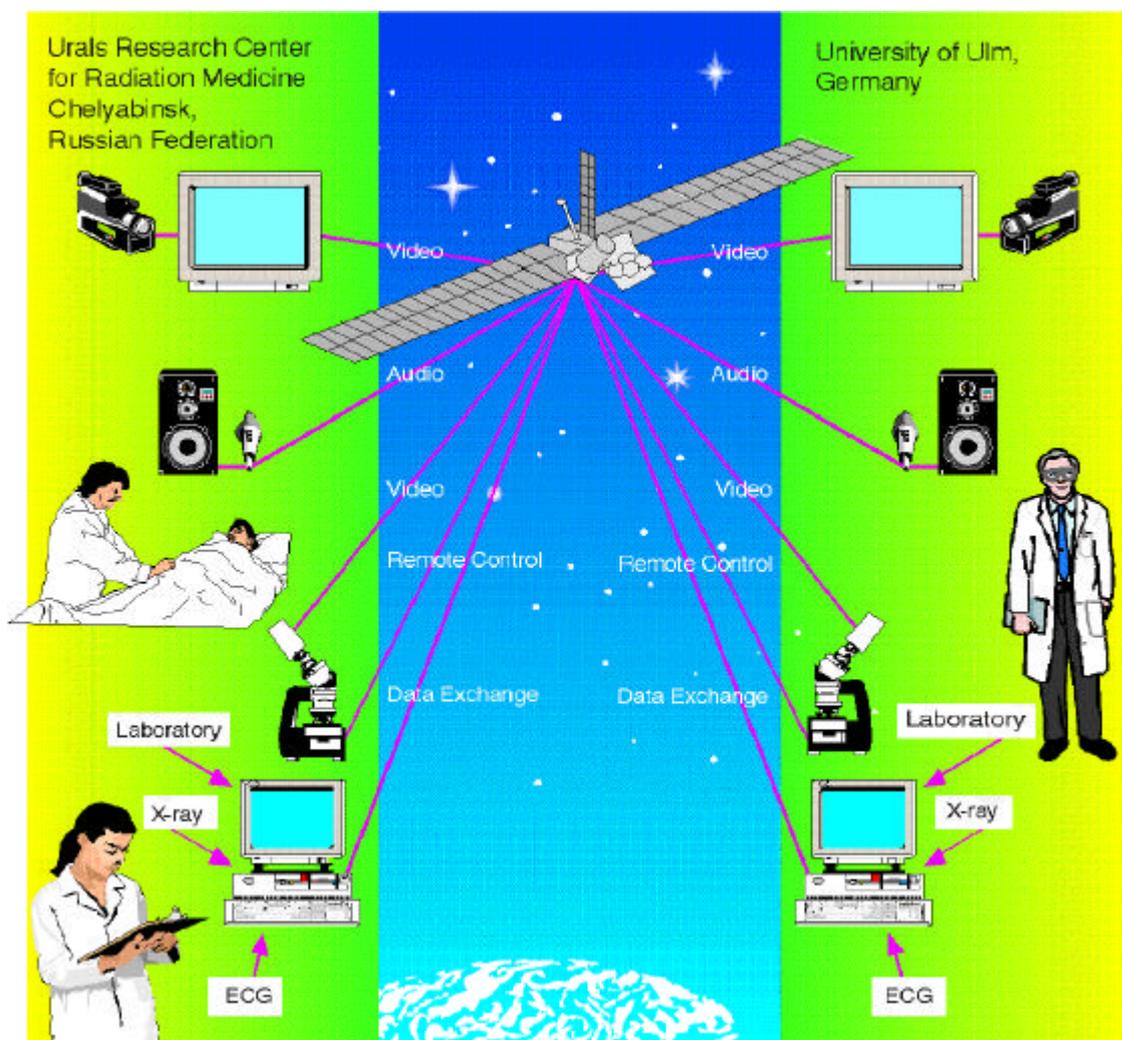


# Teleconsultation in Radiation Medicine

Results of regular telemedicine consultations between the Health Sciences Centre of the University of Ulm, Germany and Urals Research Centre for Radiation Medicine, Chelyabinsk, Russia



**Protection of the Human Environment  
Radiation and Environmental Health**

**Geneva, 2002**

WORLD HEALTH ORGANIZATION

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Akleyev A.V., Varfolomeyeva T.A. (Chelyabinsk)

Geneva, 2002

# Teleconsultation in Radiation Medicine

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## Teleconsultation in Radiation Medicine

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## Preface

This publication provides information on the success of organizing teleconsultations in radiation medicine between the Health Sciences Centre of the University of Ulm, Germany, and Urals Research Centre for Radiation Medicine, Chelyabinsk, the Russian Federation. Both these institutions are members of a global network of WHO collaborating centres: Radiation Emergency Medical Preparedness and Assistance Network (REMPAN).

WHO established REMPAN in 1987, shortly after the Chernobyl accident, with the objective of meeting its requirements under the Conventions on Early Notification and Assistance in the case of nuclear and radiation accidents. At present, REMPAN consists of 14 WHO Collaborating Centres located in specialized radiological institutions in Armenia, Australia, Brazil, Finland, France, Germany, Japan, the Russian Federation, Ukraine, United Kingdom and USA. Radiation emergency preparedness covers activities that strengthen global, regional and national capacity to manage efficiently any medical consequences of nuclear or radiological accidents.

The primary objectives of REMPAN are as follows.

- To promote medical and public health preparedness for radiation accidents among WHO Member States;
- To provide medical and public health advice and assistance in the case of a radiation accident or radiological emergency;
- To assist in medical follow-up studies of the population exposed to radiation

REMPAN Collaborating Centres serve as WHO focal points related to planning and management of radiation emergencies. They also provide training courses, seminars and on-site assistance for victims of radiation accidents. REMPAN members disseminate material developed within the network to appropriate liaison institutes within their own geographical region, and act as training centres; and participate in international preparedness exercises. To facilitate training and research in the diagnosis and treatment of radiation injuries, and medical monitoring of radiation victims, a WHO International Computer Database on radiation exposure case histories has been established at the University of Ulm within the REMPAN network. The database contains some 800 case histories from 70 accidents in 17 different countries from the years 1945 to 1994 including over 100 follow-up case histories for up to 40 years. This database includes information on:

- Acute radiation exposure
- Patient follow-up
- Chronic or ill-defined exposure

Upon request, WHO helps establish a link between the country making the request and the REMPAN assisting centre(s), keeping all REMPAN centres informed about the details of the accident and progress of its management. REMPAN has access to more than 200 specialists with expertise in radiation medicine, radiation epidemiology, radiation protection and medical dosimetry. Depending on the type of radiation emergency, WHO/REMPAN collaborating centres can provide a wide spectrum of assistance such as the following:

- Send a team for on-site emergency treatment, biological dosimetry or collecting biological samples for further medical investigations
- Provide specialized medical care to severely exposed patients
- Advise on the management of exposed persons
- Provide relevant equipment or protective materials
- Recommend appropriate medical experts
- Assist in the development of medical measures necessary to limit health effects
- Follow-up medical supervision and treatment
- Assist in the development of procedures to strengthen the ability of a country to manage radiological accidents for themselves

When a transboundary accident occurs, the accident country should notify the IAEA under the requirements of the Early Notification Convention. IAEA then notifies WHO and other UN agencies. IAEA has an emergency response medical team to assist immediately upon notification. In the earliest phase of the accident WHO coordinates the REMPAN response in close co-operation with IAEA. In some cases the IAEA medical emergency response teams will coordinate with WHO/REMPAN centres. These teams are designed to work in a site of radiation emergency in order to evaluate medical consequences, to advise local medical staff and health authorities on medical monitoring of overexposed people, and provide initial medical care to radiation victims, as required. If continued care of radiation victims is not feasible within a country then diagnosis, treatment, rehabilitation and follow-up of overexposed persons are addressed under the framework of WHO/REMPAN.

The REMPAN centre at the University of Ulm is experienced in diagnosis of radiation-induced haematological disorders and, through affiliated departments of haematology and dermatology, can provide assistance in treatment of radiation haematological syndrome and cutaneous radiation syndrome.

The REMPAN centre located at the Urals Research Centre for Radiation Medicine, Chelyabinsk has extensive experience in managing and follow-up of patients with acute or chronic radiation syndrome and is conducting important research on the dosimetry and health effects of radiation-exposed persons.

