsk, the US and RF teams reviewed the detailed FIB-1 clinical and dosimetric records of a 10% subset of the 59 Mayak workers that were diagnosed as having the Acute Radiation Syndrome (ARS). This confirmed the impression gained from a pilot inspection of 4 ARS case records at FIB-1 in March 1996 that the information was available in sufficient detail to justify continuation of the project.

Task 3 : In December 1996, both teams began a review of the WHO/Fliedner-Baranov data extraction questionnaire (FBQ) in detail for applicability to the Mayak ARS case records. During a joint work period in Pittsburgh in mid February,1997, it was concluded that the FBQ was much more extensive than needed for the project and necessary modifications of the FBQ were agreed upon.

Task 4 : The RF team began the work of data extraction and computer entry into the study data base in March, 1997. Items whose extraction was completed and entered for all 59 cases now include identification data, vital status, work history, health behaviors, reproductive history, dosimetric information and clinical laboratory test results including hematological and biochemical studies. Bone marrow study findings were also included in 43 cases in which these were performed.

1. Description of the ARS section of the FIB1 NC Mayak/Pitt computer database

The ARS database was developed using a modified version of the WHO's Fliedner-Baranov data extraction instrument and Visual Fox Pro, Version 3. The design and programming were done by Andre Fevralev and Richard Day at the University of Pittsburgh in the course of a DOE and NRC-funded project.

A random sample of 260 collected cases in the database were stratified into four data subsets of radiation injury including a random subset of the ARS cases. Subsequently, as part of this NIOSH-funded study, all of the 59 ARS cases recorded at FIB-1 have been included.

1.1. Topic codes of the data sets for ARS

All relevant patient information was collected into the computer database and classified in the following topic codes:

Subject identifier
Medical history
Demographic data
Work history data
Health behaviors history
Monthly occupation gamma exposure (1948-1963)

Yearly occupation gamma exposure (1948-1993)
Total occupation gamma exposure
Hematological data
Blood pressure
Bone marrow data
Cytogenetic data
ARS accident background
ARS clinical signs and symptoms
ARS treatment
ARS biochemical data

1.2. Clinical database for ARS cases

A total of 59 ARS cases were collected in the database .including clinical, dosimetric and laboratory information as follows :

1.2-1. Radiation exposure: the ARS exposure dose data set includes both neutron and gamma exposure data, as indicated.

1.2-2. Work places::

Plant A: Nuclear reactor facility ;
Plant B: Radiochemical separation plant;
Plant C: Plutonium production plant;
Plant D: Other affiliated facilities.

1.2-3 Symptoms and treatment:

The features of ARS utilized were selected from the more extensive Fliedner-Baranov data extraction questionnaire (22-23) with some additional modifications. They includes the following information:

1.2-3-1. Prodromal syndrome features:

Death; Anorexia; Nausea; Vomiting: Diarrhea; Bloody diarrhea; Abdominal pain; Erythema of skin; Headache; Dizziness; Temporal disorientation; Incapacitation/disorientation; incapacitation/prostration; Somnolent state; Coma; Fatigue/weakness; Sweating; Tachycardia; Hypertension; Hypotension; Fever; and Weight loss.

1.2-3-2. Gastrointestinal tract and kidney features:

Abdominal distension; X-ray abnormalities (distension, ulceration or perforation); Peritonitis; Jaundice; Hepatomegaly; Ascites; Hepatic encephalopathy; Pancreatitis; X-ray abnormalities of small intestine or pancreas; Abnormalities of kidney; Anuria; Hematuria; Polyuria; Proteinuria; Oliguria; Edema, generalized or pedal; and Dysuria.

1.2-3-3. Nervous system, heart and lung features:

Disturbance of reflexes; Disturbances of sensation; Ataxia; Other disturbances of motor functions; papilledema; Acute encephalopathy; Late encephalopathy; EEG abnormalities; Cardiac X-ray abnormalities; Cough; X-ray abnormalities of lung; Pneumonitis (local); and Pneumonitis (interstitial diffuse).

1.2-3-4. Other organs and systems features:

Conjunctival hyperemia; Other lesions of conjunctiva; Cataract (including opacities); Changes of the optic fundus; Blisters; Ulceration; Necrosis of skin; Scalp pain; Epilation; Purpura; Hemorrhage; Thyroid tenderness; Thyroid enlargement; Testicular atrophy; Oligospermia; Aspermia; Temporary amenorrhea; Permanent amenorrhea; Osteitis; Osteomyelitis; Pain in bone; and Tenderness of bone.

1.2-3-5. Treatment:

Sedatives; Analgesics; Antiemetics; Antispasmodics; Parenteral fluids: Electrolytes; Whole blood; Plasma; Platelets; Vasoconstrictors; Vitamins; Antibiotics; Hematinics; Steroids; Peripheral blood counts; Bone marrow aspiration or biopsy; other/miscellaneous.

1.3 Hematological database

These data sets were composed of complete blood counts with differential analyses, including following data: Clinical I.D. number; Diagnosis (primary and secondary); Sampling time (day/month/year); Erythrocytes; Hemoglobin; Reticulocytes; Thrombocytes; Leukocytes; Basophils (%); Eosinophils (%); Metameylocytes (%); Bands (%); Polymorphonuclear leukocytes (%); Lymphocytes (%); Monocytes (%);

Plasma cells (%); other cells; Systolic blood pressure; Diastolic blood pressure; Thrombocytopenia; and Leukocytopenia.

Using a Microsoft Excel program, absolute peripheral lymphocyte and neutrophil counts were calculated from the leukocyte count and differential percentile count.

1.4 Biochemical database:

The biochemical data set was composed of following clinical chemistry parameters: Clinical I.D. number; Diagnosis (primary and secondary); Sampling time (post-exposure day); Blood sugar; Total protein; Albumin; Globulin; Bilirubin; Chlorides; Cholesterol; Blood urea nitrogen; Alkaline phosphatase and Transaminase.

Where appropriate, SI units were converted into the conventional US units in both hematological and biochemical tests for convenience.

2. Utilizing clinical, hematological and biochemical data from the computer database and reconstructing detailed clinical data summaries.

The codes of clinical symptoms and signs as well as hematological and biochemical data were downloaded from the computer database, In order to deal with the extensive number of individual items, 77 clinical variables recorded over 90 days for each case, it was necessary to reconstruct a detailed clinical summary giving all the key findings of each patient's entire course from the data set, essentially converting the tables into words. The transformations were carried out by Dr. Zhang, with detailed review by Dr. Wald. and then they jointly converted them into detailed clinical descriptions. These are presented in Appendix A.

For the purpose of quality control assessment, the clinical descriptions were then submitted to FIB-1 colleagues to compare with the original medical records to order to insure accuracy of the reconstructions and to assure the inclusion of the relevant information in the medical records. Detailed feedback obtained from FIB-1 regarding translation errors, misinterpretations or discrepancies was incorporated into the database.

Following the extraction of all 59 records, the US investigators returned to Ozersk to carry out a quality assessment of the extraction procedure. Ten cases were randomly selected for detailed quality assessment. In this process, the data in the FBDEI was checked against the material in the clinical, dosimetric and laboratory records and vice versa with the help of a Russian speaking US investigator. The goals of this routine quality assessment/quality control procedure were threefold: (a) to insure that the data in the records were accurately transferred to the FBQ; (b) to insure that all of the information in the FBQ can be found in the records; and (c) to insure that all of the relevant information in the records has been transferred to the FBQ. Following the completion of this QA/QC procedure, completed copies of the FBQ were transported back to the University of Pittsburgh. The data provided to US investigators included only FIB-1 clinical record numbers as identifiers. No personal identifiers (e.g., names) were included in the data that might allow the independent identification of the individual workers

In May, 1997, Dr. Day visited FIB-1 and reviewed progress on this task. It was agreed that somewhat more detailed information on symptoms and treatment of ARS was available in the medical records than the format in use had collected. Accordingly, modifications were made to the extraction procedure and collection began of the additional information. It was then inserted into the database that had been appropriately modified. (See Appendix D and its Attachments 1, 2 and 3.)

Task 5: Mr. Fevralev visited the University of Pittsburgh in February 1998 to install the modified database and to work with Dr. Day on the development and testing of additional functions for analyses and data export. A resultant fully revised Database Code Book reflecting the changes was completed and delivered to the RF group in April,1998.

Task 6: It had been planned that data sets would be drawn from the joint database at FIB-1 by Mr. Fevralev and transferred by internet to the US group for development of data analyses. An RF policy decision precluded that procedure and therefore, Dr. Day and Mr. Vergona proceeded to perform the generation of the necessary data sets for analyses of the database content. By September 1998 a suitably accurate library of data sets was completed.

Task 7: The initial phase of the data analysis was carried out by Drs. Wald and Day. In the first step, Dr. Day made available to Dr. Wald all of the relevant hematological data, while keeping Dr. Wald blind to the data on signs and symptoms, clinical outcome (death/recovery), gender and estimated dose. Based solely on the hematological data, Dr. Wald calculated the cumulative blood count profile scores using a method developed in a previous study[1] and classified each patient into one of the five radiation injury groups based on these profiles.

In the second phase of the analysis, Dr. Wald was presented with the data on signs and symptoms, while being kept blind to the patient's hematological data, clinical outcome, gender and estimated dose. He again classified each patient into one of the five radiation injury groups based solely on the clinical signs and symptoms.

In the third phase of the analysis, Dr. Wald was presented with each patient's hematological data, clinical signs and symptoms, and clinical outcome, while remaining blind to estimated dose.

Several months later, based on all of this material, Drs. Wald and Zhang independently made a final classification of each patient into one of the five radiation injury groups. The correlation of these injury group assignments by the two independent examiners was high, with only one disagreement by one category in a borderline case.

Task 8: The fourth stage of the data analysis involved Dr. John Mahoney, the head of the University Medical Center's Emergency Medicine Department, and three members of the

department, Drs. Clifford Callaway, Sue Dunmire and Ron Roth. They were given the information on each patient required to implement the triage schema for a preliminary evaluation of clinical radiation injury following overexposure[1]. This information included blood counts and data on the occurrence of prodromal symptoms including nausea, vomiting and diarrhea during the first 72 hours following exposure. Based solely on these data, the Emergency Medicine physicians were asked to classify each patient into one of the five radiation injury groups

In an effort to test the feasibility of this stage, another physician, Dr. Theodore Sofish, modified the clinical reconstructions to cover only the first 72 hours of data. This requirement reduced the usable number of cases to 23, 15 males and 8 females. The cases were recoded to minimize recognition although this could not be ruled out. Both Drs. Wald and Zhang classified the cases using the 72 hour reconstructions and the full clinical course ones.

Task 9. Data analysis and preparation of final report for publication were completed in collaboration with the RF team.

Results and Statistical Analyses:

The results of the quality assessment/quality control exercise are presented in Appendix D to this report. Error rates for all three components of the QA/QC exercise did not exceed 1% and were acceptable to continue the project.

The results of the exercise carried out under Task 8 are reported in Table 7. Using the data in Table 1, kappa statistics were calculated to measure the agreement between the emergency room doctors and the gold standard assessment provided by Dr. Wald. The kappa results are presented on Table 8.

Conclusions:

1. Analysis of the results of the initial trial of application of the Thoma-Wald triage scheme to the 29 Mayak PA worker ARS patients' clinical summaries revealed some deficiencies in prognostic accuracy but were of sufficient quality to warrant .

The triage scheme being tested was modified to reduce the observation period from 7 days to 72 hours to make it more practical for field situations involving large numbers of potential Acute Radiation Syndrome (ARS) patients. This reduced the five grades of radiation injury severity to three, ie., I. Survival Probable (including old injury classification 1. no clinical effects and 2., minor laboratory test abnormalities); II. Survival Possible (including old injury classification 3. major hematologic abnormalities and 4. gastrointestinal damage); and III. Survival Improbable including old injury classification 5. neurovascular damage).

2. The clinical data for application of the modified triage scheme (MTS) were available in 22 of the 59 ARS cases from FIB-1. None of these underwent the neurovascular form of the syndrome.

3. The four physicians participating in the MTS trial were able to distinguish correctly between Injury Grades I and II but erred in overclassifying some old injury classification 4 cases as Injury Grade III instead of II because of severe clinical symptomatology described, to which they gave greater weight than to the less severe hematologic findings.

4. Inadequacies in the short instructions for use of the triage scheme may have contributed to the errors and should be reviewed. Also the logic of the modifications to the triage scheme should be reexamined.

5. It would be highly desirable to enlarge the database with additional cases with appropriate clinical and laboratory data to evaluate the modified triage scheme more adequately.

This final report was written and reviewed in close collaboration by the US and RF scientific teams. A draft of the study and its findings is also being prepared for a peer-reviewed scientific publication.

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Figure 1:

Preliminary Evaluation of Acute Radiation Injury Following Overexposure
Modified from Thoma and Wald (1959)

EVALUATION PROCEDURES

1. Observe and record time of onset of clinical signs and symptoms
2. Perform daily blood count

FINDINGS	**POTENTIAL OUTCOME**
Neither nausea and/or vomiting nor any blood count derangement in 2 days	**No Clinical Radiation Injury**

Nausea and/or vomiting and some blood count derangement in 2 days	Mnor Hematologic Syndrome
Nausea and/or vomiting in 2 days and marked leucocyte and lymphocyte count derangement in 3 days	Major Hematologic Syndrome
Nausea and/or vomiting in 2 days and diarrhea within 4 days and marked platelet derangement within 6 to 9 days	Gastrointestinal Syndrome
Nausea, vomiting, diarrhea within minutes. Ataxia, disorientation, shock, coma in minutes to hours	Neurovascular Syndrome

Table 1

Modified Thoma-Wald (1959) injury group classifications.

Group	Prognosis	Clinical features
I	Survival assured	Generally asymptomatic or with minimal prodromal anorexia and nausea (few hours). No significant impairment.
II	Survival probable	Mild ARS. Prodromal nausea and vomiting (1-2 days). Mild hematological abnormalities with no or little consequent clinical impairment for at least 2-3 weeks.

III	Survival possible	Classical ARS prodroma (1-2 days). Possible performance decrement from fatigue thereafter with major hematological derangement producing life-threatening complications in 2 to 3 weeks and requiring major supportive therapy.
IV	Survival improbable	Accelerated severe ARS prodroma, including diarrhea, followed by weakness and recurrent GI problems. Major hematological complications if survival exceeds 1-2 weeks.
V	Survival impossible	Immediate violent ARS prodroma with disturbances in consciousness and homeostasis leading to shock, coma and death in hours to 1-2 days.

Table 2

The stratification of 23 Mayak PA ARS cases using Thoma-Wald radiation injury classifications.

Group	Total Cases	ARS Case No:
I-II	13	432, 541, 3666, 4409, 12409, 12888, 14529, 19471, 25539, 29190, 29395, 40044, 40482
III	6	15189, 17087, 20096, 28562, 32510, 34406
IV	4	2119, 9685, 25864, 53992

Table 3

The clinical radiation injury grouping of 8 female ARS workers

Group	Total Cases	ARS Case No:
I-II	3	14529, 29190, 40482
III	4	17087, 28562, 32510, 34406

IV	1	9685

Table 4

The clinical radiation injury grouping of 15 male ARS workers

Group	Total Cases	ARS Case No:
I-II	10	432, 541, 3666, 4409, 12409, 12888, 19471, 25539, 29395, 40044
III	2	15189, 20096,
IV	3	2119, 25864, 53992

Table 5

ARS patients' clinical injury groupings and their estimated radiation doses.