One of the important aspects of REMPAN activities is improving communication and information between REMPAN members. In line with this, results of the first experience in organizing teleconsultation in radiation medicine between two WHO/REMPAN collaborating centres indicates the great usefulness of this modern communication approach to strengthening the operational state of REMPAN. This publication describes the usefulness of telemedicine for medical handling of radiation victims through the development of the Radiation Accident Telecommunication Medical Assistance System (RATEMA) between the University of Ulm, Germany and the Research Centre for Radiation Medicine, Chelyabinsk, Russia.

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# 1. Introduction

## 1.1 Scope and purpose

The purpose of the RATEMA project is to establish the usefulness of telemedical application for the evaluation of rare clinical entities in a multidisciplinary and international project. The scope of the project included:

- Installation and regular use of telemedical consultations via satellite between Ulm and Chelyabinsk based on multimedia patient records
- Scientific analysis of the "Chronic Radiation Syndrome"
- Improvement of medical care of persons with health effects after chronic radiation exposure
- Standardisation of diagnostic and therapeutic methods
- Assessment of telecooperation methods in interdisciplinary and international environment
- Evaluation and regular use of the RATEMA - database for education and research

## 1.2 Initiation and evolution of the RATEMA project

The idea to launch the RATEMA project was agreed at the 4<sup>th</sup> REMPAN Meeting held at the University of Ulm between December 1 and 4, 1992. Teleconsultation in radiation accident management was demonstrated by conducting a videoconference between Ulm and Moscow and between Ulm and Oak Ridge. It became evident that videoconferencing would be a new tool for transmitting scientific data worldwide. The meeting in Ulm also recommended that videoconferencing facilities become available to each centre with a view to including videoconferencing as an efficient and effective means of expert advice on the follow-up and medical management of radiation accident victims.

The University of Ulm explored ways to implement these recommendations on telemedicine. Project RATEMA was initiated with the financial support of German Telekom (DeTeBerkom) to develop a pilot application for telemedicine consultation showing the conceptual and technological requirements, for mutual international assistance, especially in the case of rare diseases. Results and experiences gained from such a project were to be carefully monitored and documented to provide a realistic assessment of the strengths and weaknesses of international telemedical assistance systems.

After Dr. Fliedner's visit to the Urals Research Centre for Radiation Medicine in Chelyabinsk in 1994, it was decided to establish such a radiation telemedicine consultation link between the University of Ulm and the Urals Centre. This was felt to be particularly useful to evaluate patients exposed intermittently or continuously to low-level ionizing radiation, to jointly study the effects of chronic radiation exposure at different levels of biological organization, and render necessary consultative assistance to persons with late onset health effects.

To implement the project it was necessary to establish a direct satellite connection between Ulm and Chelyabinsk. German Telekom, together with the Russian Satellite Communication Company was responsible for establishing this connection. A 2.4

meter-satellite antenna was installed at the University of Ulm and a 3.7 meter-satellite antenna was installed at the Urals Research Centre for Radiation Medicine. It was also necessary to develop a multimedia database to systematically collect and utilize available information.

With the help of German Telekom, the Urals Research Centre for Radiation Medicine received technical and medical equipment to match the facilities at the University of Ulm. In December 1997 the first telemedicine conference was held. Through a cooperative agreement, signed between German Telekom, the State Government of Baden-Wuerttemberg and the Ministry of Health of the Russian Federation, it was possible to conduct more than 50 teleconsultation sessions throughout 1998. This allowed physicians and scientists from the Urals Research Centre for Radiation Medicine to discuss Russian patients diagnosed with chronic radiation sickness and several other diseases, with their German colleagues from the University of Ulm. In addition, physicians and scientists from the University of Ulm presented a number of patients with health impairments matching clinical problems presented on the Russian side.

### **1.3 History of the Techa River contamination**

In the 1950s major radiation contamination occurred at the Mayak plutonium production complex located near Chelyabinsk. Imperfect waste management technologies and lack of expertise in managing huge amounts of wastes that were accumulated as a result of plutonium processing, represent the main factors causing radioactive contamination of extensive territories in the Urals region and exposures of the population living in the region [1,2]. Between 1949-1956, medium- and high-level wastes were discharged into the Techa-Isset-Tobol river system. Riverside village populations were, for many years, chronically exposed to external gamma radiation and internal radiation through consumption of river water and food produced in areas contaminated by the spills.

On September 1957 a thermo-chemical explosion occurred in a storage tank containing liquid waste with total activity of  $2 \times 10^7$  Ci. The radioactive cloud following the blast passed over Chelyabinsk, Sverdlovsk and Tyumen Oblasts and led to the formation of the East-Urals radioactive trace (EURT). Residents of villages located on the EURT territory were chronically exposed to the radiation.

In both radiation incidents  $^{90}\text{Sr}$ ,  $^{89}\text{Sr}$ ,  $^{137}\text{Cs}$ ,  $^{95}\text{Zr}$ ,  $^{95}\text{Nb}$ ,  $^{103}\text{Ru}$  and  $^{106}\text{Ru}$  were the main radionuclides, although other nuclides, such as rare earth elements, also contributed significantly to the radiation doses received. The skeleton and bone marrow were the critical organs in the population exposures. To prevent further radiation exposure, 18 thousand people resident in the most heavily contaminated areas were relocated. In addition, a number of technical, administrative and agricultural measures were implemented in the contaminated area to reduce population exposure. These measures proved to be inefficient because of a delay in their implementation. As a result, over 50 thousand residents received doses to their bone marrow in excess of 5 mSv during the period of maximum radiation exposure. The highest doses were received by the residents of the Techa riverside villages. Residents of the upper reaches received total doses to bone marrow up to 4-5 Sv.

Medical examinations of riverside residents commenced about 2 years after radioactive waste was first released into the river. These examinations were made by mobile teams of specialists from the Institute of Biophysics of the USSR's Health Ministry and Medical Sanitary Department. These examinations had little effect since the number of exposed residents was much higher than expected. Thus, in the early years (1951-1956) 940 cases of chronic radiation sickness were diagnosed among residents of the upper reaches. Providing medical assistance to exposed people was difficult because people lived in small or medium-sized villages scattered over a vast territory of 4 oblasts (Chelyabinsk, Sverdlovsk, Kurgan and Tyumen) of the Urals region. These were far from large cities where specialized medical establishments were available.

There was a lack of experience in diagnosing and treating injuries caused by chronic exposure (primarily due to  $^{90}\text{Sr}$  intakes). In 1962 Branch 4 of the Institute of Biophysics was established in Chelyabinsk on the basis of 3 institutions: a specialized dispensary, a branch of the Leningrad Research Institute for Radiation Hygiene and an Agricultural Laboratory. In 1992, Branch 4 was reorganized into the Urals Research Centre for Radiation Medicine (URCRM) within the Federal Office of Medical and Emergency Issues of Russia's Health Ministry.

The results of long-term research and observations conducted at the URCRM served as a basis for the provision of medical assistance for exposed residents in the Urals region. The medical rehabilitation system at the URCRM included:

- availability of an exposed population registry and medical-dosimetric database;
- development of the Techa River Dosimetry System (TRDS-96) and reconstruction of exposure doses for residents;
- ability to conduct clinical-epidemiological analysis of the data from long-term medical follow-up of exposed people and their offspring (4 generations); and
- development of medical measures to reduce late exposure effects.

The medical-dosimetric database "MAN", which commenced in 1967, assists medical follow-up of exposed populations and their offspring, and the analysis of late effects of exposure. Information contained in the database (MMDB) includes identification, whether still living or deceased, summary of diagnoses, family history and dosimetric data. Currently the database contains information on over 98,000 persons (and their offspring) exposed to Techa River releases or the 1957 accident. A portion of the exposed Techa residents (2,255 persons) were exposed to radioactive contamination from the river and on the EURT.

Dosimetric studies of the environment started in 1951 have continued to the present day. These studies include:

- measurements of radionuclide content of river water and sediment, and soil from the riverbanks;
- radiochemical measurement of  $^{90}\text{Sr}$ ,  $^{137}\text{Cs}$  and of other radionuclides as well as Pu sampling of the environment;
- dosimetry of external gamma-radiation, including measurements conducted using thermo-luminescent dosimetry.

Individual dosimetry for residents of the Urals region incorporates:

- radiometrical and radiochemical analysis of autopsy material and biological discharges;
- beta-radiometry of frontal bone and front teeth;
- measurements in the whole body counter (WBC) SICH-9.1;
- biological dosimetry (FISH, analysis of somatic mutations in peripheral blood cells, measurement of activity on tooth enamel using EPR-dosimetry).

Dosimetric measurements of Techa residents has allowed the reconstruction of doses from internal exposure and external gamma exposure adjusted for age, site of exposure and duration of residence.

Late effects manifested by increased cancer and leukemia death rates were only observed among a portion of residents of the riverside villages on the Techa who received the highest doses [1, 2]. The leukaemia death rate calculated per 100,000 person-years was 6.40 (4.22-9.34) which was significantly higher than the respective value for the controls: 3.27 (2.55-4.13). Total mortality from cancer at all sites, except for hemoblastosis and osteosarcoma, was estimated for exposed people as 175.3 (163.0-188.27) which also was higher than for controls - 153.4 (147.88-158.92). It should be noted that up to now an increased level of chromosome aberrations (mostly translocations and dicentrics), as well as TCR mutant lymphocytes, can still be detected in a portion of the exposed people.

Experience gained over many years by the URCRM clinic has shown that screening, based on a differential approach to patients, is the most effective and productive method for rendering medical aid to exposed people. Screening for diagnosing late effects among exposed people is conducted by the identification of high risk groups, primarily for malignant neoplasms. This approach allows an increase in the efficacy of primary prophylaxis, early diagnosis and, therefore, treatment of diseases. As indicated by the results of studies conducted in 1995-1996, the environmental situation in the area, influenced by the operation of the Mayak PA, is still very complicated. To date, vast territories in the Urals region are still contaminated with long-lived  $^{90}\text{Sr}$  and  $^{137}\text{Cs}$ . Factors contributing to the hazardous environmental situation include a high level of environmental pollution due to heavy concentrations from industrial enterprises of ferrous and non-ferrous metals, and fuel and energy complexes. The results of environmental monitoring conducted in the region indicate significant contamination of soils, water and atmosphere with heavy metals, benzopyrene, arsenic, etc., which in combination with radiation exposure, produces effects that have not yet been adequately investigated.

A critical character of the environmental situation in the area influenced by Mayak's operation is also determined by a high concentration of radioactive waste at the facility's industrial site. A considerable portion of the radioactive waste is stored in open hydrological systems (lakes, swamps) which presents a potential threat to the health of local residents.

## **2. Preparatory activities**

### **2.1 Satellite connection for telecommunication**

The telecommunication connection between Ulm and Chelyabinsk was a direct satellite link via EUTELSAT II F4. Deutsche Telekom together with the Russian Satellite Communication Company (RSCC) was responsible for establishing the satellite connection. A 2.4 m satellite antenna was installed at the University of Ulm and a 3.7 m antenna was installed at the URCRM in Chelyabinsk.

### **2.2 Technical set up in Chelyabinsk**

Over the period 1995-1997 URCRM carried out substantial preparatory work involving shipment and installation of the medical, computer, video and satellite equipment intended for the RATEMA Project. The earth station equipment for satellite communication installed at the URCRM included the following items:

- ANDREW Antenna, 3.7 m, equipped with an anti-icer device
- Transmitter ASAT-S1214 KU-BAND, capacity: 8 W
- Low-noise converter LNB s/n 5988
- Modem SDM-650B s/n 5743 with a RS449 interface
- 3Com Router, ESPL-310 model
- Picture Television System-4000 equipment for transmitting digitized information, with 2 video-cameras for direct demonstration of images, two TV sets for viewing both newly-developed and original images, ZEISS electronic microscope, a router and a computer
- X-Ray scanner RSU-1
- Two computers allowing images to be digitized directly from the microscope; the software installed on the computers included Windows NT Server, RDBMS as the operating system Oracle 8 which served as a basis for creating a multimedia database on the patients
- Uninterrupted power supply
- ECG Cardiovit AT-10 (Schiller, Switzerland)

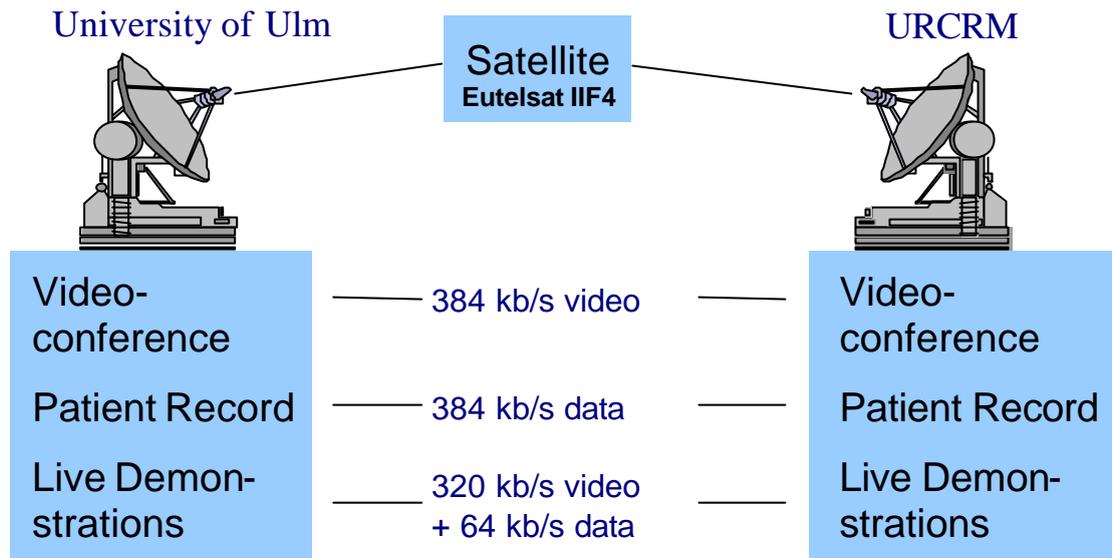
The earth station was provided with a Standard-S3 satellite communication line for transmitting digitized video information via the communication satellite EUTELSAT II F4 at a longitude of 7 degrees east, using a frequency band of 14107, 160-14143, 160 MH.

This satellite communication system allowed three types of communication between the partners (Fig. 1):

- videoconferences at 384 kb/s which allowed to conduct regular videoconferences;
- data exchange with 384 kb/s between Chelyabinsk and Ulm;
- videoconference and data exchange in parallel: up to 64 kb/s was used for data exchange, and 320 kb/s are available for video/audio communication.

### 2.3 Technical set up in Ulm

In 1989 Ulm University was equipped with a videoconference studio. In the past a switched broadband network-technique (140 Mb/s) was used for normal videoconferences (international conferences in most cases with 2Mb/s), for LAN-LAN-connections, and for telepathology and telemedical conferences with Moscow and Oak Ridge. Ulm University Computing Centre has been experienced in the field of remote control for several years. In 1990 in Brussels the first remote control of a Zeiss-microscope developed within the ULKOM project was presented.



**Fig. 1: The satellite communication system**

### 3. Creation of a multimedia patient record database (MMDB)

#### 3.1 Overview

The multimedia medical database (MMDB) has been used for medical teleconferences. The MMDB was created to achieve the following purposes:

- preparation and systematization of complete data on patients;
- preview of information by experts on each side before the teleconference;
- simultaneous review of information in the MMDB during videoconferences;
- subsequent scientific analysis of clinical data.

To cope with these tasks it was necessary that the MMDB structure be based on the use of multimedia equipment which would display video material, microscope images of bone marrow and blood preparations, x-ray films, images of endoscopic examinations, etc. as shown in Table 2. The multimedia file containing the patient data is transferred during a transmission session to the other side a few days before the conference. This enables physicians and experts to discuss the information received during conferences.

The digitizing of different material (e.g. microscope images, x-ray, CT-images, ECG, video clips) has been performed as shown in Fig. 3. The digitized information is inserted into the database. For convenience English was chosen by the Russian-German task group as the working language. Both the MMDB and clinical results were recorded in English.

#### 3.2 Software/Hardware used

**Software:** A Multimedia medical database was developed using the relational database management system (RDBMS) Oracle 8.0 software package for Windows NT 4 operational system. **Hardware:** Pentium II-266 PC; Pentium-90 Pro PC; Video controller and an X-Ray RSU-1 scanner.