Group	Male			Female		
	Case No.	Dp* (cGy)	Da** (cGy)	Case No.	Da* (cGy)	: Dp** (cGy)
I-II	432	292	33	14529	11.2	150
	541	33	21.6	29190	0	150
	3666	239	50	40482	0	300
	4409	169	50			
	12409	488	50			

	12888	401	150			
	19471	27	150			
	25539	379	33			
	29395	0	150			
	40044	305	250			
III	15189	220	961	17087	0	580
	20096	715	1000	28562	167	581
				32510	0	1201
				34406	0	1213
IV	2119	11.7	12451	9685	0	4603
	25864	1.4	4870			
	53992	9.3	13131			

* represents the pre-accident cumulative occupational exposure dose estimate.
** represents the accidental exposure dose.estimate

Table 6. The average pre-accident and accident radiation exposures (Gy) in male and female patients.

Group	Male		Female		All Cases	
	Da*	Dp**	Da*	Dp**	Mean+/-SME	Median
I-II	2.33	0.97	0.04	2.00	1.18+/- 0.24	1.50
III	4.68	9.80	0.42	8.90	9.35+/- 1.16	9.80
IV	0.06	101.50	0	46.03	87.64+/-23.29	86.60

* represents the pre-accident cumulative occupational exposure dose estimate.
** represents the accidental exposure dose.estimate

Table 7
Medical Rater Scoring (1-4) and Gold Standard *(G)* By Case

Case Number	Survival Category Probable (1)	Possible (2)	Improbable (3)
432	1,2,3,4 *(G)*		
541	1,2,3,4 *(G)*		
2119		*(G)*	1,2,3,4
3666	3 *(G)*	1,2,4	
4409	1,2,3,4 *(G)*		
9685		1*(G)*	2,3,4
12409	1,2,3,4	*(G)*	
14529	1,2,3,4*(G)*		
15189		1,2,3,4 *(G)*	
17087	1,2,3,4	*(G)*	
19471	1,2,3,4	*(G)*	
20096	1,3,4	2 *(G)*	
25539	1,2,3,4 *(G)*		
25864		1,2,4*(G)*	3
28562	2,3	1,4*(G)*	
29190	1,2,3,4*(G)*		
29395	1,2,3,4*(G)*		
32510		1,3,4 *(G)*	2
34406		1,2,3,4*(G)*	
40044	1,2,3,4*(G)*		
40482	1,2,3,4 *(G)*		
53992		*(G)*	1,2,3,4

Table 8.

Individual and Overall Rater Agreement with the Gold Standard Assessment of the Likelihood of Patient Survival (Triage Group) for n=22 Russian Acute Radiation Cases

Rater	Kappa	Std. Error	95% CI	P-Value
1	0.407	0.139	0.136-0.679	0.0042
2	0.535	0.101	0.337-0.733	0.0036
3	0.526	0.100	0.330-0.722	0.0063
4	0.527	0.116	0.300-0.754	0.0082
Overall	0.449	0.058	0.385-0.614	>0.0001

Appendix A

CLINICAL RADIATION INJURY GROUPS I and II

ARS 432 (DOB 10-5-1926)

A 27-year-old male nuclear facility worker, with a history of chronic radiation syndrome, came to the clinic after receiving a whole body radiation exposure at Plant A on September 18, 1953. He was employed at Plant B in 1949 and transferred to Plant A in December 1950. His past medical history revealed Chronic Radiation Syndrome since October 10, 1950. His psychosocial history indicated smoking (1 pack/day) and moderate alcohol consumption.

Upon arrival, he complained of headache, sweating and ataxia. On physical examination (P/E), there was asymmetry of deep tendon reflexes. Laboratory tests showed mildly elevated leukocytes (neutrophils: 4140/mm3; lymphocytes: 4876/mm3), compared the baseline values on June 12, 1953 (neutrophils: 2989/mm3; lymphocytes: 2531/mm3). He was treated with sedatives and antibiotics.

Twenty-four hours post exposure (day 2), the patient developed fever and hypotension. Disturbance of reflex continued. Laboratory tests showed: chlorides: 539 mg/dL, albumin: 4.16 g/dL and globulin: 2.76

g/dL, and the blood count was back to the pre-exposure level (neutrophils: 2490/mm3; lymphocytes: 2520/mm3).
On day 3, the patient continued to show fever and disturbance of reflexes. The next two days, he remains hypotensive. Vitamins were given on day 4. A blood count showed a significant decrease in neutrophils (1180/mm3) and mildly decrease in lymphocyte (lymphocytes: 2160/mm3). Antibiotics were withheld and parenteral fluids were given on day 5.
On day 6, hypotension ended but the patient had fever again. There were no significant changes on blood count compared to that on day 4. The next day, the patient's conditions were unchanged except for headache, which intermittently reoccurred until day 29. On day 8, the patient was friable. P/E confirmed ataxia and disturbance of reflexes.
On day 9, the patient continued with fever. On day 10, the symptoms and signs improved and supplements of the electrolytes were initiated. Blood counts on days 4, 6 and 10 showed mild decrements in neutrophils, but lymphocytes were not changed.
On day 11-14, the patient was stable. Laboratory tests showed chlorides: 431 mg/dL and no changes on albumin and globulin. On day 15-16, the patient had fever again and antibiotics were resumed. The fever spiked several times even with continued antibiotics. However, the fever did resolved on day 28. On day 19, urine analysis showed hematuria.
On day 24-26, two episodes of abdominal pain were described. On day 29, chemistry test showed albumin: 3.0 g/dL and elevated globulin: 3.66 g/dL. On day 36, there was one episode of tachycardia.
On day 46, tachycardia and sweating was noted. An episode of hypotension on day 54. Ataxia and asymmetry of deep tendon reflexes remain constant during the course of his hospitalization.
The clinical care of this individual ended on 54th post-exposure day, with his physical condition improving. He continued work at Plant A until 1975 and was under continuing medical surveillance until his death in 1994.

ARS 541 (DOB 1-8-1920)

A 31-year-old male nuclear facility worker came to the clinic after receiving a whole body radiation exposure on December 15, 1951. He was an employee at Plant C in 1949 and transferred to Plant A where he remained until 1971. His past medical history was negative. His psychosocial history revealed smoking (1/2 pack/day) and moderate alcohol consumption.

Upon arrival, he complained of nausea, vomiting, dizziness and fatigue. On physical examination (P/E), he had tachycardia and hypertension. Laboratory tests showed mildly elevated neutrophils (3355/mm3) and slightly lower lymphocytes (1622/mm3), compared the baseline values on Oct. 12, 1951 (neutrophils: 2185/mm3 and lymphocytes: 1886/mm3).

Twenty-four hours post exposure (day 2), vomiting, dizziness and hypertension were no longer present. The next day, the patient had an episode of hypertension. Laboratory test showed that neutrophils had returned to pre-exposure level (2299/mm3) but lymphocytes remained lower (1102/mm3).The next two days, his condition was unchanged.

On day 7, the patient had an episode of hypertension. Laboratory studies showed neutrophils at 1862/mm3 and slightly lower lymphocytes (1159/mm3).
By the day 30, a blood count showed decreased neutrophils (1115/mm3) and lymphocytes (874/mm3), and thrombocytopenia (88,000/mm3). Reexamination 4 days later revealed neutrophils, lymphocytes and thrombocytes were slightly higher i.e., 1472/mm3 , 1131/mm3, and 99,000/mm3 respectively. On day 38,the thrombocytopenia was no longer present. The neutrophils and lymphocytes returned to pre-exposure levels on day 45 and day 85, respectively.

Nausea and fatigue persisted until day 41. That day the patient had one episode of hemorrhage, headache and sweating. P/E showed asymmetry of deep tendon reflexes and ataxia. On day 47, hepatomegaly was noted. Between Day 48 and 60, the patient was asymptomatic.

This individual was on reduced follow up as of 60th post exposure day, with his physical condition improving. Intermittent hematological studies were satisfactory until his employment ended in 1971. He died in 1972.

ARS 3666 (DOB 6-14-1926)

A 27-year-old male nuclear facility worker arrived at the clinic on Oct. 14, 1953 after a whole body irradiation. He had been an employee in Plant A since 1948. His past medical history was negative. His psychosocial history revealed smoking (1 pack/day) and alcohol-related domestic abuse.

Upon arrival, he complained of nausea, headache, sweating and fatigue. On physical examination (P/E), he had hypertension. The blood count showed mildly lower neutrophils (4161/mm3) and increased lymphocytes (1368/mm3) compared pre-exposure values on September 9, 1953 (neutrophils: 3250/mm3 and lymphocytes: 1500/mm3) and September 19, 1953 (neutrophils: 5046/mm3 and lymphocytes: 464/mm3).

Twenty-four hours post exposure (day 2), sweating and fatigue subsided, but the patient had an episode of diarrhea and abdominal pain. The neutrophil and lymphocytes counts returned to the pre-exposure levels, e.g., 5046/mm3 and 464/mm3), respectively.

On day 3, the patient developed erythema of the skin and nausea, cough, fatigue, tachycardia and conjunctival hyperemia were also noted. The blood count showed neutrophils: 4930/mm3 and lymphocytes: 1326/mm3.

On day 4, hypertension ended. P/E revealed asymmetry of the deep tendon reflexes and ataxia. A blood count gave neutrophils: 7097/mm3 and lymphocytes: 1739/mm3. He was treated with electrolytes, antibiotics and vitamins.

On days 5-6, headache, erythema of the skin and tachycardia ended. The patient was asymptomatic. Laboratory tests on day 6 showed total protein: 5.74 g/dL, albumin: 3.74 g/dL, globulin: 2.0 g/dL and chloride: 552 mg/dL, neutrophils: 4900/mm3 and lymphocytes: 1610/mm3.

Headache recurred the next day. He also had an episode of hypertension. On day 8, the patient's condition was unchanged. A blood count showed neutrophils: 3976/mm3 and increased lymphocytes: 2343/mm3. The next day he had an episode of sweating and hypertension for which sedatives were given. By days 10-11, the patient's condition was stable and the blood count was neutrophils: 2300/mm3 and lymphocytes: 1000/mm3. Similar hematological findings were also noted between days 12 and 16.

On day 13, the patient's tachycardia returned. He became hypotensive (110/60 mmHg). By days 14-15, headache stopped but hypertension was back. Tachycardia and hypertension intermittently recurred during the rest of his hospitalization. The patient had an episode of headache and proteinuria on day 16. Sedative and antibiotics discontinued. Over the next three days he complained of headache, which recurred intermittently until day 36. The blood count on day 18 showed thrombocytopenia (84,000/mm3). Sedatives resumed on that day. Thrombocytopenia persisted in the later repeated hematological tests, while changes in neutrophil and lymphocyte counts were not significant.

On day 20, the patient had an episode of fever and erythema of the skin. This was followed by an episode of sweating the next day and antibiotics were resumed.

On days 22-29, his symptoms abated. Sedatives were withheld between days 22 and 24, and completely discontinued on day 29. On day 30, the patient developed hematuria and proteinuria. The hematuria last only for one day, and the proteinuria subsided by the next day. A whole blood transfusion was given.

On day 33, he was asymptomatic. The next two days sweating recurred, followed by an episode of hematuria on day 36.

Between days 37-65, his condition was stable, except for fatigue on day 55 and cough on day 60. A whole blood transfusion and hematinics were given on day 48 and day 55, respectively. However, electrolytes, antibiotics and vitamins were discontinued on day 52.

On day 66, the pateint had an episode of diarrhea, abdominal pain and fatigue. Between days 67-75, was asymptomatic except an episode of anorexia on day 69. Hematinics were discontinued on day 70. On day 76, transient anorexia and sweating was noted.

Clinical care on this individual ended on 77th post-exposure day, with his physical condition improved. His hematological results continued to improve and the thrombocytopenia was no longer present on May 15, 1954. This individual returned to work at Plant A and left on May 1, 1955. His medical surveillance ended on December 14, 1954.

ARS 4409 (DOB 6-1-1908)

A 45-year-old male, nuclear facility worker was brought to the clinic after whole body irradiation on October 14, 1953. He had been an employee in Plant B since 1948 and was transferred to Plant A on April 28, 1952. His past medical history was negative. His psychosocial history revealed that he was a smoker (1.5 pack/day) and moderate consumer of alcohol.

Upon arrival, he complained of headache. Physical examination (P/E) was negative. A blood count showed mildly increased neutrophils (4131/mm3) and decreased lymphocytes (765/mm3) compared his previous values on September 24, 1953 (neutrophils: 3596/mm3 and lymphocytes: 1334/mm3).

Twenty-four hours post exposure (day 2), the patient noted fatigue, and an episode of anorexia and nausea. On day 3, the patient's condition was unchanged. The blood count showed no additional changes in neutrophils: 4275/mm3 and lymphocytes: 855/mm3. He was treated with sedatives, parenteral fluids and vitamins. By day 4, anorexia returned and had an episode of sweating. P/E revealed ataxia and disturbance of motor functions. A transient elevation in neutrophils (4590/mm3) and lymphocytes (1666/mm3) was observed. Biochemical test showed total protein: 6.87 g/dL, albumin: 4.99 g/dL, globulin: 1.88 g/dL and chloride: 534 mg/dL.

By day 5, the headache and fatigue had subsided. The blood count on day 6 again showed decreases in both neutrophils (2709/mm3) and lymphocytes (903/mm3). He was asymptomatic up to day 7. The next day, asymmetry of the deep tendon reflexes was noted.

Between day 9 and day 16, he was asymptomatic. A blood count on day 9 showed neutrophils: 2310/mm3 and lymphocytes: 1144/mm3. Antibiotics were given on day 11. Sedatives were stopped on day 14. Abnormalities of motor functions (other than the deep tendon reflexes) subsided on day 15. Electrolytes were given on that day.

On day 17, epilation was noted. Parenteral fluids and electrolytes were discontinued. The next day, the patient had an episode of headache and hypertension. Although he was asymptomatic on day 19, he had erythema of the skin on day 20 and noted sweating on day 21. Epilation stopped and sedatives were resumed. The findings of the later hematological tests were non-significant except for thrombocytopenia noted on day 20, which continued until day 70.

On day 22, the patient noted a headache. Subsquently, his condition was unchanged between day 23 and 31, except for disturbances of sensation and motor functions revealed by examination on day 27. Biochemical testing on day 29 showed chloride: 539 mg/dL.

On days 32-33, he had headaches. A fall of neutrophils (1844/mm3) was observed, which gradually returned to near pre-exposure level by the end of his hospitalization. By day 34, P/E revealed disturbance of the deep tendon reflexes and ataxia, but disturbance of sensation and other motor dysfunction subsided. On days 35-36, the patient had an episode of headaches.

Between days 37 and 79, the patient was asymptomatic, except for fatigue on day 55 and anorexia on day 77. The disturbance of the deep tendon reflexes and ataxia subsided by day 43. Treatment with antibiotics was stopped on day 46, while sedatives and vitamin supplements were discontinued on day 51. He was treated with hematinics between days 55 and 68.

This patient's clinical care ended on 79th post exposure day, with his physical condition improved. He returned to work at Plant A and left on March 24, 1966. He continued to be under medical surveillance until June 5, 1966.