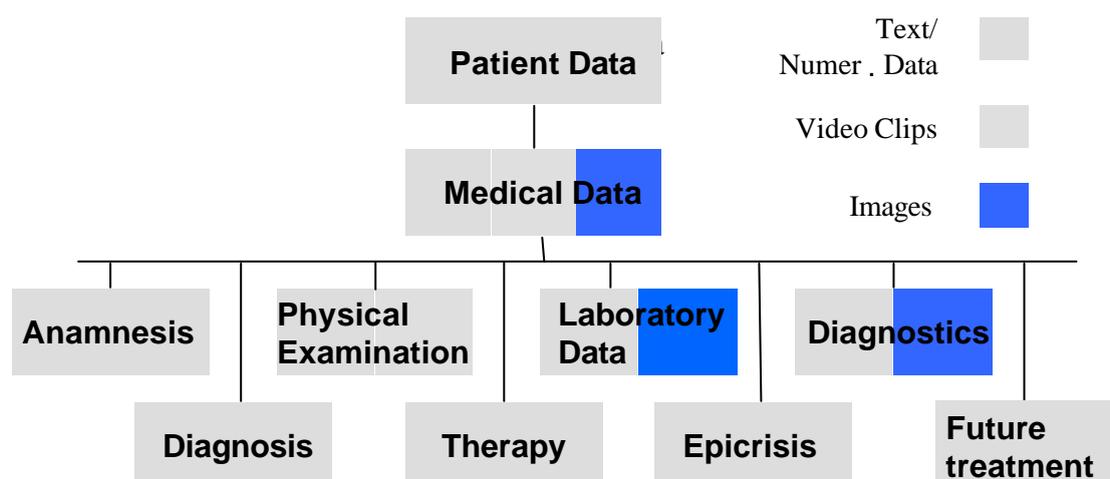
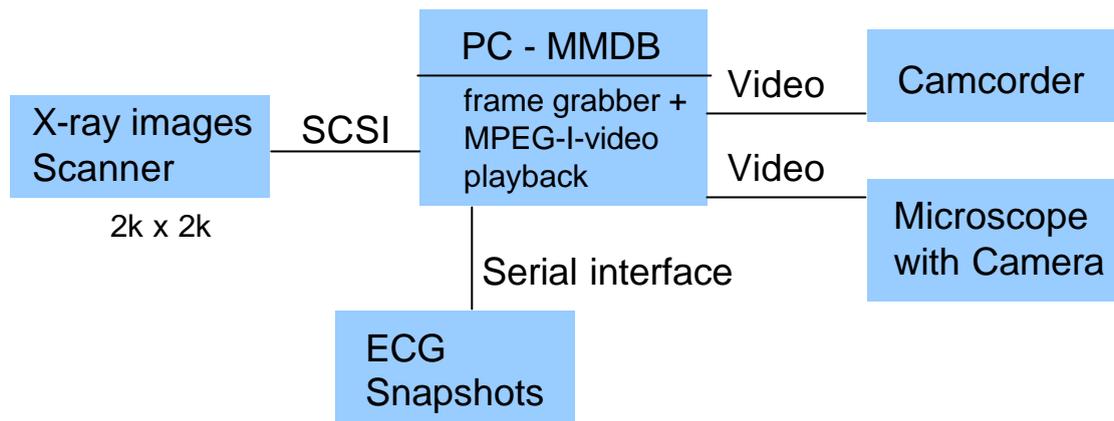


Fig. 2: Multimedia patient record



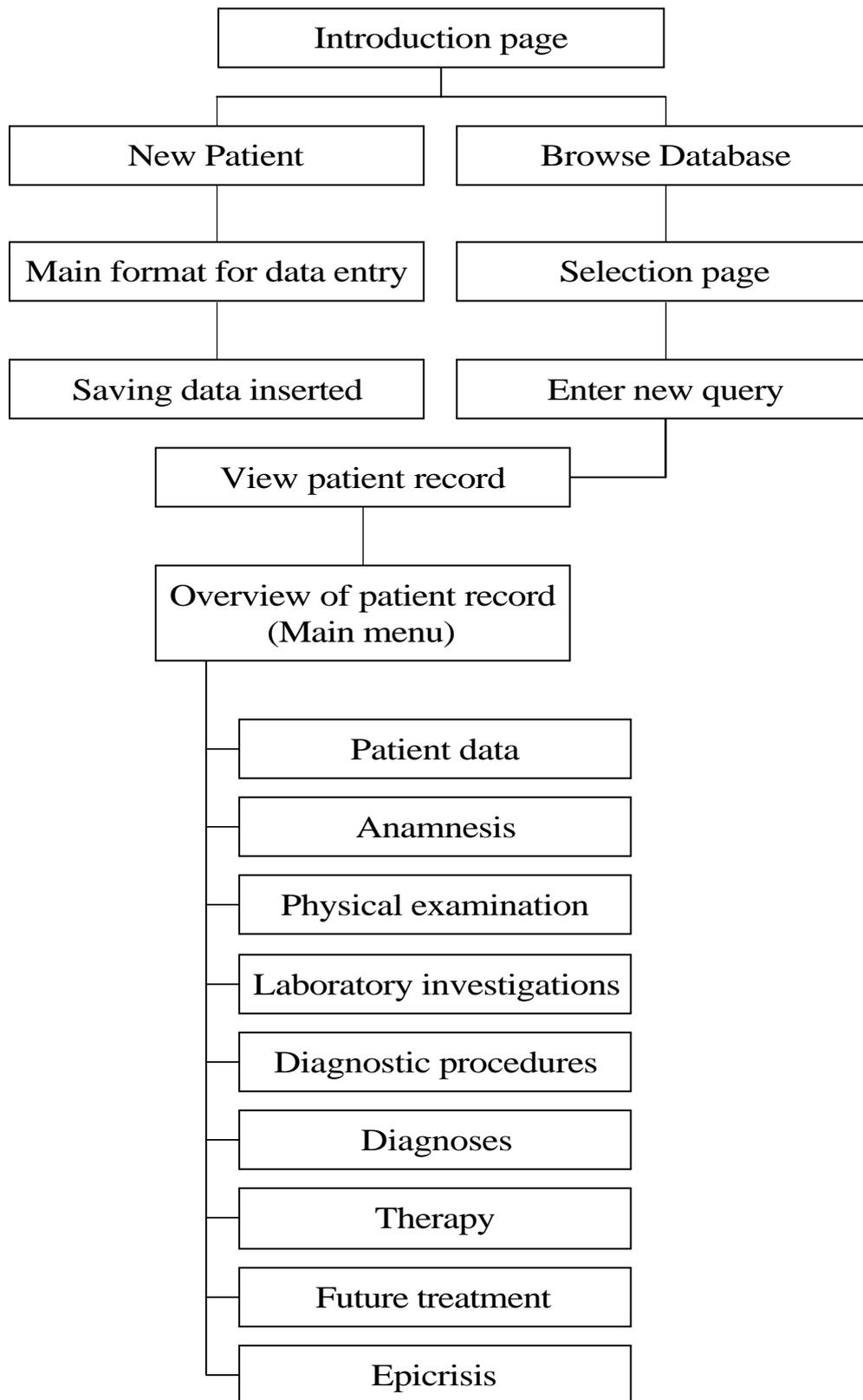
**Fig. 3: Digitizing of the material**

### **3.3 General structure of the MMDB**

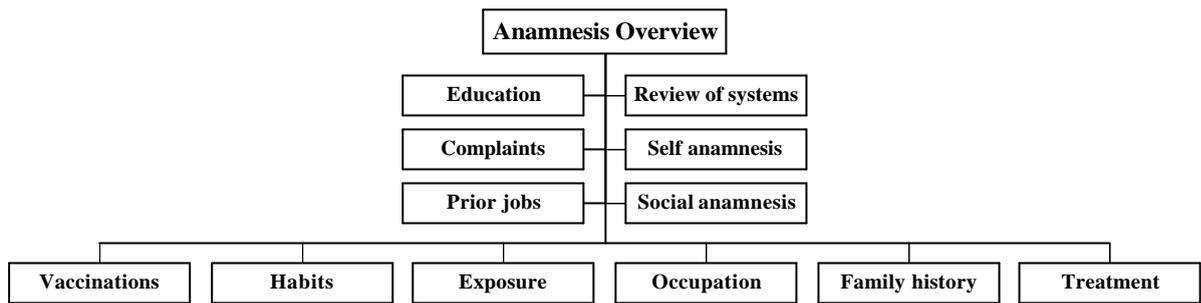
The MMDB is operated in 2 modes; entry and viewing (see Fig. 4):

Several charts were filled out for every patient, with the date of examination indicated on each of them. The first mode is operated when information on a new patient is entered (a new file is created), or when the information on a patient already included in the MMDB is updated (e.g., the results of the latest examination). The second mode allows for a review and update of information inserted earlier. Links between data files are activated through an individual digital code which is assigned to the patient automatically.

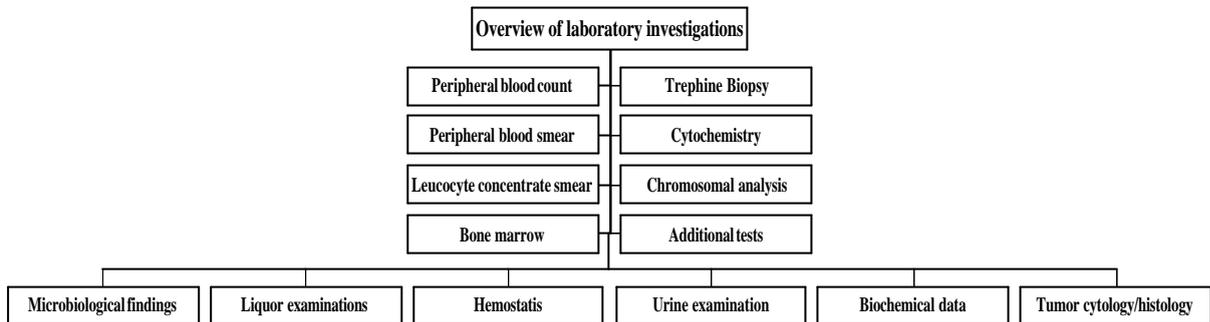
For easy search of patient data and entry of new information, the following database structure was developed: a general section (“introduction page”) and a specific section designed for working on an individual patient file. The general section allows user registration (he/she is granted access to browsing or editing data), preview (numerical only) of all patients entered into the database, or search of a patient using his/her identification number, creating a new patient file. The second section only allows work on a specific patient file involving entry of data, updating of data, adding data on new diagnostic examinations, etc.



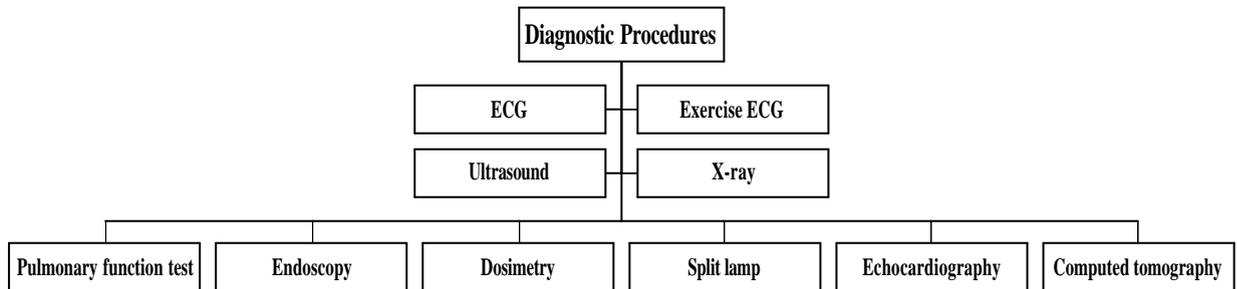
**Fig. 4: Elements of the database**



**Fig. 4a: Elements of the section “Anamnesis”**



**Fig. 4b: Elements of the section “Laboratory Investigations”**



**Fig. 4c: Elements of the section “Diagnostic Procedures”**

The opening page of the database entitled “*Introductory page*” enables the user to choose a mode of MMDB operation (Fig. 4). The next page, “Patient Selection”, contains general information on the patient: the patient’s individual number in the MMDB, last name, first name, patronymic, gender and birth date. Also, all dates at which the patient was examined are indicated on this page. These dates are automatically inserted when the respective sections of the MMDB are filled out. Via this page the “main menu” can be accessed in accordance with the mode of MMDB operation. Figs. 5 and 6 show the step-by-step opening of pages in the MMDB.

## Fig. 5: Stepwise opening of the MMBD to review patient records

### Fig. 6: Work on the DB. Sub-sections “Review of Systems” and “Self-Anamnesis” 3.4 Structural elements

For each patient 9 sections were foreseen:

- general information on the patient
- anamnesis
- physical examination
- laboratory investigations
- diagnostic procedures
- diagnoses
- therapy
- further treatment
- epicrisis

The 3 major sections ( anamnestic information, diagnostic procedures and laboratory investigations) were divided into sub-sections.

**Patient Data Section** includes the patient’s general personal information derived from the patient’s passport:

- family name
- first name
- second name
- birth date
- gender
- nationality
- blood group and Rhesus index
- address
- place of residence at the time of the radiation accident
- marital status
- postal code (index)

**Anamnesis Section** contains information on the patient’s health and social status. It includes 12 sub-sections (Fig. 4a):

- complaints
- exposure
- social anamnesis
- prior jobs
- occupation
- self anamnesis
- vaccinations
- family anamnesis
- education

- habits
- treatment
- review of systems
- therapy.

**Physical Examination Section** contains objective information on the patient’s general physical status, nutritional status, and the status of his/her inner organs and organ systems (Table 1).

**Table 1: The scope of physical examination of the patient’s organ systems and their functions**

Body parts or system	Status of organs
<b>1. Head</b>	<b>General examination:</b> mobility; tenderness on compression or percussion
	<b>Eyes:</b> Vision acuity, light reaction, sclerae, eye fundi, color vision
	<b>Ears:</b> Auditory canal, tympanic membranes, whisper test
	<b>Nose and sinuses:</b> nasal vestibule, nasal septum, mucous membranes
	<b>Mouth/Throat:</b> tongue, teeth, tonsils, pharyngeal ring
	<b>Thyroid:</b> circumference, results of specific examinations
<b>2. Thorax</b>	<b>General examination:</b> thoracic cage, breasts
	<b>Heart:</b> heart borders, rhythm, auscultation
	<b>Blood pressure:</b> systolic and diastolic on both arms in recumbent position; pulse rate, pulse deficit (present/absent)
	<b>Lungs:</b> motility, lung borders, percussion <b>Auscultation:</b> respiration rate, respiration sounds; additional sounds
<b>3. Abdomen</b>	<b>Abdominal wall:</b> soft/rigid, tender/non-tender, presence of scars (position); hernia (present/absent)
	<b>Liver:</b> hepatomegaly (costovertebral angle)
	<b>Spleen:</b> splenomegaly
<b>4. Spine</b>	Mobility, course of the spine, Lasègue, fingers-to-floor distance
<b>5. Upper extremities</b>	Mobility, muscular strength, peripheral pulse, palmar surfaces, finger prints, amputations
<b>6. Lower extremities</b>	Mobility, muscular strength, peripheral pulse, varicosity, edema, amputations
<b>7. Nervous system</b>	Status of cranial nerves, Achilles reflex on the right and the left, patellar reflex, triceps reflex on the right and left, abdominal reflex on the right and the left, presence of pathological reflexes, tremor, coordination, sensory function, paresthesia
<b>8. Lymphatic system</b>	Peripheral lymph nodes (if palpable): location, size, tenderness, consistency, mobility
<b>9. Skin and its appendages</b>	Color, turgor, white/red dermographism, rashes, lesions, tenderness, vulnerability, atrophy, hypertrophy, fibrosis, abnormal changes of pigmentation, telangiectasia, lymphangioma, malignant neoplasms, etc.
<b>10. Additional findings</b>	

The MMDB software allows insertion of videoclips into the MMDB making it possible to demonstrate the patient’s functional status, severity of disease, status of the integument, etc. (Fig. 7).