ARS 12409 (DOB 0-0-1927)

A 26-year-old male nuclear facility worker came to the clinic after a whole body irradiation on December 28, 1953. He had been an employee in Plant A since 1951. His past medical history was negative. His psychosocial history revealed that he was a smoker (1 pack/day) and moderate alcohol consumer.

Upon arrival, he complained of anorexia, nausea, vomiting and fatigue. Physical examination (P/E) was negative.

Twenty-four hours post exposure (day 2), nausea and vomiting stopped. The blood count showed no significant changes of neutrophils (3312/mm3) and lymphocytes (805/mm3), compared the previous

values on December 11, 1953 (neutrophils: 3243/mm3 and lymphocytes: 987/mm3).

On day 3, the patient was stable. The blood count showed neutrophils: 2860/mm3 and lymphocytes: 820/mm3. By day 4, anorexia and fatigue stopped.

He was asymptomatic up to day 7. Neutrophil and lymphocyte counts were unchanged, and thrombocytopenia (94,000/mm3) was observed. The hematological findings in the later course confirmed the persistency of thrombocytopenia, but neutrophil and lymphocyte counts were stable.

On day 8, the patient had an episode of hypertension and EEG abnormality, which was treated with parenteral fluids and vitamins. Between days 9-15, he was asymptomatic, except transient hypertension on day 13. Laboratory tests on day 9 showed total protein: 7.8 g/dL, albumin: 4.29 g/dL, globulin: 3.51 g/dL and chloride: 561 mg/dL.

On day 16, the patient was febrile. By the next day, he had an episode of sweating. Thereafter, he was asymptomatic until day 22. Antibiotics and electrolytes were given on that day. The next day, he had an episode of sweating. P/E revealed disturbance of the deep tendon reflexes and ataxia, which persisted during the remaindr of his hospitalization.

He was asymptomatic on day 24. Laboratory tests showed total protein: 7.60 g/dL, albumin: 4.56 g/dL, globulin: 3.04 g/dL and chloride: 568 mg/dL. The next day, he was febrile. Although he was asymptomatic on day 26, hemorrhage and EEG abnormalities were found the next day. He was stable on day 28, but became hypotensive on day 29.

On day 30, hemorrhage was no longer seen and the patient became hypertensive. P/E revealed other disturbance of motor function in addition of those noted previously. A whole blood transfusion was given. On days 31-36, sweating recurred again. A whole blood transfusion was given on day 33. The patient had fever and complained of fatigue the next day. On days 35-36, he became hypotensive. The next day, sweating stopped. A whole blood transfusion was given.

The patient was asymptomatic on day 37-38, but EKG abnormalities were noted on day 39. Parenteral fluids and vitamins were discontinued, however, hematinics were given.

On days 40-41, he had an episode of fever. A whole blood transfusion was given on day 41. On days 42-43, he had another episode of sweating. Antibiotics and electrolytes were discontinued.

The patient was asymptomatic until day 67. Whole blood transfusions were given on days 46 and 53, respectively. Hematinics were withheld between day 55 and 63. Antispasmodics were given on day 64. He had sweating, fatigue and hypertension on day 67.

Between days 68-70, the patient was asymptomatic. On day 71, he had an episode of sweating. Ataxia subsided, but disturbance of the deep tendon reflexes and other motor function changes persisted. There were no complain between days 72-79. Antispasmodics and hematinics discontinued on day 73.

This man's clinical care ended on 80th post-exposure day, with his physical condition improved. His hematological results continued to improve and the thrombocytopenia was over by June 17, 1955. He returned to work at Plant A and left on June 26, 1956. His medical surveillance ended on March 8, 1956.

ARS 12888 (DOB ?-?-1908)

A 45-year-old male nuclear facility worker was seen at the clinic after receiving whole body irradiation on December 28, 1953. He had been employed at the Plant A since 1952. His past medical history was negative. The psychosocial history revealed that he was a smoker (one pack/day) and moderate alcohol consumer.

Upon arrival to the medical facility, he complained of anorexia, nausea and vomiting, headache and fatigue. The physical examination (P/E) showed necrosis of skin.

Twenty-four hours post-exposure (day 2), the nausea ended. Laboratory tests showed mildly increased neutrophils (3082/mm3) and decreased lymphocytes (1057/mm3) compared the pre-accident values of March 21, 1953 (neutrophils: 2850/mm3 and lymphocytes: 1650/mm3).

On day 3, anorexia, vomiting and fatigue had ended but nausea returned. The next day, nausea stopped but anorexia was present. The blood count on Day 4 showed neutrophils: 3850/mm3 and lymphocytes: 775/mm3. Two days later, his appetite returned. A blood count showed neutrophils: 3225/mm3 and lymphocytes: 881/mm3.

On days 6 and 7, the patient's condition was unchanged. Vitamins were given. On Day 7, there was a further fall in neutrophils: 2502/mm3 and lymphocytes: 720/mm3. The next day, anorexia returned and intermittently reappeared until day 43. Laboratory tests showed chlorides: 535 mg/dL, globulin: 2.75 g/dL, albumin: 4.13 g/dL, neutrophils: 2576/mm3 and lymphocytes: 1288/mm3.

The patient developed hypertension, tachycardia and EEG abnormality on the 9th day post-exposure day. Laboratory tests showed neutrophils: 2583/mm3 and lymphocytes: 943/mm3. The next day, a headache was present. A blood count on following day showed neutrophils: 3225/mm3 and lymphocytes: 881/mm3.

On day 12, headache, hypertension and tachycardia subsided, but hypotension was noted. Hypertension and tachycardia intermittently recurred until day 56 and day 71, respectively. By days 13-14, the patient's condition was unchanged. The next day, he had another episode of hypotension. The blood count showed neutrophils: 2478/mm3 and lymphocytes: 1218/mm3. Two days later, the patient complained of headache, which intermittently recurred until Day 34.

On days 17-23, he had two episodes of abdominal pain, and was treated with antibiotics on day 20.

The patient complained of fatigue and had an episode of sweating on day 24. P/E revealed asymmetry of deep tendon reflexes and ataxia. Blood counts showed neutrophils: 2992/mm3, lymphocytes: 1192/mm3 and thrombocytes: 113,000/mm3. The disturbance of deep tendon reflexes and ataxia, as well as mild thrombocytopenia continued during the rest of his hospitalization.

On day 25, Laboratory tests showed chlorides 576 mg/dL, globulin 2.28 g/dL, albumin 4.27 g/dL.

On days 32, 37, 41 and 45, the patient received whole blood transfusions. On days 33-35, he had fever. On day 37, hematinics were given. Antibiotics were discontinued on day 47. On day 67-72, parenteral fluids were given.

On day 45, biochemical tests showed chlorides: 478 mg/dL, globulin: 2.72 g/dL and albumin: 4.08 g/dL.

Clinical care ended on the 72nd post-exposure day, with his physical condition improved. His hematological also results continued to improve and the thrombocytopenia subsided but leukocyte counts remained lower than the pre-exposure levels as noted on June 17, 1954, the last recorded observation. He continued to work at the Plant A until September 1, 1954.

ARS 14529 (DOB 6-10-25)

A 32-year-old female nuclear facility worker came to the clinic after receiving a whole body radiation exposure on April 22, 1957. She had been an employee at Plant C in 1949 and transferred to Plant D in 1959, where she remained until 1974. Her past medical and psychosocial history was negative.

Upon arrival, she complained of nausea, vomiting, headache, dizziness and weakness. On physical examination (P/E), she had asymmetry of the deep tendon reflexes, ataxia and disturbances of sensation. Blood count showed an decreased neutrophils (1890/mm3) and slightly elevated lymphocytes (1911/mm3), compared the baseline values on December 18, 1956 (neutrophils: 4031/mm3 and lymphocytes: 1450/mm3). She was treat with antibiotics, parenteral fluids, electrolytes and vitamins.

Twenty-four hours post exposure (day 2), all complaints had subsided. A blood count showed neutrophils: 2379/mm3 and lymphocytes: 1053/mm3. All medications were discontinued.

On days 3 to 5, she was asymptomatic. Blood count On day 4 showed neutrophils: 2100/mm3 and lymphocytes: 1207/mm3. The next day, a blood count showed neutrophils: 2997/mm3 and lymphocytes: 1701/mm3.

On day 7, the patient had an episode of weakness. Between days 8 to 12, her condition was unchanged. A blood count On day 9 showed neutrophils: 3355/mm3 and lymphocytes: 1705/mm3. Three day later, a blood count showed neutrophils: 4087/mm3 and lymphocytes: 1809/mm3.

On day 14, the patient had an episode of weakness. From days 15 to 33, she was asymptomatic. Blood counts on days 17, 24, 30 and 33 showed non-significant changes.

On day 34, the patient had an episode of weakness. Examination revealed asymmetry of the deep tendon reflexes. The next four days, she was asymptomatic. Then, on day 39, she had an episode of anorexia, headache and weakness. A blood count showed neutrophils: 3874/mm3 and lymphocytes:

1890/mm3, which suggested a return to the pre-exposure levels.

This individual was follow up as of 39th post-exposure day, with her physical condition improved. Intermittent hematological studies were satisfactory until discontinued on September of 1996.

ARS Case 19471 (DOB 0-0-1930)

A 21-year-old male nuclear facility worker was seen at the clinic after a whole body irradiation on December 11, 1951. He had been an employee in Plant A since July 10, 1951. His past medical history was negative. His psychosocial history revealed positive for smoking (1 pack/day) and moderate alcohol consumption.

Upon arrival to the medical facility, he complained of nausea, vomiting, headache, dizziness, erythema of the skin, weakness, dyspnea, cough and sweating. Physical examination (P/E) revealed tachycardia and asymmetry of the deeper tendon reflexes. The blood count showed no major differences of neutrophils (6063/mm3) and lymphocytes (2064/mm3) compared the somewhat elevated pre-exposure values (neutrophils: 5520/mm3 and lymphocytes: 3128/mm3 on July 11, 1951; neutrophils: 6273/mm3 and lymphocytes: 5412/mm3 on Nov. 3, 1951). Biochemical tests showed total protein: 7.8 g/dL, albumin: 5.05 g/dL, globulin: 2.75 g/dL, bilirubin: 0.28 mg/dL, chlorides: 343 mg/dL and BUN: 37 mg/dL. He was treated with parenteral fluids and electrolytes.

Twenty-four hours post exposure (day 2), vomiting, dizziness, erythema of the skin, fatigue, dyspnea, cough and sweating had subsided. However, the patient became hypotensive. A marked drop of lymphocytes (870/mm3) and, to a lesser degree, neutrophils (4553/mm3) was observed. The next day, the patient was less symptomatic. His blood count showed neutrophils: 5715/mm3 and lymphocytes 1136/mm3.

On day 4, the patient was still anorexic. Tachycardia recurred, and persisted throughout the remainder of his hospitalization.

On day 5, headache returned and recurred intermittently until day 65. Next 5 days, the patient's condition was unchanged. On day 7, there were a decrease of neutrophils (3094/mm3) and a mildly increase of lymphocytes (1846/mm3). By day 9, a further fall in neutrophils (1802/mm3) and lymphocytes(1435/mm3) was noted. Parenteral fluids discontinued.

On day 11, he became febrile. Fever stopped the next day but recurred on day 13. A marked drop of lymphocytes (672/mm3) was observed without changes in neutrophils (2144/mm3). Thrombocytopenia (125,000/mm3) became evident as well.

On days 14-24, the patient was stable. Electrolytes were discontinued on day 17. Blood counts became significantly lower on days 23 and 24 (neutrophils: 592/mm3, lymphocytes 968/mm3 and platelets: 39,600/mm3).

On day 25, anorexia returned, which intermittently recurred until day 53. Parenteral fluids were resumed. He was also treated with one whole blood transfusion.

The following day, fever returned. Severe neutropenia: 180/mm3 , lymphopenia: 775/mm3 and thrombocytopenia (22,350/mm3) were noted. Antibiotics and vitamins were given. The patient was asymptomatic on the next day. By day 28, the patient hypotensive and febrile again. He also had sweating and had developed purpura. The neutrophil count was done to 74/mm3, lymphocyte count was 920/mm3 and platelets were down to 4,120/mm3.

Hypotension and purpura subsided on day 30, but the blood count was not improved (neutrophils: 71/mm3, lymphocytes: 836/mm3 and platelets: 4,390/mm3)). The patient remained febrile until day 31.

On days 32-49, the patient's condition was unchanged, except for episodes of hypotension on days 35 and 42, respectively. The neutropenia remained but the lymphocyte and platelet counts were slightly improved. Biochemical test on day 32 showed total protein: 6.89 g/dL, albumin: 4.07 g/dL, globulin: 2.82 g/dL, bilirubin: 0.28 mg/dL, chlorides: 351 mg/dL and BUN: 25 mg/dL. The repeated test on day 35 was unremarkable, except an increased BUN: 34 mg/dL. Parenteral fluids were discontinued on day 36 and antibiotics on day 44. Hematinics were started on day 47 and gradual recovery granulocytes and platelets was noted.

On day 50, he had an episode of sweating. P/E revealed disturbance of the deep tendon reflexes

and other motor functions.

During days 51-66, the patient was clinically stable. Hematinics were discontinued on day 58. The blood counts gradually improved but remained in lower ranges. Biochemical testing on day 56 showed total protein: 6.8 g/dL, albumin: 5.1 g/dL, globulin: 1.7 g/dL and chlorides: 352 mg/dL.

This patient's clinical care ended on the 66th post-exposure day, with his physical condition improved. Although the same trend was also true for his blood counts, the return to the pre-exposure levels was not seen until the end of medical surveillance on Feb. 7, 1955. This individual returned to work at Plant A and left on August 10, 1955.

RS 25539 (DOB 10-1-1927)

A 26-year-old male nuclear facility worker was brought to the clinic immediately after receiving whole body irradiation at Plant A on September 18, 1953. He was an employee at Plant A since 1948. His past medical history was negative. His psychosocial history included smoking (1 pack/day) and moderate to marked alcohol consumption.

Upon arrival to the medical facility, he complained of headache. On physical examination (P/E), he had tachycardia, ataxia, and disturbances of the deep tendon reflexes. Blood counts showed a mild increase in neutrophils (4970/mm3), a mild decrease in lymphocytes (1645/mm3) and an elevation of platelets (316,000/mm3), compared the pre-accident values of July 25, 1953 (neutrophils: 2916/mm3, lymphocytes: 2268/mm3 and platelets: 234,000/mm3). He was treated with antibiotics and sedatives. Twenty-four hours post exposure (day 2), headache and tachycardia stopped but the patient became somewhat hypotensive (100/60 mmHg). Laboratory tests showed neutrophils: 3960/mm3, lymphocytes: 3240/mm3; total protein: 7.9 g/dL, albumin: 4.35 g/dL, globulin: 3.55 g/dL and chloride: 524 mg/dL. Although he was asymptomatic on days 3-4, decrements of neutrophils (2401/mm3) and lymphocytes (2107/mm3) were observed.

On day 4, P/E revealed asymmetry of the deep tendon reflexes. The next day, hypotension came back (110/65 mmHg). Asymmetry of the deep tendon reflexes remained. Antibiotics discontinued He was treated with parenteral fluids and vitamins. By day 6, the hypotension subsided and the patient was asymptomatic. The blood count showed neutrophils: 2722/mm3 and lymphocytes: 1952/mm3. The next day, headache recurred, and continued to return intermittently throughout the course of his hospitalization. On day 8, the patient was febrile, but the blood count was unremarkable (neutrophils: 3190/mm3 and lymphocytes: 1705/mm3). The next day, weight loss was noted. Electrolytes were given. The following day the fever subsided. On days 11-12, the patient's condition was unchanged.