**Laboratory Investigations Section** has 14 sub-sections: see Table 2 and Fig 4b.

**Table 2: Parameters of laboratory investigations**

Subsection	Parameters investigated
<b>1. Peripheral blood count</b>	Leukocytes, erythrocytes, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, reticulocytes, thrombocytes, ESR
<b>2. Peripheral blood smear</b>	Cell count; additionally, the presence of atypical cells, abnormal mitoses, micronuclei; cytochemical findings (a picture can be inserted)
<b>3. Leukocyte concentrate smear</b>	Cell count (a picture can be inserted, see Fig. 8)
<b>5. Bone marrow</b>	Punctuation site, cellularity, myelofibrosis; myelopoietic tissue; erythropoietic tissue; megacaryopoietic tissue; myeloid-erythroid ratio; mitotic abnormalities of myelopoiesis and erythropoiesis (a picture can be inserted, see Fig. 9)
<b>4. Trepine biopsy</b>	<b>Puncture site, staining, bone trabecules:</b> thickness, cellularity of osteoblasts and osteoclasts <b>Hemopoiesis:</b> cellularity of myelopoietic, erythropoietic, megacaryopoietic tissue, myeloid-erythroid ratio, cell pyknosis, lysis of cells, blood vessels, bone marrow stroma, connective tissue, additional findings (a picture can be inserted)
<b>6. Cytochemistry</b>	Staining; PAS, Peroxidase, Leucocyte Alkaline Phosphatase, Acid Esterase, Silver impregnation
<b>7. Immunological studies</b>	Cellular and humoral immunity, Electrophoresis; direct and indirect Coomb's test; oncogenen expression
<b>8. Tumor Cytology/Histology</b>	Description (a picture can be inserted)
<b>9. Cytogenetic data</b>	Chromosomal aberrations: dicentrics, tracentrics, multicentrics, centric and acentric rings, minutes, gaps; chromatid aberrations; aneuploid cells; polyploid cells; additional findings (a picture can be inserted)
<b>10. Biochemical studies</b>	biochemical parameters; endocrinological parameters; analysis of blood gases; additional findings; hemostasis
<b>11. Liquor</b>	Cell count; differentiation; contents of total protein, albumin, glucose, lactate, Ig G, LDG (a picture can be inserted)
<b>12. Urine tests</b>	General analysis of urine and urine sediment; quantitative analysis (24 hour): volume, specific gravity, protein, K <sup>+</sup> , Na <sup>+</sup> , Ca <sup>+2</sup> , osmolality; additional findings.
<b>13. Microbiological studies</b>	Blood culture Urine culture Stools culture Throat culture

**Diagnostic Procedures Section** consists of 11 sub-sections (Fig. 4c):  
ECG examination (Fig. 10); Exercise ECG; Lung function examination;  
Echocardiography; Ultrasound examination (Fig. 11); Computer tomography;  
Endoscopy; X-ray examination (Fig. 12); Slit-lamp examination; Dosimetry; and  
Additional examinations



**Diagnostic Section:** gives a retrospective list of all the relevant diagnoses for the present health status based on the pathological changes observed in the patient over the period of follow-up. Previous diagnoses of health impairments are included in the section on anamnesis.

**Therapy Section:** contains the following sub-sets of information: general plan of therapy, medicinal preparations, dates of beginning and termination of the course for each of the preparation, INN name of the preparation, INN code of the preparation, and the dose administered.

**Epicrisis Section:** contains a concise overview of the patient's health status at discharge made by the patient's attending physician.

**Future Treatment Section:** includes recommendations concerning further treatments developed as a result of discussion during the teleconference.

### **3.5 Harmonization of methods and terminology**

#### ***Methods of examination and measurement units***

Prior to data being entered into the MMDB effort was made to unify the examination methods and measurement units for all data to be entered. The use by all clinicians of comparable methods for laboratory and diagnostic procedures contributed to the effectiveness of the joint work on the MMDB.

At the URCRM clinic there is an automatic analyzer for the measurement of 14 peripheral blood parameters; and biochemical studies of blood serum using a FP-901 M analyzer. Microscopic examinations of histological and hematological preparations were conducted using Axioskop microscope. Microscope incorporating a videocamera made it possible to transfer images to the partner site for diagnosis. The use of a light pointer installed in the microscope ensured that experts could focus on sites of interest.

Analysis of the cardio-vascular system and lungs was conducted on an automatic electrocardiograph Cardiovit AT-10 that allows measurement of ECG parameters, assessment of external breathing and other parameters. It meets all current international requirements.

To undergo certain examinations aimed at evaluating the status of inner organs (USE, CT, endoscopic examinations) patients are referred to the Regional Diagnostic Centre. Measurement of activity accumulated in bone tissues have been conducted on a regular basis since 1974 using the whole-body counter SICH-9.1 developed at the URCRM. From these measurements the staff of the Biophysics Laboratory are able to estimate equivalent individual exposure doses: cumulative doses for the entire period of exposure, and dose rates per year from internal and external exposure. The results of dosimetric measurements and calculations are entered into the database: an equivalent dose was expressed in Sieverts, contents of  $^{90}\text{Sr}$  in bone tissue in Becquerels, absorbed dose in Grays, etc.

The exact names and INN-codes of medicinal preparations used on patients were referred to in the reference book International Nonproprietary Names (INN) for Pharmaceutical Substances, WHO, 1992. This avoided confusion in the names of those medicinal preparations that are made in Russia and are unknown to physicians in European countries.

### ***Terminology***

All clinical diagnoses that had been established since the beginning of patient observations were correlated with ICD9. The diagnoses made in earlier years, were reviewed and retrospectively based on the retained original records and entries in the patients' case histories.

## **3.6 Sources of information**

The patient's case history is the key source of information entered into the MMDB. Case histories are stored in the medical archives of the URCRM's clinical department. Case histories, along with out-patient charts, contain complete medical information and general information on the patient and his/her family. This information is collected carefully by the URCRM's clinical staff and updated with new data on a regular basis. Some sub-sections of the section "Anamnesis" (Habits, Social Anamnesis, Family Anamnesis, Occupation, Education) are completed by the physician from personal interviews of patients, or on information derived from a questionnaire conducted in earlier years. The latter approach was mostly applied to deceased patients. The following sources of additional (visual) information were used: blood and bone marrow preparations, X-ray films and other visual materials.

### **Blood and bone marrow preparations**

- peripheral blood smears
- leukocyte concentrate smears
- bone marrow smears
- trephine biopsy preparations
- cytogenetic preparations

Bone marrow and cytogenetic preparations for the entire follow-up of the patient have been stored for a long time in the hematological archives.

X-ray films are also stored at the archives, with the exception of those whose quality has diminished with time. These include films of the:

- spine
- joints of upper and lower extremities
- chest
- stomach, duodenum, etc.

### **Other visual materials**

- electrocardiograms
- graphic presentation of ultrasonic examination, computer tomography and endoscopic examinations

### **Video material**

Video materials included in the MMDB were made with the specific aim of highlighting the peculiarities of the patient's outward appearance (habitus), loco-motor function (e.g., in cases of disorders of the bone-muscular system), the condition of the skin and its integuments and other signs of interest. On some occasions video filming was conducted at the patient's home. The quality of the video, stored as MPEG I-Video, is excellent.

### **3.7 Concluding remarks**

The MMDB currently contains information on 37 patients. Among them 30 patients are from the clinical department of the URCRM, and 7 from the University Hospital of Ulm. The MMDB contains information on 14 patients with a past history of chronic radiation sickness associated with the contamination of the Techa River. Of the 30 patients from Chelyabinsk, 19 suffer from hematological disorders, such as leukemia of various etiology (14 cases), osteomyelosclerosis (1 case), erythremia (1 case), Marchiafava-Micheli syndrome (1 case), B<sub>12</sub>-deficient and sideroachrestic anemia (2 cases). 10 other patients included in the MMDB suffer from diabetes mellitus, osteoarthritis, spondylosis deformans, chronic gastritis, pruriginous atopic dermatitis. The multimorbidity of these patients is noticeable.

Seven patients from the University of Ulm are included. One patient suffers from osteomyelofibrosis, one from chronic myeloid leukemia, another from chronic myelomonocytic leukemia, one from myelodysplasia, one from plasmacell leukemia, one from Parvovirus B-19 infection with bone marrow aplasia and one patient suffers from a severe radiation injury of the skin.

## **4. Organization of teleconsultations**

### **4.1 Overview**

The “RATEMA” project envisaged the establishment of a permanent channel for satellite and computer communication between clinicians and researchers of the URCRM and those at the University of Ulm. Among the issues discussed at the videoconferences were medical aspects of the health status of persons exposed to radiation, the diagnostic approach, treatments and outcomes of illnesses.

### **4.2 Patient selection**

Patients presented during the joint videoconferences can be divided into 3 groups: those diagnosed with chronic radiation sickness; those with malignant neoplasms (including deceased persons); exposed patients who did not develop chronic radiation sickness. The following issues were identified as having the highest priority:

- presentation of exposed patients with a history of chronic radiation sickness (CRS);
- discussion of case histories of exposed patients diagnosed with disorders of a hematological nature (hypo- and aplastic conditions of the hematogenous system, leukemia, etc.);
- “live” patient demonstrations to allow consultative assistance from clinicians at the University of Ulm. Some of the patients were demonstrated repeatedly for diagnosing in light of new data, discussing the adequacy of therapy, etc.

The Chelyabinsk RATEMA Team focused on the presentation of patients with a history of chronic radiation sickness, a condition which is unique in the sense that it has only been observed among residents of the Techa riverside villages and Mayak workers. The Techa population was exposed for many years to ionizing radiation at fairly high doses, due to releases of radioactive waste from the Mayak facility into the Techa River [1, 2]. Since this clinical situation is being debated by many scientists, it was interesting to discuss the issue with German colleagues. CRS represents a number of non-specific alterations in certain body systems – primarily the hemopoietic system, nervous system, cardiovascular, immune and osteal systems - which may also be induced by non-radiation factors. In the 1950s the diagnosis of CRS was established based on the occurrence of a typical symptom-complex (most often, leuco- and neutropenia, vegetative disorder, ostealgic syndrome, syndrome of micro-organic nervous system disturbances, and immunity inhibition), and on the person’s residential history - whether or not he/she lived on the territory contaminated by radioactive wastes.

At that time no account was taken of dosimetry data, which undoubtedly does not rule out diagnostic mistakes. Over 45 years experience gained by the URCRM’s clinicians in the observation of patients diagnosed with CRS (940 patients) allowed a thorough analysis of CRS diagnosis. The presentation of patients with CRS pathology was conducted using estimates of individual doses absorbed in various organs and tissues.

### **4.3 Examination of patients**

When a patient was selected for videoconference he was admitted to the URCRM to undergo a comprehensive medical examination. During examination the doctor

recorded the patient's complaints and the results of the physical examination and laboratory investigations. All patients were measured for  $^{90}\text{Sr}$  body and electrocardiography. Depending on any pathology, the patients underwent x-ray examination, ultrasound, endoscopy, nuclear medicine imaging and other diagnostic examinations. Women also have a gynecological examination. In addition, advice was sought from neuropathologist (all patients with CRS were given neurological check-ups), oncologist, surgeon, ophthalmologist, otorhinolaryngologist, dermatologist, etc.

The presentation of a patient at the videoconference was preceded by a discussion of his/her case history at the weekly rounds made by Prof. A.V.Akleyev. The doctor in charge presented an analysis of the patient's history, present disease, results of the laboratory and instrumental investigations, the main trends in the medical treatment and the dynamics of the underlying illness for the period of observation. Confirmation or rejection of the CRS diagnosis was thoroughly analyzed. Special attention was paid to the estimate of the individual exposure dose to red bone marrow, the presence of clinical manifestations of CRS and their relationship to their radiation exposure, and to the presence of concomitant somatic and infectious diseases.

#### **4.4 Preparation of material for presentation**

At the preparatory stage the doctor processed the original medical information on the patient health status over the entire period of observation. All patient records available at the URCRM's archives were reviewed and the information entered into both the Russian and the English versions of the data bases.

There was a slight difference between the information on the patient presented at the conference (the attending doctor's presentation) and that contained in the database. The data base information was normally complete encompassing the entire period of follow-up (about 5 decades). All data relevant on the patient were forwarded to other participants before the teleconference which allowed the presenting physician to draw attention to the current health problems.

Presentation of the patient's case history at a videoconference (Supplements 1, 2) was prepared and made by the attending doctor. All presentations included the following points:

- patient identification;
- date of last admission to the URCRM or the University clinic in Ulm, the patient's complaints on admission and details of the clinical diagnosis;
- patient's history, the history of diseases, date of onset, substantiation of diagnosis of present illness (complaints, results of physical examination and laboratory investigations);
- therapy currently taken by the patient;
- patient's current health status;
- medication currently taken by the patient;
- clinical course and the underlying disease prognosis.

Special emphasis was put on how many years the exposed person resided in a settlement contaminated by radioactive wastes. The following characteristics were recorded: distance between the settlement and the site of release of radioactive wastes; position of the house in relation to the Techa River, use of contaminated water:

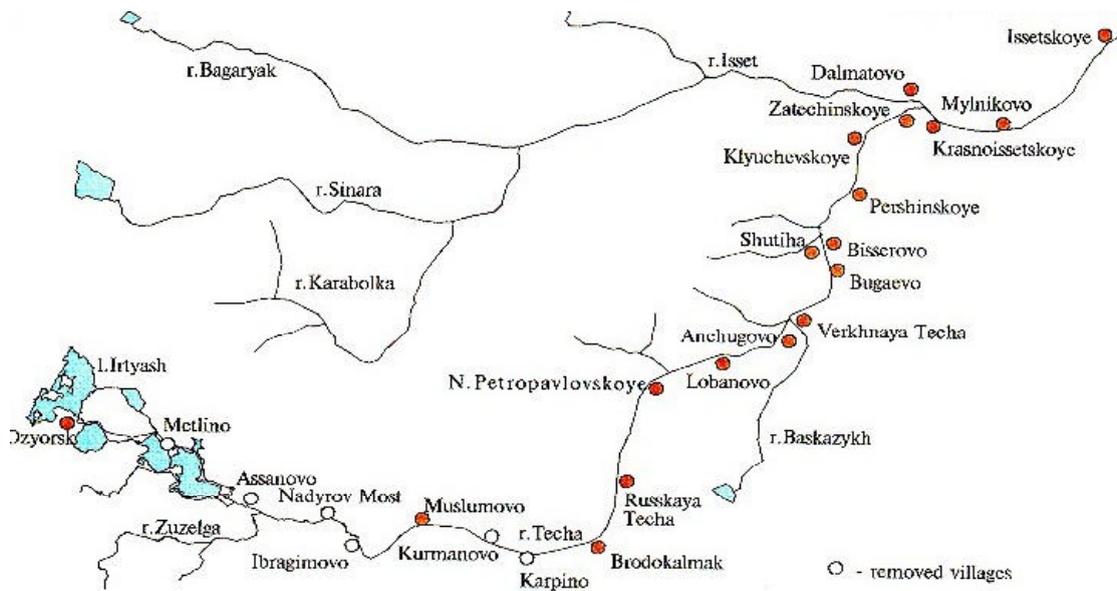
whether well water was available or the family used river water for their domestic needs (drinking, preparing food, laundry, bathing, watering kitchen-gardens, etc.), and whether or not they ate fish from the river. If the patient had CRS, the presentation included a description of his/her complaints, anamnestic information and the findings of laboratory investigations which served as the basis for making the diagnosis, as well as the dynamics of the course and the outcome of CRS were also described.

The dosimetry data represented individual total exposure doses to red bone marrow (both external and internal components), the dose rate at the time of the diagnosis was made, as well as  $^{90}\text{Sr}$  body (skeleton) contents.

In selected cases live demonstrations of the patient during the teleconference were practised. The purpose of such demonstrations was to achieve, – in addition to visualization effect - a direct contact with the patient, use of the opportunity offered by the telecommunication line to ask some specific questions, acquaintance with the patient's own opinion on the course of his/her sickness and the efficacy of the treatment administered to him/her.

To make the presentations more vivid they were, as a rule, accompanied by the demonstration of visual materials such as: the schematic map of the patient's village and the position of the house in relation to the Techa River (Fig. 13), graphs describing the dynamics of the following parameters: accumulation of exposure dose in the red bone marrow (Fig. 14), findings of laboratory investigations: leukocyte counts in peripheral blood for different years (Fig. 15) and changes in blood parameters in the course of treatment (Fig. 16), etc. The peripheral blood counts and the myelographic findings were presented in a tabulated format. Besides, the dynamics of occurrence of the main pathological syndromes (lesions of cardiovascular system, locomotor system, nervous system, etc.) was also presented in a table (Fig. 17).

When patients had features of interest such as a gait typical of patients with locomotor system pathology, outward manifestations (forced body position, difficulties getting out of bed, deformed joints, etc.), or cutaneous pathology, the presentation was also accompanied by a video sequence. When hepato- and/or splenomegaly was present, the borders of the patient's liver and spleen were marked on the anterior abdominal wall. Use of video sequences certainly made it easier for the participants of the teleconference to understand the patient's current problems.