On day 13, he had an episode of tachycardia. The next two days the fever recurred. Biochemical tests showed abnormal chemistry values: total protein: 6.7 g/dL, albumin: 4.53 g/dL, globulin: 2.17 g/dL and chloride: 566 mg/dL.

On day 16, fever subsided but the patient had an episode of tachycardia. Antibiotics were resumed. Blood counts showed neutrophils: 3559/mm3 and lymphocytes: 2142/mm3. On days 17-18, his condition was unchanged. Parenteral fluids and electrolytes were discontinued. Blood counts on day 18 showed neutrophils: 3430/mm3 and lymphocytes: 2520/mm3. On day 19, he had an episode of fever. Biochemical tests showed bilirubin: 0.6 mg/dL.

While he was stable on days 20-21, the patient was intermittently febrile on day 22 and 24. Sedatives were withheld. On days 25-28, his condition was stable. Antibiotics discontinued on day 26 and the sedatives resumed on day 28.

The patient had another episode of fever on day 29. Biochemical tests showed the following values: total protein: 6.44 g/dL, albumin: 3.39 g/dL, globulin: 3.05 g/dL and chloride: 434 mg/dL.

Over the next two days, the patient was asymptomatic. Sedatives and vitamins were discontinued. On day 33, the patient became hypertensive and electrolytes were resumed. On day 34-35, he was asymptomatic. On day 36, he complained of sweating and scalp pain, but on days 37-45, the patient was again asymptomatic. Electrolytes were discontinued on day 45. The hematological findings between day 11 and 41 were unchanged.

The clinical care on this individual was ended on Day 46-post exposure, with his physical condition

improved. A single dose of vasoconstrictors was given on the same day. He returned to work at Plant A and was transferred to Plant D in December 11, 1971 and left on December 2, 1997. He continued to be under medical surveillance until Oct. 15, 1996.

ARS 29190 (DOB ?-?-1931)

A 26-year-old female nuclear facility worker was brought to the clinic after receiving whole body irradiation on April 22, 1957. She had been an employee at the Plant C since April 15, 1955. Her past-medical history and the psychosocial history were non-contributory.
Upon arrival, she complained of anorexia, nausea, headache, dizziness, fever and fatigue. The physical examination (P/E) was negative. The blood count showed mildly increased neutrophils (3770/mm3) and mildly decreased lymphocytes (1450/mm3) compared the pre-accident values of December 13, 1956 (neutrophils: 2725/mm3 and lymphocytes: 1875/mm3). She was treated with parenteral fluids, electrolytes, antibiotics and vitamins.

Twenty-four hours post-exposure (day 2), all complaints stopped, but the patient became hypotensive (90/60 mmHg). Both neutrophils and lymphocytes increased (4224/mm3 and 1988/mm3, respectively). The next day, fever returned.

On day 4, the hypotension subsided and the patient was asymptomatic. A blood count showed neutrophils: 3965/mm3 and lymphocytes: 1787/mm3. The next day, hypotension recurred and the patient had an episode of dizziness and tachycardia. Vasoconstictors were started.

On day 6, she had an episode of anorexia and headache. Neutrophil and lymphocyte counts (2548/mm3 and 1950/mm3, respectively) returned to pre-exposure levels. By day 7-8, the patient was asymptomatic although P/E revealed asymmetry of the deep tendon reflexes and disturbance of other motor functions.

On day 9, fever and tachycardia recurred. On day 10-11, the patient was asymptomatic. Disturbance of other motor functions (not including deep tendon reflexes) stopped. She was febrile and complained of anorexia and fatigue on day 12. Hypotension returned on day 13. Electrolytes and antibiotics were withheld.

Although the patient was asymptomatic on day 14, she became febrile and had an episode of hemorrhage next day. By days 16-17, the fever stopped, but hypotension recurred. Electrolytes and antibiotics were resumed.

The patient was without symptomes on days 18-20, except for an episode of sweating on day 19. All medications were discontinued. On day 21, she complained of dizziness. Between day 22 and 28, she was asymptomatic, except for an episode of tachycardia on day 24.

On day 29, anorexia, dizziness, fatigue, sweating, tachycardia and hemorrage recurred. P/E revealed ataxia and motor dysfunction. However, the patient was asymptomatic on days 30-33. On day 34, fatigue, sweating, tachycardia and hypotension recurred. Ataxia stopped and only the disturbance of deep tendon reflexes was noted. She was asymptomatic the next three days.

The patient complained of headache and dizziness again on days 38-40. By day 41, the dizziness stopped but headache remained. An episode of sweating and hypotension were also noted. P/E showed asymmetry of deep tendon reflexes.

On days 42-43, her condition was unchanged. By day 44, she sweated and complained of fatigue again, but was asymptomatic on days 45-47. P/E showed asymmetry of deep tendon reflexes and disturbance of other motor functions, which persisted through the course of her hospitalization. By day 48, the patient was hypotensive again.

Between days 49 and 68, the patient was asymptomatic. On day 69, she had an episode of headache, dizziness and hypotension. She was again asymptomatic the next ten days. On day 80, headache, fatigue and hypotension were noted again, but the symptoms stopped the next day. The hematological findings between days 9 and 81 were stable.

This patient's clinical care ended on 90th post-exposure day, with her physical condition improved. She continued to work at the Plant C and left on August 1, 1962. She continued to be under medical surveillance and follow up until March 26, 1962.

ARS 29395 (DOB 4-19-1927)

A 30-year-old male nuclear facility worker appeared at the clinic after receiving whole body radiation on April 22, 1957. He was employed at the Plant A since September 17, 1953. His past-medical history included chronic radiation syndrome, which had been diagnosed on Feb. 27, 1957. The psychosocial history revealed cigarette smoking (a half of pack/day) and moderate alcohol consumption.

Upon admission, he complained of anorexia, nausea, vomiting, headache, cough, dizziness and fatigue. The physical examination (P/E) showed asymmetry of the deep tendon reflexes and conjunctival hyperemia. The blood count showed mildly decreased neutrophils: 2257/mm3 and lymphocytes: 1526/mm3, compared the pre-accident values of Feb. 27, 1957 (neutrophils: 2830/mm3 and lymphocytes: 1632/mm3). He was treated with sedatives, antibiotics, parenteral fluids, and vitamins.

Twenty-four hours past exposure (day 2), the previous symptoms had subsided, but the patient developed fever and hematuria. An increase in neutrophils (4012/mm3) was observed with a decrease in lymphocytes (1150/mm3).

On day 3, dizziness and hematuria stopped, but a headache was back. He also had an episode of tachycardia. Biochemical tests showed total protein: 6.98 g/dL; bilirubin: 1.9 mg/dL, chlorides: 556 mg/dL, BUN: 42 mg/dL. Next day, headache and weakness stopped, but he had an episode of hematuria. There was a fall in neutrophils (1786/mm3), but no changes on lymphocytes (1159/mm3).

By day 5, fever subsided but fatigue and dizziness returned. By day 6, headache stopped. Laboratory test showed bilirubin: 1.9 mg/dL and further decreases of both neutrophils (1290/mm3) and lymphocytes (899/mm3).

The next day, the patient was symptom-free. On day 8, he had an episode of headache, weakness and dizziness. P/E revealed ataxia and other disturbance of motor functions, in addition to asymmetry of the deep tendon reflexes. Antibiotics were discontinued.

Between days 9 and 15, the patient was asymptomatic. Laboratory test on day 9 showed cholesterol: 192 mg/dL, neutrophils: 2350/mm3 and lymphocytes: 1551/mm3. The blood counts reached their pre-exposure levels by day 15.

On day 16, the patient became febrile. Biochemical tests showed bilirubin: 0.7 mg/dL, cholesterol: 175 mg/dL and chlorides: 484 mg/dL. He had an episode of hematuria on the next day.

On days 19-26, the patient was unsymptomatic, except an episode of tachycardia on day 24. Ataxia subsided on day 22. Parenteral fluids and sedatives were discontinued on day 19 and 23, respectively, but hematinics were given on day 24.

On day 27, headache, weakness and tachycardia recurred. The patient had an episode of hypotension. P/E showed asymmetry of the deep tendon reflexes. The next few days (28-33), the patient's condition was unchanged. On day 34, he had an episode of sweating. Headache stopped on next day.

By day 39, weakness stopped and the patient was asymptomatic, but he had an episode of anorexia the next day. Vitamins and hematinics were discontinued. The patient was asymptomatic between days 41 and 80 except for a headache on day 66. However, asymmetry of the deep tendon reflexes persisted during the entire course of his hospitalization. The blood counts between days 18 and 80 were unremarkable.

Clinical care ended on 80th post-exposure day, with his physical condition improved. He returned to work at Plant C. Then, he was transferred to Plant D at June 27, 1961 and left on 1985. He continued to be under medical surveillance until June 4, 1997.

ARS 40044 (DOB 7-17-1930)

A 20-year-old male nuclear facility worker was brought to the clinic immediately after receiving a whole body irradiation at Plant B on September 28, 1950. He was an employee at Plant B since 1948. He had been diagnosed with chronic radiation sickness since Aug. of 1949. His psychosocial history included smoking (1 pack/day) and moderate to marked alcohol consumption.

Upon arrival to the medical facility, he complained of nausea, headache, fatigue, fever, weakness, dizziness and cough. On physical examination (P/E), he had tachycardia. Blood counts showed no

significant changes of neutrophils (5040/mm3) and lymphocytes (1152/mm3) compared the pre-accident values of September 11, 1957 (neutrophils: 4662/mm3 and lymphocytes: 1071/mm3). He was treated with parenteral fluids.
Twenty-four hours post-exposure (day 2), tachycardia stopped. Laboratory tests showed an increased neutrophils (7906/mm3) and a decrease of lymphocytes (921/mm3) compared to the values of the first day; and abnormal chemistry values: total protein: 6.91 g/dL, albumin: 2.72 g/dL, globulin: 4.19 g/dL and chloride: 344 mg/dL, bilirubin: 1.0 mg/Dl and BUN 22.4 mg/dL. A whole blood transfusion was given.
On day 3, weakness subsided. The blood counts were stable (neutrophils: 7515/mm3 and lymphocytes: 900/mm3). He was treated with antibiotics and vitamins. The next day nausea and dizziness stopped.
On day 4, nausea and dizziness stopped, but tachycardia recurred the next day. The patient developed jaundice. He also noted anorexia, erythema of the skin, incapacitation, weakness and scalp pain. P/E revealed asymmetry of the deep tendon reflexes, which was persistent through his hospitalization. Blood counts showed a decrease in neutrophils (3619/mm3) and lymphocytes (470/mm3).
On day 6, the patient was oliguric. A blood count showed neutrophils: 2976/mm3 and lymphocytes: 888/mm3. Parenteral fluids and vitamins were resumed and electrolytes were also given. Over the next few days, jaundice and tachycardia subsided. He developed hypertension (145/90 mmHg). Laboratory tests on day 7 showed total protein: 7.0 g/dL, albumin: 4.2 g/dL, globulin: 2.8 g/dL and chloride: 304 mg/dL, bilirubin: 0.55 mg/dL, BUN 34.7 mg/dL. A blood count showed neutrophils: 2796/mm3 and lymphocytes: 1104 /mm3, and a similar result was found on day 8.
On day 9, the hypertension subsided, but the patient had some EKG abnormalities. A blood count was unchanged (neutrophils: 3172/mm3 and lymphocytes: 832/mm3). Antibiotics were discontinued. The next day, he had an episode of ataxia. A blood count showed neutrophils: 3360/mm3 and lymphocytes: 963/mm3. The next day the patient was febrile. On days 12 and 13, his condition was unchanged. A blood counts on day 12 revealed neutrophils: 2967/mm3 and lymphocytes: 1104/mm3 , and on day 13 neutrophils: 3360/mm3 and lymphocytes: 963/mm3. A whole blood transfusion was given, and electrolytes were discontinued.
The next few days, the patient was asymptomatic, but on days 17-19, the patient was febrile again. Biochemical tests on day 19 showed total protein: 6.98 g/dL, albumin: 1.92 g/dL, globulin: 5.06 g/dL and chloride: 330 mg/dL, bilirubin: 0.52 mg/dL and BUN 15.7 mg/dL. By day 20, the fever subsided.

Between days 21-24, the patient was asymptomatic, but on days 25-27, he had fever again. On day 28, this subsided and parenteral fluids were discontinued.

On day 29, he had an episode of weakness. Biochemical test showed total protein: 7.02 g/dL, albumin: 4.19 g/dL, globulin: 2.83 g/dL and chloride: 332 mg/dL, bilirubin: 1.2 mg/dL and BUN 26.9 mg/dL. The hematological findings between day 14 and 29 were unchanged.
The clinical care on this individual was ended on 30th post-exposure day, with his physical condition improved. He returned to work at Plant B and was transferred to Plant A in Feb. 1, 1951. He was then transferred to Plant A in Nov. 4, 1958 and left on April 1, 1990. He continued to be under medical surveillance until Oct. 3, 1997.

Case 40482 (DOB 6-19-1929)

A 28-year-old female nuclear facility worker presented to the clinic after receiving whole body irradiation on April 22, 1957. She had been an employee at the Plant C since Oct. 15, 1956. Her past medical history and psychosocial history were negative.
Upon arrival to the medical facility, she complained of nausea, headache and fatigue. The physical examination (P/E) revealed erythema of the skin. A blood count showed markedly increased neutrophils (9450/mm3) and decreased lymphocytes (1100/mm3) compared her pre-accident values of March 27, 1957 (neutrophils 4576/mm3 and lymphocytes 3740/mm3). She was treated with antibiotics and vitamins.

Twenty-four hours post exposure (day 2), the patient was hypotensive and had a poor appetite. However, all other symptoms subsided. P/E showed tachycardia, hypoactive deep tendon reflexes and disturbances of motor functions. Electrophysiological test showed EEG abnormalities. A marked drop of

neutrophils (3789/mm3) was observed with a mild increase of lymphocytes (1245/mm3).

On day 3, the patient noted dizziness, but P/E was negative. A blood count was unremarkable (neutrophils: 3877/mm3 and lymphocytes: 1292/mm3). A whole blood transfusion was given. She was also treated with a single dose of parenteral fluids and electrolytes.

On day 4, hypotension subsided, but recurred intermittently until day 74. There was a decrease in neutrophils: 2466/mm3 and lymphocytes: 954/mm3, however, the next day's blood count showed neutrophils: 2900/mm3 and lymphocytes: 1825/mm3. Dizziness stopped. Parenteral fluids and electrolytes, as well as a plasma transfusion were given.

By day 6, hypoactive deep tendon reflexes and disturbances of motor functions recurred. A blood count showed neutrophils: 2527/mm3 and lymphocytes: 1102/mm3.

On day 7, the patient was clinically stable, but an episode of fatigue was noted on the next day. A blood count showed neutrophils: 2665/mm3 and lymphocytes: 1127/mm3.

On days 9-10, her condition was unchanged. On day 11, P/E revealed asymmetry of the deep tendon reflexes and ataxia. Ataxia subsided on the next day, but asymmetry of the deep tendon reflexes recurred intermittently until day 73.

On day 12, a single dose of parenteral fluids and electrolytes, as well as a plasma transfusion were given. The next day, tachycardia was noted and recurred intermittently until day 74. Although neutrophil and lymphocyte counts were stable at the lower ranges, thrombocytopenia was first observed on day 14 and persisted intermittently until day 43.

On day 16, parenteral fluids and electrolytes, as well as one whole blood transfusion were given, while on days 20 and 24, she was treated with parenteral fluids and electrolytes, as well as a plasma transfusion. Disturbances of motor functions was noted on day 22.

On day 27, the patient was treated with electrolytes, which ended on day 32, while on day 31, parenteral fluids and a whole blood transfusion were given. On day 37, ataxia was noted. Between days 38 and 90, she was clinically stable, except for headache on days 47 and 59.

Clinical care ended on 90th post-exposure day, with her physical condition improving. The same was also true for her hematological results, which gradually returned to the near pre-exposure level by September 11, 1957. She continued to work at the Plant C and was transferred to Plant D on August 8, 1957. Then, she was transferred to Plant A on July 19, 1973 and left on October 1, 1974. She continued to be under medical surveillance until November 17, 1997.

Appendix B

RADIATION INJURY GROUP III

ARS 15189 (DOB 1-18-1916)

A 41-year-old male, nuclear facility worker came to the clinic after whole body irradiation on April 22, 1957. He had been employed in Plant C since 1949. His past medical history and psychosocial history were negative.

Upon admitted, he complained of nausea, vomiting, and erythema of the skin, headache, sweating, tachycardia, fatigue and fever. Physical examination (P/E) revealed disturbance of the deep tendon reflexes. Laboratory tests showed markedly increased neutrophils (9460/mm3) and decreased lymphocytes (330/mm3) compared the pre-accident values of March 25, 1957 (neutrophils 3240/mm3 and lymphocytes 1620/mm3), and biochemical values: total protein: 7.7 g/dL, bilirubin: 0.7 mg/dL, and cholesterol: 556 mg/dL. He was treated with one whole blood transfusions. Sedatives, analgesics, antispasmodics, parenteral fluids, electrolytes, antibiotics, vasoconstrictors and vitamins were started.

Twenty-four hours post exposure (day 2), nausea, vomiting, sweating and tachycardia had ended, but the patient was anorexic and had hematuria. The blood count showed further elevation in neutrophils (13575/mm3) and decreased lymphocytes (300/mm3). Analgesics, antispasmodics, electrolytes and vasoconstrictors were discontinued.

On day 3, anorexia and fever subsided, but tachycardia recurred. P/E revealed ataxia, disturbance of sensations and motor functions. Severe lymphopenia (166/mm3) was noted, along with neutrophilia (10434/mm3). One plasma transfusion was given.

Headache and tachycardia stopped the next day. He complained of nausea. A blood count showed neutrophils: 8463/mm3 and lymphocytes: 227/mm3. Electrolyte administration was resumed.

By day 5, erythema of the skin and hematuria had stopped, but fever and headache recurred. A fall of the neutrophil count (3403/mm3) to the pre-exposure level was noted, but lymphopenia remained (266/mm3). One whole blood transfusion and a single dose of analgesics were given. Anorexia was noted the next day. A blood count showed neutrophils: 2856/mm3 and lymphocytes: 204/mm3. A plasma transfusion was given.

The patient was stable on day 7, but erythema of the skin was recurred on day 8. The patient developed thrombocytopenia, which persisted until day 27. However, both neutrophil and lymphocyte

counts were slightly increased (3600/mm3 and 600/mm3, respectively). Steroids were started. Single doses of analgesics and antispasmodics were given.

Headache and tachycardia recurred on day 9, as well as fatigue and anorexia on the following day. Neutrophil (1897/mm3) and lymphocytes changes were unremarkable (660/mm3). Whole blood transfusions were alternated with plasma transfusions every other day or two until day 31.

Headache, fatigue, fever and tachycardia appeared intermittently during the course of his hospitalization.

The patient was stable on days 11 and 12. Ataxia subsided. Epilation was noted on day 13. The blood counts were unchanged. Single doses of analgesics and antispasmodics were given.

On day 14, weight loss was noted, while the patient was stable. The next few days, an episode of proteinuria on day 18 and hematuria on day 19 were noted. Ataxia returned, he became hypotensive (100/60 mmHg) transiently on day 20. Single doses of analgesics and antispasmodics were given.

The patient's condition was unchanged between days 22 and 24. He complained of dizziness on days 25 and 26, but ataxia and disturbance of sensations stopped. On day 27, dizziness and epilation stopped.

Between days 28 and 31, the patient's condition was stable. Sedatives, parenteral fluids and electrolytes discontinued. By day 32, the patient was hypotensive again, and this recurred intermittently during the rest of his hospitalization.

There were step-wise decrements of neutrophils between days 16 and 32, which reached the lowest level on day 25 (224/mm3), with a wide fluctuation of lymphocytes (528/mm3 and 1207/mm3).

The patient's condition was unchanged between days 33 and 46, except for ataxia and disturbance of sensations on day 36. Whole blood transfusions were given on days 34 and 38, respectively, and hematinics between days 40 and 46.

On day 47, ataxia and disturbance of sensations stopped. The patient's condition was unchanged between days 48 and 58. On day 59, he complained of sweating, which stopped on day 70. P/E revealed asymmetry of the deep tendon reflexes and disturbances of sensation.

Between days 60 and 90, the patient's condition did not change significantly, except for dizziness on days 67 and 69. Sedatives, analgesics and vasoconstrictors were resumed on day 62. The latter were discontinued on day 82. Antibiotics resumed on day 69 and discontinued on day 86. Hematological findings continued to improve between day 34 and 87, and were back to the pre-exposure level on day 90.

The patient's clinical care ended on 90th post-exposure day, with his physical condition improved. This individual returned to work at Plant C and left on September 1, 1976. He continued to be under medical surveillance, and was diagnosed to have Pu pneumosclerosis in Nov. 21, 1961. The patient died on September 27, 1976.

ARS 17087 (DOB 10-11-1932)

A 25-year-old female nuclear facility worker came to the clinic after receiving whole body irradiation on April 22, 1957. She was employed at Plant C since 1954. Her past medical history and psychosocial history were negative.

Upon arrival to the medical facility, she complained of nausea, vomiting, headache, fever and fatigue. The physical examination (P/E) showed asymmetry of deep tendon reflexes, ataxia and other motor dysfunction, as well as thyroid enlargement. She was treated with parenteral fluids, electrolytes, antibiotics and vitamins. The blood count showed an elevated neutrophil count (5610/mm3) and reduced lymphocytes (748/mm3) compared the pre-accident values of March 16, 1957 (neutrophils: 1567/mm3 and lymphocytes: 1452/mm3).

Twenty-four hours post-exposure (day 2), the patient's symptoms improved except for the vomiting. Laboratory tests showed total protein: 7.42 g/dL, bilirubin: 2.5 mg/dL, chlorides: 579 mg/dL, neutrophils: 2362/mm3 and lymphocytes: 525/mm3. Sedatives were started.

On day 3, the vomiting had subsided, but nausea persisted. The patient also had fever and tachycardia. P/S revealed asymmetry of deep tendon reflexes, ataxia and other motor dysfunction, which persisted during the course of her hospitalization. A whole blood transfusion was given.

The next day, nausea, fever and tachycardia had subsided, but jaundice was noted. A blood account showed neutrophils: 1512/mm3 and decreasing lymphocytes: 315/mm3. By Day 5, fever had subsided. Laboratory tests showed bilirubin 2.0 mg/dL, neutrophils: 2044/mm3 and lymphocytes: 434/mm3.

The patient's condition was relatively stable on days 6-8 except for an episode of polyuria on day 6. A blood count on day 6 showed neutrophils: 1750/mm3 and lymphocytes: 475/mm3. The patient was given a whole blood transfusion , but sedatives were withheld on day 7. By day 8, jaundice disappeared, however, a definite drop of neutrophil counts (672/mm3) and thrombocytopenia (117,000/mm3) were noted.

On day 9, the patient had an episode of fever and oliguria. A blood count showed a further fall in neutrophils (429/mm3) and no changes in lymphocytes (495/mm3). Thrombocytopenia persisted during the remainder of her hospitalization. A plasma transfusion was given.

Over the next three days, the patient complained of headache and fatigue, and had an episode of polyuria and incapacitation. A blood account on day 10 showed neutrophils: 731/mm3 and lymphocytes: 561/mm3 with similar hematological findings on days 11 and 12. Clinical chemistry tests on day 12 showed bilirubin: 1.1 mg/dL and chlorides: 573 mg/dL. The patient received another whole blood transfusion on day 11.

On days 13-15, headache, tachycardia, hypotension and fever were noted. These recurred intermittently during the patient's further hospitalization. On Day 13, laboratory tests showed neutrophils 595/mm3 and lymphocytes 420/mm3. Another plasma transfusion was given. On Day 14-15, the neutrophil count increased to 1863/mm3 and lymphocytes 607/mm3. The patient lost weight and steroids were started.

On the 16th post-exposure day, the patient developed epilation. Sedatives were resumed and antibiotics discontinued. Laboratory tests showed neutrophils: 3332/mm3 and lymphocytes: 731/mm3.

On days 17-18, the patient noted some scalp pain and polyuria. P/E revealed disturbance of sensations. Analgesics were discontinued and antibiotics resumed. There were no significant changes on hematological tests. A whole blood transfusion was given. Sedatives were withheld. The next day, the patient again noted polyuria.

On day 20, the patient developed purpura. Blood counts showed platelets: 58,000/mm3. One plasma transfusion was given.

The patient's conditions were unchanged for the next few days. Her chemistry tests showed bilirubin 0.9 mg/dL and chlorides 579 mg/dL. Parenteral fluids, electrolytes, antibiotics and steroids were withheld.

On day 25-26s, epilation subsided. The patient developed erythema of skin. Antibiotics and electrolytes were resumed. Blood counts showed a marked fall in neutrophils (193/mm3) and lymphocytes (519/mm3).

On days 27-30, the patient noted fatigue and one episode of polyuria. Laboratory test showed a further fall in neutrophils (73/mm3) but unchanges of lymphocytes (588/mm3). A plasma transfusion was given on day 27 and a whole blood transfusion on day 31. However, there was no significant change in blood counts. The administration of hematinics began two days later. No significant improvement in blood counts between days 27 and 37.

By day 38, the patient had an episode of hypertension. A plasma transfusion was given. The blood count continued to show low neutrophils (287/mm3) and lymphocytes (805/mm3). The erythema of the skin remained, and sedatives and steroids were resumed on days 39 and 40.

Two days later, antibiotics were discontinued. Laboratory test showed slight improvement of the counts of neutrophils: 541/mm3 and lymphocytes: 950/mm3.

On days 47-48, the patient noted dizziness, nausea and vomiting. Hematinics and steroid were discontinued, antibiotics were resumed and a whole blood transfusion was given. A blood count on day 52 showed further improvement in neutrophils: 1116/mm3 and lymphocyte counts:828/mm3.

The patient had an episode of headache and vomiting on 58th post-exposure day. Blood counts showed neutrophils: 1364/mm3 and lymphocytes: 616/mm3. Vasoconstrictors were administrated. On day

69, sedatives, vasoconstrictors and vitamins were discontinued, but antibiotics resumed on dat 79.

This clinical care ended on 90th post-exposure day, with the patient's physical condition improved. The same was also true for her hematological results, which gradually returned to the pre-exposure level by September, 1957.

This worker continued to work at the Plant C until September 1, 1958. She was transferred to Plant D on August 12, 1959 and left on June 2, 1986, but continued to be under medical surveillance until Feb. 7, 1997.

ARS 20096 (DOB ?-?-1914)

A 41-year-old male nuclear facility worker came to the clinic after whole body irradiation on March 15, 1953. He was employed in Plant D on January 7, 1949 and transferred to Plant B in December 1, 1949. His past medical history was unremarkable and psychosocial history revealed that he was a smoker (5 packs/day) and heavy alcohol consumer. By 1951-1953, his initial leukocyte level of about 7,500/mm3 and platelets of about 220,000/mm3 had declined to a range of 5,000 and 120,000/mm3, respectively. Upon arrival, he complained of anorexia, nausea, vomiting, headache and fever. Physical examination (P/E) was negative. A blood count showed mildly increased neutrophils (5712/mm3) and lymphocytes (2436/mm3) compared the pre-accident values of Feb. 19, 1953 (neutrophils: 4200/mm3 and lymphocytes: 1200/mm3).

Twenty-four hours post exposure (day 2), nausea, vomiting, and headache were not noted, but the patient complained of weakness, which persisted until day 54. His appetite remained hearty until day 11. The next day, the patient noted an episode of erythema of the skin. A blood count showed a mild fall in neutrophils (4428/mm3) but a significant one in lymphocytes (540/mm3).

The patient's condition was stable on day 4. The next day, he complained of abdominal pain, and erythema of the skin and purpura were noted. The later last for 28 days. P/E revealed tachycardia, edema and tenderness of the bone. Fever and tachycardia persisted throughout the course of his hospitalization. A blood count showed neutrophils: 4872/mm3 and lymphocytes: 560/mm3. Sedatives, parenteral fluids, electrolytes and vitamins were started.

On day 6, the patient developed peritonitis and abdominal distention. An episode of vomiting, headache, sweating and dizziness was also noted. P/E revealed disturbances of sensations and deep tendon reflexes, as well as other motor functions. A blood count showed neutrophils: 8234/mm3 and lymphocytes: 644/mm3. Antibiotics were started and a dose of analgesics was given, but sedatives were discontinued.

On day 7, purpura subsided but an episode of oliguria was noted. A blood count showed neutrophils: 5705/mm3 and lymphocytes: 910/mm3, and platelets: 127,000/mm3. Thrombocytopenia persisted during the rest hospitalization. Over next 4 days, abdominal pain and distention and peritonitis were not present, but hypertension was noted on day 10. Blisters appeared on day 12, as was hypotension the next day. Although his condition was unchanged on day 14, he lost his appetite again and developed hematuria and epilation in the next two days. Anorexia and hematuria, as well as hypertension recurred intermittently during the remainder of his hospitalization. Parenteral fluids and electrolytes were discontinued on day 15 and 16, respectively. Biochemical tests on day 16 showed total protein: 6.34 g/dL, albumin: 4.13 g/dL, globulin: 2.21 g/dL and chloride: 526 mg/dL.

The patient's condition was stable from days 17 to day 20, except for a headache on day 20. Bone tenderness stopped on day 19. The patient became hypotensive again on day 21. Antispasmodics and sedatives were started on days 18 and 20, respectively. Parenteral fluids and electrolytes were resumed on day 20.

The patient noted bloody diarrhea on day 22, but his condition was stable the next two days. Abdominal distention and purpura were noted on day 25, and abdominal pain on day 26. Vasoconstrictors were given.

On day 27, the blistered area developed into cutaneous ulceration and necrosis. Cutaneous ulceration lasted for 27 days, while necrosis of the skin persisted until day 88 (last for 61 days). On 28th day, epilation stopped, but abdominal pain recurred again and was present intermittently until day 60.

The patient's condition was stable the next 4 days, except proteinuria on day 31. Headache subsided on day 29 and blisters on day 31. Antispasmodics were stopped on day 30, but vasoconstrictors were given the next day. By day 33, the patient was noted to be in the somnolent state, which last for the next 19 days.

By the following 3 days, the patient developed hemorrhage, which persisted until day 63. Biochemical test on day 34 showed total protein: 5.18 g/dL, albumin: 2.85 g/dL, globulin: 2.33 g/dL, BUN 18 mg/dL and chloride: 551 mg/dL, and a similar finding was noted at day 39. P/E revealed abdominal distension, which last 11 days. Hematinics were started at day 35. Weight loss was noted on day 37 and he failed to return his previous body weight during the remainder of his hospitalization. An episode of dyspnea was also noted. Vasoconstrictors were discontinued. Over the next three days, transient purpura and polyuria were noted.

Between days 41 and 45, polyuria and oliguria recurred alternately, as well as an episode of arrhythmia. Vasoconstrictors were resumed on day 44. Antispasmodics were resumed between day 42 and 53. The patient's condition was unchanged from days 46 to 59, except for abdominal distension on day 52. Biochemical tests on day 52 showed total protein: 5.47 g/dL, albumin: 3.65 g/dL, globulin: 1.91 g/dL, bilirubin: 0.3 mg/dL, BUN: 22 mg/dL and chloride: 481 mg/dL. The similar biochemical results were noted on day 69. However, he had abdominal pain on day 60 and oliguria the next day. Parenteral fluids and electrolytes were discontinued on day 69.

Paralleling thrombocytopenia, but delayed in onset by two days, there was a progressive fall, with some fluctuations, in both neutrophil and lymphocyte counts beginning on day 9. These reached a nadir of 352/mm3 on day 34 and 330/mm3 on day 27, respectively. In contrast to thrombocytopenia, a stepwise recovery of both neutrophils and lymphocytes began on day 56 and was complete on day 80.

The clinical course from then on was uneventful and this patient's care ended on the 90th post-exposure day, with his physical condition improved. The same was also true for his platelet count, which return the pre-exposure level by December 3, 1953. This individual returned to work at Plant B, and was transferred back to Plant D at May 17, 1954 and left on September 15, 1961. He was under medical surveillance until August 31, 1961.

ARS 28562 (DOB 9-25-1918)

A 39-year-old female nuclear facility worker came to the clinic after receiving whole body irradiation on April 22, 1957. She had been an employee at the Plant C since April 19, 1949. Her past-medical history and the psychosocial history were negative.

Upon arrival, she complained of vomiting and headache. The physical examination (P/E) revealed hypotension (110/60 mmHg), asymmetry of the deep tendon reflexes, ataxia and other motor dysfuctions. The blood count showed markedly increased neutrophils (9800/mm3) and decreased lymphocytes (896/mm3), compared the pre-accident values of March 28, 1957 (neutrophils 3333/mm3 and lymphocytes 2360/mm3). She was treated with antibiotics and vitamins.

Twenty-four hours past exposure (day 2), vomiting and hypotension were not present, but the patient was febrile and complained of anorexia and tachycardia. Sedatives were started.

Both neutrophils and lymphocytes significantly decreased (2085/mm3 and 570/mm3, respectively).

On day 3, anorexia, fever and tachycardia were not present, but she was hypotensive again. The blood count showed neutrophils: 2275/mm3 and lymphocytes 980/mm3. A whole blood transfusion and parenteral fluids, as well as electrolytes, were given.

The next day, hypotension subsided, but headache was back and return intermittently until day 19. A blood count showed neutrophils: 2534/mm3 and lymphocytes: 962/mm3.

By day 5, ataxia stopped. An episode of hypotension and cough were noted. The patient was febrile, which recurred intermittently until day 25. Laboratory tests showed BUN: 30 mg/dL and no changes in both neutrophils and lymphocytes (2304/mm3 and 752/mm3, respectively).

On day 6, she complained of fatigue. P/E showed disturbance of sensations. A blood count showed neutrophils: 2142/mm3 and lymphocytes: 518/mm3, respectively. A whole blood transfusion and parenteral fluids, as well as electrolytes, were given. By day 7-8, tachycardia, fever and hypotension were

noted. Headache, tachycardia, ataxia and hypotension were noted intermittently throughout the course of her hospitalization.

On days 9 and 10, the patient was stable. One plasma transfusion was given. By day 11, disturbance of sensations stopped. Between day 12 and 18, the patient's condition was not changed, except for weight loss noted on day 13 and the subsidence of ataxia on day 15. While neutrophil and lymphocyte counts during this period were stable, she developed thrombocytopenia on day 12, which persisted through day 38. Biochemical tests on day 17 showed total protein: 5.68 g/dL, bilirubin: 0.5 mg/dL and chlorides: 570 mg/dL. A whole blood transfusion, parenteral fluids and electrolytes were given on day 12 and 18, respectively. A plasma transfusion was given on day 15.

On day 19, polyuria and epilation were noted. Sedatives were discontinued. On days 20-24, the patient's condition was stable, but ataxia recurred on day 22. The results of biochemical tests were unremarkable. A plasma transfusion was given on day 22, and electrolytes were started the same day.

An episode of vomiting on day 25 and nausea on day 26 were noted. A whole blood transfusion and parenteral fluids were given. Biochemical tests on day 26 showed total protein: 6.4 g/dL, bilirubin: 0.6 mg/dL, chlorides: 582 mg/dL, BUN: 18 mg/dL and cholesterol: 250 mg/dL. While the patient was stable between day 27 and 31, she developed nausea again on day 32. A plasma transfusion was given day 29, and one whole blood transfusion and parenteral fluid were admitted on day 32.

Between days 33 and 36, the patient's condition was not changed. A whole blood transfusion and parenteral fluids were given and electrolytes discontinued on day 33. Hematinics were started on day 34. By day 37, she complained of sweating, which recurred intermittently during the rest of her hospitalization.

The patient's condition was stable on days 38-51. Blood counts, which were stable before 27, showed a significant decrement of neutrophils (the lowest level: 569/mm3) was noted between days 29 and 45, with a fluctuation of lymphocytes (within a range of 667-1316/mm3). Biochemical test on day 38 showed total protein: 7.5 g/dL, albumin: 4.89 g/dL, globulin: 2.61 g/dL, bilirubin: 0.5 mg/dL and chlorides: 576 mg/dL. A plasma transfusion was given on day 38. The patient was treated with steroids between days 39 and 49. Antibiotics and hematinics were discontinued on day 48 and 50, respectively. A whole blood transfusion and parenteral fluids, as well as electrolytes, were given on day 50. On day 52, patient noted a cough again, which intermittently recurred until day 90.

The patient was stable between days 53 and 71. Anorexia was reported on day 72 and the patient had abdominal pain the next day. An episode of dyspnea was noted on day 74 and diarrhea on day 75. Biochemical tests on day 75 showed total protein: 7.5 g/dL, albumin: 5.25 g/dL, globulin: 2.25 g/dL and bilirubin: 5.0 mg/dL. Analgesics and electrolytes were started on that day.

The next day, abdominal pain stopped, but the patient was nauseated again the next day. On days 78-79, anorexia stopped. Biochemical test on day 79 showed total protein: 7.7 g/dL, albumin: 5.19 g/dL, globulin: 2.51 g/dL, bilirubin: 5.7 mg/dL and cholesterol: 194mg/dL. Analgesics were discontinued. The patient's condition was stable between day 80 and 90, except for nausea on day 81 and dyspnea on day 83. Bilirubin fell to 2.8 mg/dL on day 83 and 2.2 mg/dL on day 86.

This patient's clinical care ended on 90th post-exposure day, with her physical condition improved. The same was also true for her hematological results, which gradually returned to the near pre-exposure level by day 76. She continued to work at the Plant C and left on August 15, 1961. She continued to be under medical surveillance and follow up until July 27, 1961.

ARS 32510 (DOB 4-25-1938)

A 19-year-old female nuclear facility worker presented to the clinic after receiving whole body irradiation on April 22, 1957. She had been an employee at the Plant C since November 10, 1956. Her past-medical history and the psychosocial history were negative. Upon arrival, she complained of nausea, vomiting, abdominal pain, erythema of the skin, and headache. The physical examination (P/E) revealed tachycardia, hypotension (110/60 mmHg), disturbance of the sensations, asymmetry of the deep tendon reflexes and other motor dysfuctions, conjunctival hyperemia, papilledema and changes of the optic fundus. The blood count showed markedly increased neutrophils (15930/mm3) and decreased lymphocytes (450/mm3), compared the pre-accident values of March 27, 1957 (neutrophils: 3690/mm3,

lymphocytes: 1680/mm3, and thrombocytes: 129,000/mm3). A whole blood transfusion was given, as well as parenteral fluids, electrolytes, antibiotics and vitamins.

Twenty-four hours post-exposure (day 2), abdominal pain and tachycardia had subsided, but the patient was febrile and complained of anorexia and dizziness. P/E revealed jaundice and ataxia. She also had hematuria. Both neutrophils and lymphocytes were 6930/mm3 and 192/mm3, respectively, with a borderline normal platelet count (151,000/mm3).

On day 3, anorexia, nausea, vomiting, dizziness and hypotension were absent. The blood count showed a further decrease; neutrophils: 3344/mm3 and lymphocytes: 209/mm3. Thrombocytes were also reduced: 81,900/mm3. A plasma transfusion was given.

On day 4, fever and hematuria subsided. The patient was hypotensive again. The blood count showed neutrophils: 3740/mm3 and lymphocytes: 506/mm3. Thrombocytes incresed to 210,000/mm3. The next day, erythema of the skin and ataxia were gone. Lymphocytes decreased again (304/mm3) with on changes of neutrophils and a platelet count of 155,000/mm3 in the lower normal range.

On day 6, hypotension was not present, but tachycardia and ataxia recurred. The patient complained of fatigue. A slightly increase of neutrophils (4752/mm3) and lymphocytes (378/mm3) was noted. Thrombocytopenia continued (136,000/mm3) and persisted until day 32. A whole blood transfusion was given. The next day, tachycardia was not present, but hypotension was back. Tachycardia recurred the next day. Neutropenia (992/mm3) and lymphopenia (328/mm3) were noted, which persisted until days 29 and day 45, respectively.

The patient had an episode of hematuria on day 9 and fatigue on day 10. A plasma transfusion was given. Electrolytes withheld and hematinics were started. Tachycardia, hypotension, fever and fatigue recurred intermittently through the course of her hospitalization.

The patient was asymptomatic on day 11, but erythema recurred the next day. A whole blood transfusion was given.

Epilation and weight loss were noted on days 13 and 14. A plasma transfusion was given. While the patient was stable on day 15, she developed blisters and had an episode of hematuria on day 16. A plasma transfusion was given.

The patient was stable on day 17, but hematuria recurred on day 18. Erythema of the skin subsided. An episode of purpura was noted and a whole blood transfusion was given. She complained of anorexia and had weight loss on day 19. Weight loss recurred intermittently in her rest hospitalization. A whole blood transfusion was given. She became jaundiced again on day 20.

On days 21 and 22, the patient's condition was unchanged. The neutrophil count reached its lowest level (8/mm3). A whole blood and plasma transfusion were given and electrolytes were resumed as were analgesics and antispasodmics.

By day 23, blisters and hematuria subsided. A whole blood transfusion was given and hematinics were withheld. Between day 24 and 27, the patient's condition was unchanged, except for erythema of the skin and dizziness on day 25 and anorexia on day 27. The lowest lymphocyte count (125/mm3) was noted on day 25. A single dose of sedatives was given that day and a whole blood transfusion was given the next day.

Jaundice subsided on day 28. The patient had an episode of abdominal pain on day 29 and hematuria on day 30. A whole blood and plasma transfusions were given and analgesics were started. A single dose of antispasodmics was given on day 29. Parenteral fluids and electrolytes were discontinued on day 30.

The patient's condition was unchanged between day 31 and 64, except for an episode of hematuria on day 39 and anorexia on day 57. X-ray abnormalities of lung were reported on day 59. Epilation stopped on day 35. A whole blood transfusion was given on day 32, 36, 41 and 62 and the patient was treated with hematinics between day 31 and 44. Analgesics discontinued on day 34. Antibiotics were withheld between days 45 and 56, and discontinued on day 61.

Jaundice was noted on day 65, but subsided the next day. A whole blood transfusion was given. She had episode of hematuria on day 69. Hematological findings between day 45 and 69 were stable, which gradually returned to the near pre-exposure level by day 64. A whole blood transfusion was given on

day 68.

Between day 70 and 90, she was stable. Asymmetry of the deep tendon reflexes, ataxia and other motor dysfuctions, papilledema and changes of the optic fundus remained persistently during the course of her hospitalization. The patient was treated with sedatives between day 73 and 86.

This patient's clinical care ended on 90th post-exposure day, with her physical condition improved. She continued to work at the Plant C and left on August 1, 1961. She was diagnosed to have radiation cataracts on February 24, 1960. She continued to be under medical surveillance and follow up until July 27, 1961.

ARS 34406 (DOB 11-17-1924)

A 34-year-old female nuclear facility worker was sent to the clinic after receiving whole body irradiation on January 2, 1958. She was employed at the Plant A in February 15, 1953 and had been transferred to Plant D on December 15, 1953. Her past-medical history included a diagnosis of radiation cataracts on May 7, 1956. Her psychosocial history was negative. Upon admission, she complained of nausea, vomiting, and erythema of the skin, fever and fatigue. The physical examination (P/E) revealed conjunctival hyperemia. Laboratory tests showed a increased neutrophils (13931/mm3), lymphocytopenia (372/mm3), total protein: 7.85 g/dL, albumin: 5.13 g/dL, globulin: 2.72 g/dL, bilirubin: 0.5 mg/dL, cholesterol: 556 mg/dL, BUN: 28 mg/dL and chloride: 556 mg/dL. There were no pre-exposure laboratory records for this patient. Whole blood and plasma transfusions were given, as were sedatives, parenteral fluids, electrolytes, antibiotics and vitamins.

Twenty-four hours post-exposure (day 2), nausea, vomiting and fatigue subsided, but the patient developed jaundice and had some EKG abnormalities. A blood count showed neutrophils: 7636/mm3 lymphocytes: 415/mm3.

On day 3, erythema of the skin, jaundice and EKG abnormalities subsided. The patient became mildly hypertensive (130/90 mmHg). A blood test showed a further fall in both neutrophils (4581/mm3) and lymphocytes (147/mm3). A another whole blood transfusion was given, and whole blood and plasma transfusions were alternated every other day until day 14. Occasional doses of analgesics and antispasmodics were given.

On day 4, hypertension subsided, but anorexia, vomiting and some EKG abnormalities recorded. P/E revealed asymmetry of the deep tendon reflexes. The next day, vomiting and EKG abnormalities subsided, but fatigue was again noted. A blood count showed neutrophils: 2653/mm3 and lymphocytes: 72/mm3, as well as thrombocytopenia (89,000/mm3).

On day 6, she complained of loss of appetite, abdominal pain and dysuria. She was nausea and vomiting again. P/E revealed asymmetry of the deep tendon reflexes and disturbance of other motor functions. Biochemical testing showed total protein: 7.00 g/dL, albumin: 4.2 g/dL, globulin: 2.8 g/dL, bilirubin: 1.3 mg/dL, BUN: 36 mg/dL and chloride: 544 mg/dL. Analgesics and antispasmodics were started.

There was a progressive fall in the neutrophil and lymphocyte counts for the next 20 days, reaching a nadir of 172/mm3 on day 21 and 9/mm3 on day 7, respectively. A stepwise recovery of the neutrophils and lymphocytes began thereafter and was nearly complete on day 31. The nadir of the thrombocytopenia was parallel to that of the neutrophils, but recovery was complete by day 24.

There was intermittent remission of these initial symptoms and signs, including anorexia, nausea, vomiting, fever, fatigue and tachycardia and asymmetry of the deep tendon reflexes and other motor dysfunctions, toward the end of her hospitalization.

On days 7 and 8, the patient had episodes of somnolence and abdominal pain. Erythema of the skin was noted on day 9 and recurred intermittently until day 44, and diarrhea on day 10.

On day 11, transient hypotension was observed, which recurred intermittently during the rest of her hospitalization. P/E revealed ataxia and epilation. Biochemical tests showed total protein: 7.00 g/dL, albumin: 4.03 g/dL, globulin: 2.97 g/dL, bilirubin: 0.5 mg/dL, BUN: 39 mg/dL and chloride: 547 mg/dL. By the next day, blisters were noted, which recurred intermittently until day 34. Transient somnolence recurred.

On days 13-16, the patient was relatively stable. Ataxia subsided. Steroids were started; however, analgesics and antispasmodics were discontinued.

On days 17-19, ulceration of the skin was noted. Biochemical tests showed total protein: 7.5 g/dL, albumin: 3.75 g/dL, globulin: 3.75 g/dL, bilirubin: 0.5 mg/dL, BUN: 39 mg/dL and chloride: 541 mg/dL. Whole blood and plasma transfusion, analgesics and antispasmodics were given on day 17 and 19, respectively.

The patient was stable on day 20. By day 21, the end of epilation was observed, but disturbance of sensation recurred. Between days 22 and 25, the patient's condition was unchanged. Oliguria was noted on day 26 and weight loss on the next day. Whole blood and plasma transfusions, analgesics and antispasmodics were given on day 22. Another whole blood transfusion, as well as analgesics and antispasmodics were administrated on day 25.

Oliguria subsided on day 28 and the disturbances of sensation on day 29, but ataxia returned. Biochemical tests showed total protein: 8.2 g/dL, albumin: 5.74 g/dL, globulin: 2.44 g/dL, bilirubin: 0.4 mg/dL, cholesterol: 321 mg/dL and chloride: 576 mg/dL. Whole blood transfusion, analgesics and antispasmodics were given.

Between days 30 and 39, the patient was stable, except for disturbance of sensation on day 33. Electrolytes were discontinued on day 32. Whole blood transfusion, analgesics and antispasmodics were given on day 37. On day 40, she had another episode of oliguria.

Between days 41-47, the patient's condition was unchanged, except for dysuria on day 46. Biochemical tests on day 43 showed total protein: 7.8 g/dL, albumin: 5.08 g/dL, globulin: 2.72 g/dL, bilirubin: 0.5 mg/dL, cholesterol: 250 mg/dL, and chloride: 550 mg/dL. Steroids were discontinued on day 41, but were resumed between days 47 and 53. A whole blood transfusion, analgesics and antispasmodics were given on day 43. However, hematuria was noted on day 48 and 50.

The clinical course from days 51 to 73 was uneventful, except for headache and edema on day 68 and weight loss on day 71. Antibiotics were discontinued on day 63. Edema recurred on day 74 and persisted throughout the next 16 days. Electrolytes were resumed on day 78. A biochemical test on day 70 showed total protein: 7.9 g/dL, albumin: 4.35 g/dL, globulin: 3.55 g/dL, bilirubin: 0.4 mg/dL, BUN: 30 mg/dL, and chloride: 582 mg/dL. Similar results were noted on day 80. A whole blood transfusion and parenteral fluids were given on day 85.

This patient's clinical care ended on the 90th post-exposure day, with her physical condition improved. The same was also true for hematological findings, which gradually reached the normal range by this time. She returned to work at the Plant D and left on July 16, 1965. She continued to be under medical surveillance and follow up until August 9, 1967.

Appendix C

CLINICAL RADIATION INJURY GROUP IV

ARS 2119 (DOB 12-30-1927)
A 31-year-old male nuclear facility worker was brought to the clinic immediately after receiving a whole body exposure to ionizing radiation at Plant C on Jan. 2, 1958. He had been an employee at Plant C since 1949. His past medical history was negative. His psychosocial history included smoking (1 pack/day) and moderate to marked alcohol consumption.
Upon arrival to the medical facility, he complained of vomiting, diarrhea, abdominal pain, fever, headache, fatigue, weakness, erythema of the skin. On physical examination (P/E), he had hypotension, dyspnea, tachycardia, asymmetry of deep tendon reflexes and disturbance of sensations. Laboratory showed markedly elevated neutrophils (13340/mm3) and decreased lymphocytes (797/mm3), compared the pre-accident values of December 10, 1957 (neutrophils: 3030/mm3) and decreased lymphocytes: 2040/mm3), and abnormal chemistry values: total protein: 7.3 g/dL; albumin: 4.75 g/dL; globulin: 2.55 g/dL; chloride: 582 mg/dL; BUN: 39 mg/dL; bilirubin: 0.5 mg/dL and cholesterol: 210 mg/dL. He was treated with whole blood transfusions, analgesics, antispasmodics, parenteral fluids, antibiotics and vitamins.
Twenty-four hours post exposure (day 2), abdominal pain subsided, but the patient developed an episode of nausea, EEG anormalities, purpura, conjunctival hyperemia and other lesions of the conjunctiva. Laboratory showed neutrophils: 14960/mm3 and lymphocytes: 160/mm3, and chemistry values: chloride: 477 mg/dL; bilirubin: 0.9 mg/dl. Plasma and a platelet transfusion were given. Vasoconstrictors and a single dose of sedatives were added to the treatment regime.
On day 3, diarrhea and fatigue subsided, but abdominal pain reoccurred. The patient developed hematuria, oliguria, acute encephalopathy and an episode of incapacitation, as well as EKG abnormalities. He also complained of bone pain. Examination revealed tenderness of bone. Blood count showed neutrophils: 10388/mm3 and lymphocytes: 53/mm3. The next day, vomiting, fever and hematuria subsided. He was somnolent. Antispasmodics and vasoconstrictors were discontinued.
On day 5, headache subsided but hematuria and vomiting recurred. He also had anorexia. P/E revealed, in addition of asymmetry of deep tendon reflexes, others of motor dysfunction. Laboratory tests showed neutrophils: 10098/mm3 and zero lymphocytes, and abnormal chemistry values: total protein: 6.0 g/dL; albumin: 3.9 g/dL; globulin:2.1 g/dL; chloride: 412 mg/dL and BUN: 142 mg/dL. Whole blood transfusions were discontinued, antispasmodics were resumed and electrolytes were given.
Even with intensive medical intervention, the patient's conditions continued to deteriorate. He developed temporal disorientation and coma, and expired on 6th post exposure day.

ARS 9685 (DOB 10-20-1931)
A 26-year-old female nuclear facility worker was admitted to the clinic immediately after receiving a whole body exposure to ionizing radiation on April 22, 1957. She had been an employee at Plant C since 1956. Her past medical and psychosocial history was negative.
Upon arrival to the medical facility, she complained of anorexia, nausea, vomiting, abdominal pain, and erythema of the skin, fever, headache, and fatigue. On physical examination (P/E), she had hypotension (100/60 mmHg), tachycardia, edema, conjunctival hyperemia, ataxia, hypoactive deep tendon reflexes and other motor dysfunction, disturbance of sensations. Laboratory tests showed markedly elevated neutrophils: 16625/mm3 and lymphocytopenia: 475 /mm3, compared the baseline values on April 15, 1957 (neutrophils: 3021/mm3 and lymphocytes: 2280 /mm3), and chemistry values: total protein: 6.8; chloride: 570 and bilirubin: 2.0. She was treated with whole blood transfusion, parenteral fluids, electrolytes, vasoconstrictors, antibiotics and vitamins.
Twenty-four hours post exposure (day 2), nausea, abdominal pain, ataxia and conjunctival hyperemia stopped but jaundice and EKG abnormalities were found. Laboratory tests showed neutrophils: 11992/mm3 and zero lymphocyte counts, total protein: 6.98 g/dL and chloride 497 mg/dL. Sedatives and analgesics as well as a single dose of antispasmodics were added on treatment regimes.
On day 3, vomiting, headache and fever subsided, but the patient had one episode of hematuria. Laboratory tests showed neutrophils: 11997/mm3 and lymphocytes: 31 /mm3, chloride: 570 mg/dL and BUN: 32 mg/dL. A plasma transfusion was given. P/E revealed asymmetry of deep tendon reflexes.
On day 4, tachycardia was subsided but hypotension remained. The patient was loss of weight. Blood count showed neutrophils: 11828/mm3 and lymphocytes: 23 /mm3. Another single dose of antispasodmics was given.
On day 5, hypotension was improved and jaundice disappeared, but tachycardia returned. The patient was in somnolent state. P/E revealed hepatomegaly. Blood count showed neutrophils: 10274/mm3 and zero lymphocyte count. She received a whole blood transfusion. Since then, whole blood or plasma transfusion was given alternately every other day.
On day 6, she had fever again. Anorexia subsided. Blood count showed neutrophils: 3492/mm3 and lymphocytes: 72 /mm3, as well as a borderline thrombocytopenia: 149,000/mm3. The next day, hypotension recurred. Hepatomagely and weight loss disappeared.
On day 8, the patient had an episode of anorexia and vomiting. Blood count showed markedly decrease in neutrophils: 7/mm3 and lymphocytes: 7/mm3, as well as a thrombocytopenia: 77,000/mm3.
On day 9, erythema of the skin was fading, but the patient developed localized pneumonia. Blood count showed neutrophils: 4/mm3 and lymphocytes: 29/mm3, as well as thrombocytopenia: 32,000/mm3.
On day 10, she developed diarrhea, dyspnea, cough, purpura and hemorrhage of the skin and was in somnolent state. Blood count showed zero neutrophil counts and lymphocytes: 44/mm3, as well as thrombocytopenia: 30,000/mm3. Vasoconstrictors were resumed.
On day 11, anorexia returned. Epilation was noted. Even with intensive medical intervention, her conditions continued to deteriorate. Blood count showed zero neutrophil counts and lymphocytes: 22/mm3, as well as thrombocytopenia: 33,000/mm3.
The patient died on 12th post-exposure day.

ARS 25864 (DOB 8-29-1929)
A 29 year old male nuclear facility worker was brought to the clinic immediately after receiving a whole body exposure to ionizing radiation at Plant A on Jan. 2, 1958. He was an employee at Plant A since 1953. His past medical history was negative. His psychosocial history included smoking (1.5 pack/day) and moderate to marked alcohol consumption.
Upon arrival to the medical facility, he complained of nausea, vomiting, headache, fatigue, tachycardia, weakness, erythema, fever and diarrhea. On physical examination (P/E), he had mild hypotension (90/60 mmHg), fever, hypoactive deep tendon reflexes and other motor dysfunctions, conjunctival hyperemia and other lesions of the conjunctiva. Laboratory tests showed markedly elevated neutrophils (10829/mm3) and decreased lymphocytes (665/mm3) compared the pre-accident values of March 23, 1957 (neutrophils:

3542/mm3 and lymphocytes: 2275/mm3).
He was given whole blood and plasma transfusions. In addition, he was treated with sedatives, analgesics, antispasodmics, parenteral fluids, antibiotics and vitamins.
Twenty-four hours post exposure (day 2), the patient had an episode of abdominal pain. Otherwise, his conditions were unchanged. Hypotension persisted during the remainder of his life. The same was also true for fever, except on days 6 and 7. Laboratory tests showed high neutrophils (10416/mm3) and further reduction of lymphocytes (224/mm3) compared the first day. Biochemistry values: albumin 5.46g/dL, globulin 2.39g/dL and chloride 556mg/dL, BUN 36mg/dL, bilirubin 1.1mg/dL and cholesterol 321mg/dL. Blood transfusions were discontinued and vasoconstrictors were added.
On day 3, nausea, vomiting, headache, fatigue, and diarrhea, nausea, abdominal pain and purpura subsided. Laboratory studies showed neutrophils 10530/mm3 but 120/mm3 lymphocytes were found. Whole blood and plasma transfusions were given alternately every other day.
On day 4, the patient noted headache and incapacitation. Examination revealed tenderness of bone and disturbance of sensations. No blood counts were done.
On day 5, No improvement was seen. The patient developed abdominal pain, dyspnea, temporal disorientation and anuria. Laboratory studies showed decrease of chlorides: 427 mg/dL, albumin: 4.2 mg/dL, globulin: 1.8 mg/dL and elevation of BUN: 87 mg/dL. A blood count showed decreased neutrophils: 7644/mm3 and zero lymphocytes, as well as thrombocytopenia (127,000/mm3).
On day 6, anuria ended. The patient complained of anorexia, vomiting, and fatigue. P/E revealed abdominal distension, dyspnea, somnolence and an episode of arrhythmia. A blood count showed neutrophils: 2205/mm3, lymphocytes: 11/mm3, and platelets: 84,000/mm3.
Fever subsided the next day but the patient developed proteinuria. A blood count showed further decrease in neutrophils: 294/mm3 and platelets: 48,000/mm3 and no lymphocytes.
On day 8, the patient developed hemorrhage, jaundice, epilation and polyuria. He complained of headache, dizziness and fatigue. Even with intensive medical intervention, the patient's conditions continued to deteriorate. The last laboratory tests showed chlorides: 395 mg/dl, bilirubin: 1.7 mg/dl and BUN: 89 mg/dl, zero lymphocytes, very low neutrophils: 56/mm3 and platelets: 20,000/mm3.
The patient had fever again and died on day 9.

ARS 53992 (DOB 10-28-1933)
A 25-year-old male nuclear facility worker was brought to the clinic immediately after receiving a whole body exposure to ionizing radiation at Plant C on January 2, 1958. He was first employed at Plant A in1953 and transferred to Plant D until January 1958. His past medical history was negative. His psychosocial history included smoking (3/4 pack / day) and moderate alcohol consumption.
Upon admission, he complained of nausea, vomiting, diarrhea, headache, weakness, abdominal pain and. On physical examination, he had erythema, fever, tachycardia, hypotension (80/35 mmHg), hyperactive deep tendon reflexes and conjunctival hyperemia. Laboratory showed significantly elevated neutrophils (12,900/mm3) and decreased lymphocytes (352/mm3) compared the pre-accident values of December 2, 1957 (neutrophils: 3153/mm3 and lymphocytes: 1325/mm3). He was treated with parenteral fluids and electrolytes.
Twenty-four hours post-exposure (day 2), the patient's condition was unchanged, except for cessation of the diarrhea. Tachycardia, hypotension and fever persisted during the remainder of his life, while vomiting persisted until day 5. P/E revealed asymmetry of deep tendon reflexes, ataxia, disturbance of sensations, purpura, other lesions (not hyperemia) of the conjunctiva and a transient change of the optic fundus. Laboratory studies showed glucose: 155 mg/dL, chlorides: 561 mg/dL, albumin: 4.94 mg/dL and globulin: 2.66 mg/dL and bilirubin: 0.7 mg/dL. A blood counts showed neutrophils: 10260/mm3 and lymphocyte: 108/mm3. Vasoconstrictors, sedatives, analgesics and antibiotics, as well as vitamins were added to therapy. The patient also received blood and plasma transfusions.
On day 3, nausea, fatigue, abdominal pain and purpura had ended, but the patient developed anorexia, abdominal distension, cough and disturbances of motor functions. Laboratory studies showed chlorides: 518 mg/dL; bilirubin: 1.3 mg/dL, and BUN: 61 mg/dL. A blood count showed markedly elevated neutrophils

(14,775/mm3) but lymphocytes had fallen to zero. Treatment was unchanged except replacement of sedatives with antispasmodics.
On day 4, the patient remained hypotensive and developed oliguria. Erythema cleared, but purpura recurred. Whole blood transfusion and antispasodmics were discontinued, but plasma infusion continued.
The next day, the patient developed temporal disorientation. Anorexia and erythema returned. Antispasmodics were resumed. Laboratory tests showed chlorides: 436 mg/dL and albumin: 3.63 g/dL and elevation of BUN: 122 mg/dL. A blood count showed neutrophils: 11,000/mm3 and no lymphocytes.
By day 6, despite intensive medical intervention, the patient's condition continued to deteriorate. A blood count showed markedly decreased neutrophils: 3700/mm3 and no lymphocytes. Whole blood transfusions were resumed.
On day 7, no improvement was seen and the patient expired. The last laboratory test showed BUN: 212 mg/dL, neutrophil counts were reduced to 120/mm3 and again, no lymphocytes were found.

Appendix D

Report on Quality Control Assessment (QCA) for the Study of
Acute Radiation Syndrome in Russian Nuclear Workers

Institute of Biophysics, Branch No. 1 (FIB-1)
Ozyorsk, Russian Federation
December 3-7, 1997

Background

As part of the NIOSH sponsored project entitled, "Acute Radiation Syndrome in Russian Nuclear Workers," the collaborating scientists from the University of Pittsburgh Graduate School of Public Health were to carry out a quality control assessment (QCA) of the information abstracted from medical records by the scientists from the Institute of Biophysics, Branch No. 1 (FIB-1).

Methodology and Sampling

The methodology and sampling procedures for the QCA are provided in the protocol dated November 1997 (see Attachment 1).

Implementation

The QCA was carried out over a four day period from December 4-7, 1997. Items for

checking were selected primarily from the following sections of the project data base:

a. Worker Identification (date of birth, sex)
b. Work History (plants and dates of employment)
c. Medical History and Vital Status (diagnosis, vital status, date and cause of death)
d. Occupational Exposure History (dates and total exposures prior to accident)
e. Hematological and Blood Pressure Data
f. Acute Radiation Exposure (date, location, high and low cumulative exposure estimate)
g. Acute Radiation Symptoms (particularly first 72 hours)
h. Treatment for Acute Radiation Syndrome
i. Biochemical Tests

The number of items checked for each subject was variable depending upon the complexity of the case and the amount of available data. As a rule, 300-400 items, including symptoms not occurring, were checked for each subject or approximately 7000 total items for the 20 patients in the QAC sample. Item selection for checking was carried out in two ways: (a) Dr. Wald (English speaking) selected items from the data base to be checked by Dr. Sheketer-Levin (Russian/English speaking) in the original medical records; and (b) Dr. Sheketer-Levin selected items from the original Russian records to be checked by Dr. Wald using data base information. The majority of items were selected using method a. in order to test whether Dr. Wald was able to reconstruct realistic case histories using the information in the data base.

Results

The detected error rate for the transcription of information from the medical records to the project data base did not exceed a 1% level, well within the limits set for the QCA procedure. A list of outstanding transcription errors requiring correction in the data is included in Attachment 2 of this report.

In addition to the correction of transcription errors, the QAC procedure also located a number of items in the data base that require inclusion or revision. These are not counted as errors, but as data base revisions that will improve the clinical accuracy of the data base and permit the construction of more informative clinical case histories from the transcribed record information. A list of the agreed upon revisions to the data base are included in Attachment 3 of this report.

Discussion and Conclusions

The findings of this QCA are very similar to previous exercises. The quality of the transcription of the information from clinical records to the electronic data base by the

FIB-1 scientists was excellent both in terms of accuracy and completeness. The QCA procedure also permitted the clinicians on the University of Pittsburgh team to work with the information contained in the data base for the first time. This provided an important opportunity to for the University of Pittsburgh clinicians to request some final modifications to the data base that would improve the clinical description of cases based on the transcribed information.

Final Agreements

The University of Pittsburgh scientists were permitted to take a copy of the current version of the data base back to Pittsburgh in order to begin work on the next phase of the Acute Radiation Study. The FIB-1 scientists estimated that it would take approximately one month to make the corrections and revisions to the data base included in Attachments 2 and 3 of this report. It was agreed that a final (corrected and revised) version of the data base would be transported by a FIB-1 representative to the University of Pittsburgh in the latter part of January 1998.

ATTACHMENT 1

ACUTE RADIATION SYNDROME IN RUSSIAN NUCLEAR WORKERS

PROPOSED QUALITY ASSESSMENT/ QUALITY CONTROL (QA/QC) PROCEDURES

NOVEMBER 1997

1. For NIOSH ARS Study the US Investigators propose using the same type of data QA/QC procedures routinely used by US National Cancer Institute (NCI) Collaborative Clinical Trials Groups.

2. As applied this our collaborative project, this procedure calls for a randomly selected 33.8% (n=20) QA/QC sample of the 59 ARS cases in the study population. All of the clinical data on these subjects should be made available for review and comparison with the computerized data base contents. The identification numbers for 75% of the sample of subjects (n=15) will be sent to the FIB-1 center one week prior to the arrival of the US team. The identification numbers for the remaining 25% of the QA/QC sample (n=5) of subjects will be provided to the FIB-1 staff on the arrival of the US team.

3. Selected data items from the clinical records will be compared to the material in the data base by the US team. All items will be rated as: present and accurate, divergent from source, or missing. All instances of items that are divergent from source or missing will be discussed by the US and RFD investigators and a final determination arrived at.

4. The data base contents will be considered acceptable if less than 5% of the data items are divergent from the source or missing. In other words, a minimum overall accuracy of at least 95% is required in order to consider that the quality of the data in the data base is acceptable.

5. If the results of the QA/QC review falls below 95% overall accuracy, the US and RF investigators will jointly develop a plan to identify the causes and improve the accuracy of the data in the data base.

QA/QC SAMPLE

A total of n=20 subjects have been randomly selected for review. Seventy-five percent (n=20) of the identification numbers are included with this protocol. The remaining 25% (n=5) of the subject identification numbers will be provided on the arrival of the US team on December 2. Complete original clinical records should be available for these subjects for review and comparison with the computer data base contents.

Records supplied prior to arrival in Ozyorsk:

PITT sequence no.	FIB-1 Clinic no.
2	18835-22547
9	5526-14529
15	3142-5552
16	92-34040
18	2536-541
33	2944-27667
37	1949-12888
41	612-32698

42	6160-15189
44	6140-8599
45	3407-3963
51	18842-9685
52	7974-29190
53	7680--56135
58	6466-29395

Records supplied on arrival in Ozyorsk:

1	3940-7518
17	1771-3733
22	3757-2372
32	14664-2250
59	18844-466

ATTACHMENT 2

Remaining Transcription Errors for Correction in Data Base

18842-9685 - Hematology data for days 1 and 2 of ARS history needs checking for transcription errors.

6466-29395 – Information for dates 22-28/04/57 actually refers to one day earlier in Hematology section.

6160-15189 – Hematology data for days 1-3 needs checking for transcription errors.

14664-2250 – Overall gamma dose estimates vary between Occupational Exposure History section and Exposure Prior to Accident in the ARS section of the data base (107 vs. 207 rads).

The 40 rad acute exposure is placed in the "upper" estimate box, it should actually be in the "lower" estimate box. The upper estimate is unknown.

1949-12888 – Hypertension scored as a symptom in the ARS section, but not given at an adequate level in the Hematology section.

6140-8599 – Error in the number of children, should read "99" (unknown) but reads "9."

Dyspena scored as symptom in ARS section on days 14-15 but not located in the clinical records.

Disturbance of reflexes and other disturbances of motor functions are scored as present in the ARS symptoms section for days 3 through 21. However, testing was done only on days 3 and 21, therefore, symptoms should be scored as present only on days 3 and 21 and scored as unknown on days 4-20.

7974-29190 – Thyroid enlargement scored as a symptom in the ARS section. However, clinical records show that this symptom occurred prior to the acute exposure and there is no evidence that it occurred as an effect of the accidental acute exposure.

The same problem as above for hypotension. This symptom pre-existed the accidental acute exposure and should not be scored as an accident consequence.

7680-56135 – Biochemical tests indicated for day "33" are actually day "3."

ATTACHMENT 3

Agreed Upon Revisions to the Project Data Base

1. Two cases of ARS are mistakenly classified as CRS: 7824-32413 and 3407-3963. These two cases will be reclassified in the pilot study data base to reflect their true status as ARS cases. This means that the pilot study data base actually contains 97 (rather than 99) CRS cases and 16 (rather than 13) ARS cases. The extra ARS case is one patient (6466-29395) who was diagnosed as having both CRS and ARS.

2. "Estimated Duration" of the acute radiation exposure will be added to the ARS section of the data base.

3. Field will be created that gives the actual date of each of the 90 sequential days following the acute radiation exposure. This variable will be placed in the ARS

section of the data base.

4. The total neutron dose for an individual is currently placed in the "prior" box in the ARS exposure section. This will be revised such that neutron dose from acute exposure is differentiated from prior and subsequent neutron dose, and placed in proper exposure box.

5. The following specific symptoms will be revised in the following manner:

a. On **Day1** of the ARS symptom section, **nausea, vomiting and diarrhea** will be rated using the following scale:

0=not present at any time
1=occurred within first hour following acute exposure
2=occurred between 1-4 hours of acute exposure
3=occurred after 4 hours following acute exposure
8=symptom occurred but time unknown
9=unknown if symptom occurred

b. **Tachycardia** will be rated using the following scale:

0=heart rate <80 per min.
1=heart rate between 80 and 100 per min. (any position)
2=heart rate >100 per min. (any position)
8=symptom occurred but unable to grade
9=unknown if symptom occurred

c. **Hypertension** defined as ≥140/90 (either or both systolic and diastolic pressures must exceed minimum).

d. **Hypotension** defined as ≤90/60 (either or both systolic and diastolic pressures must fall below defined level).

e. **Insulin deficiency** will be removed from the symptom list.

f. **Hematuria** will be scored using the following scale:

0=not present
1=micro hematuria
2=macro or gross hematuria
8=symptom occurred, but grade unknown
9=unknown if symptom occurred

g. **Disturbance of reflexes** will be rated using the following scale:

0=not present
1=hyperactive reflexes
2=hypoactive reflexes
3=asymmetry or imbalance of reflexes
8=symptom occurred but unable to grade
9=unknown if symptom occurred

h. **Disturbance of sensations** will be rated using the following scale:

0=not present
1=hyperaesthenia
2=hypoaesthenia
8=symptom occurred but unable to grade
9=unknown if symptom occurred

i. **Ataxia** will be rated using the following scale:

0=not present
1=static ataxia
2=dynamic/gross ataxia
8=symptom occurred but unable to grade
9=unknown if symptom occurred

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Public Health Service
Centers for Disease Control
and Prevention (CDC)

Memorandum

Date: July 24, 2002

From: Michael J. Galvin, Ph.D., Program Official
Office of Extramural Programs, NIOSH, E-74

Subject: Final Report Submitted for Entry into NTIS for Grant 5 R01 CC312952-02.

To: William D. Bennett
Data Systems Team, Information Resources Branch, EID, NIOSH, P03/C18

The attached final report has been received from the principal investigator on the subject NIOSH grant. If this document is forwarded to the National Technical Information Service, please let us know when a document number is known so that we can inform anyone who inquires about this final report.

Any publications that are included with this report are highlighted on the list below.

Attachment
cc: Sherri Diana, EID, P03/C13

List of Publications

Title: Acute Radiation Syndrome in Russian Nuclear Workers
Investigator: Niel Wald, M.D.
Affiliation: University of Pittsburgh
City & State: Pittsburgh, PA
Telephone: (412) 624-2735
Award Number: 5 R01 CC312952-02
Start & End Date: 12/5/1996–12/4/1999
Total Project Cost: $260,377
Program Area: NORA
Key Words:

Abstract:
Abstract:
The main objective of the parent project, Joint Collaborative Committee for Radiation Effects Research (JCCRER) Project 2.3, is the development of a database of Mayak PA workers to use for such purposes as the verification of current dose-effect models for deterministic effects of acute exposure including the acute radiation syndrome or AARS@.

The pilot research was carried out with DOE support (January 1997) to evaluate the possibility of applying primary clinical and dosimetry data available at FIB-1 and Mayak PA to the study of deterministic effects from occupational radiation exposures. During the pilot stage, the clinical- and dosimetry database was created using a stratified random sampling of the Mayak PA workers (1948-1954), and a quality control exercise on the resulting data- base. A report on work at the pilot stage of project 2.3 was submitted for the Nuclear Regulatory Commission on February 29, 1997. The work was accepted, approved of, and funded on January 15, 1998, for the long-term stage of Project 2.3.

The first stage of the long-term phase (1st year of work) was to carry out the descriptive analysis of the pilot project database and to verify the existing models of acute radiation syndrome. The next stage of the work (2nd and 3rd years) was to extend the clinical-dosimetry database from the pilot number of 225 to final database of 600 persons. The work on collecting, copying, and inputting clinical data has been completed. The dosimetry, occupational histories, demographic data and vital status have been obtained for all workers.

During the period of the NIOSH study Project 2.3 was carrying out work to complete a quality control study of the extended database; to prepare standard samples of the data and a library of Aclean@ data samples for further analysis; to prepare a final Code book; and, to test mathematical and statistical methods of dose-effect assessment for deterministic effects.

Acute Radiation Syndrome. The initial focus of effort on the NIOSH ARS project, a component of Project 2.3, was to add clinical information concerning the 59 accidentally radiation-exposed workers in the former Soviet Union during 1948 through 1958 to a similar number of accident cases collected in the Western world. The work was funded

by a National Institute of Occupational Safety and Health (NIOSH) project led by Dr. Nadezhda Okladnikova (FIB-1) and Drs. Niel Wald and Richard Day (University of Pittsburgh). The new data were to be used to test the triage scheme that had been developed by Thoma and Wald in 1959 to provide clinicians without any special knowledge about radiation effects with early diagnostic and prognostic information about the severity of such injury as a basis for medical management.

We found that 22 of the 59 cases had more than one blood count within the first 72 hours after the radiation exposure, a prerequisite for the triage injury classification method to be tested. In view of the rarity of the syndrome, all 59 cases were prepared for further study in Project 2.3 A selection was therefore made of 77 clinical and laboratory items that were of most significance and likely to be on record in most cases. In addition, demographic details, prior medical and radiation history and laboratory data were included in the data extraction questionnaire. A quality assurance study of the data extraction by the US participants revealed a low error rate of 4%.

Classification of the 22 cases into 5 injury groups was performed by Dr. Wald using clinical, laboratory and dosimetric information. A test of the ability of radiation-naive physicians to correctly classify the RF cases on the basis of 72 hours of data was completed and analyzed. This led to modification and preliminary retesting of the triage scheme. The improved results warrant further testing of the modified scheme.

Publications
No publications to date.