**Fig. 13: A schematic of villages located on the Techa River (blank circles indicate re-settled villages)**

**Fig. 14: Exposure dose accumulation in red bone marrow for patient 2.2.**



**Fig. 16: Peripheral blood changes for one of the patients presented**

<i>Hg</i> <i>g/l</i>	<i>Thrmb.</i> <i>giga/l</i>	<i>Lymph.</i> <i>% - abs</i>	<i>Basoph.</i> <i>%</i>	<i>Eosin.</i> <i>%</i>	<i>Leuco.</i> <i>giga/l</i>	<i>Neutrophils, %</i>						<i>Date</i>	<i>Therapy</i>	
						<i>blasts</i>	<i>promc</i>	<i>myel</i>	<i>metmc</i>	<i>bands</i>	<i>segm</i>			<i>abs.</i>
113	114				83,5	4,5							20.03.78	
													20.07.79	
96	41	2 - 7,84	6,5	5,5	392	4	4	20,5	21,5	21	15	337		<i>Busulfan</i>
108	31	16 - 3,8	2	2	23,8	1	0,5	17	11	19	30	18,68	24.08.79	
													24.10.79	
129		19 - 3,24		2,5	17,1		1	4,5	2,5	9,5	55	12,39		<i>Busulfan</i>
													11.07.80	
129	706	10 - 2,4	2,5	9,5	24	1	0,5	4	3	3	64,5	18,24		<i>Busulfan</i>
132	880	7 - 2,36	6,5	10,5	33,7	2,5	1	4	7	8	50	24,43	22.07.80	
													01.12.82	
96	384	1 - 0,51	6	3	51	8	3	14,5	17	25	22	45,64		<i>Busulfan</i>
100	155	12 - 0,8	5,5	2,5	6,7		2	7	8,5	30	28,5	5,09	31.01.83	
													25.06.84	
82	570	3 - 1,1	9,5	2,5	36,7	2,5	1,5	19,5	16,5	20	25	31,19		<i>Busulfan</i>
46	11,8	8 - 0,06			0,7	6				5	81	0,64	29.07.84	<i>6-Mercaptoparine</i> <i>Prednisolone</i> <i>Vinkristine</i>



Presentations made by consulting doctor were illustrated by X-ray films, both recent and archival films, to demonstrate the dynamics of any pathological processes. In addition to the doctor's oral description of the patient's health status, relevant graphic materials and charts were also demonstrated.

All participants had the opportunity to evaluate blood, red bone marrow and bone tissue preparations, X-ray films, ultrasound images, etc., during videoconferences. Thus, all tissue preparations available for the entire period of observation, stored at the URCRM, were demonstrated during videoconferences.

#### **4.5 Experiences of teleconsultations**

During one year weekly media teleconferences were conducted during which both sides discussed the health status of Russian patients chronically exposed to radiation in the South Urals Region. The German partners presented patients with comparable haematological and oncological diseases to compare radiation and non-radiation exposed patients and their health injuries. The German patients had not been exposed to radiation.

All relevant medical data were stored in the RATEMA multimedia patient record database and exchanged over the satellite link. In view of the wide scope of tasks to be tackled and the conference time limits it was necessary to ensure effective work during the conference. From conference to conference different modifications were introduced depending on the subject for discussion.

The time on air allocated for the presentation of 1 patient (2 hours, as a rule) was proportioned in the following way:

- introductions of conference participants usually took 5 minutes, on average;
- presentation of the patient's case history took about 30 minutes;
- communication between participants and the patient usually took no more than 15 minutes;
- the attending doctor's summary of the patient's pathology took 5 minutes;
- video sequence of any patient difficulties in movements or cutaneous problems, etc. took 5 minutes;
- demonstration of x-ray films, the radiologists comments;
- demonstration of the video materials: blood and red bone marrow parameters; exposure; findings of cytogenetic tests, etc.
- discussion of the patient's health status;
- clarifications provided by the doctor in charge;
- therapeutic strategy and prognosis;
- recommendations made by the Ulm RATEMA team.

## 4.6 Results obtained

In all, 51 conferences were held during 1998 by the clinicians and researchers of the URCRM and the University of Ulm. The Russian side presented 30 patients with different pathologic conditions (Table 3), 14 were patients with CRS diagnosis in the anamnesis, 5 patients had acute leukemia, and there were 5 cases of chronic myeloid leukemia. Among those presented at teleconferences there were single cases of malignant histiocytoma, Marchiafava-Micheli syndrome, osteomyelosclerosis and erythremia, B<sub>12</sub>-deficiency anemia and a female patient with a severe course of diabetes mellitus, type II.

**Table 3: Patients presented at telemedical conferences by the URCRM's RATEMA Project team**

?	Date of presentation	Vital Status	Goal of patient presentation
1	12.02.98	alive	Patient with CRS: Discussion on diagnosis and treatment
1	12.03.98	dead	Osteomyelofibrosis
2	21.12.97 9.10.98	alive	<b>Conference 1:</b> Discussion on approaches of treatment of a CRS patient with recurrent agranulocytosis <b>Conference 2:</b> Discussion on methods for treatment of a progressive renal insufficiency
3	12.02.98 19.02.98 29.10.98	alive	<b>Conference 1:</b> Patient with CRS: discussion on diagnosis verification and therapeutic procedure <b>Conference 2:</b> Assessment of the efficacy of the prescribed therapy <b>Conference 3:</b> Discussion on further treatment
4	26.02.98	alive	Patient with CRS: diagnosis and therapeutic approach
5	6.03.98 24.04.98	dead	Patient with acute leukemia
6	2.04.98	alive	Urgent consultation aimed at diagnosis verification and development of an appropriate therapeutic approach
	23.04.98 28.04.98		Patient with chronic myeloid leukemia (CML)
7	7.05.98 14.05.98	alive	Patient with CRS: development and assessment of further therapeutic strategy
8	14.05.98	dead	Exposed patient with CML
9	20.05.98	alive	Patient with CRS: development of further therapeutic strategy
10	26.05.98	alive	Patient with CRS: consultation on validity of the therapeutic approach
	04.06.98 23.06.98 20.08.98 09.10.98	alive	Cutaneous radiation syndrome
	10.06.98		Parvovirus B-19 infection with bone marrow aplasia
11	18.06.98	dead	Patient with CML who was exposed to radiation in 1957

12	18.06.98	alive	Patient with CRS: assessment of treatment effects
13	2.07.98 7.07.98	alive	Patient with CRS: verification of diagnosis and adequacy of the therapeutic approach
14	13.07.98	alive	Patient with CRS: effects of treatment
15	13.07.98 15.07.98	alive	Urgent consultation aimed at diagnosis verification and development of treatment strategy
16	15.07.98	alive	Exposed patient with Marchiafava-Micheli syndrome: consultation on further therapeutic approach
17	25.08.98	dead	Patient with osteomyelosclerosis: validation of the diagnosis
	27.08.98		Patient with myelodysplastic syndrome
18	24.09.98	dead	Patient with CRS and CML
19	15.10.98	alive	Exposed patient with erythremia (erythroleukemia?): development of a further therapeutic strategy
20	22.10.98	dead	Exposed patient (Techa River) with AML
	04.06.98 23.06.98 20.08.98 09.10.98	alive	Patient with CRS
21	05.11.98	alive	Discussion on diagnosis and treatment
22	12.11.98	dead	Exposed patient with CML
23	12.11.98	alive	Patient with CRS
24	19.11.98	alive	Patient with ALL. He is an offspring of parents belonging to the exposed Techa River population
25	26.11.98	alive	Patient with CRS
26	26.11.98	dead	Exposed patient (case history) with uterine blastoma and AML in an exposed patient
27	3.12.98	alive	Patient with CRS: evaluation of the therapeutic approach
28	3.12.98	dead	Discuss a case of AML in an exposed patient
29	10.12.98	dead	Discuss a case of CML in an exposed patient
30	17.12.98	alive	Discuss a case of CRS: consultation on further therapy
	17.12.98	dead	MDS (chronic myelo-monocytic leukemia)
	17.12.98	dead	Plasmacell leukemia

Of the 30 patients presented by the Russian team 20 were alive at the time the conferences were held. All patients received a medical consultation at the time of presentation (5 patients needed urgent medical advice). The 10 deceased patients were presented and discussed based on their case histories and other medical records. Deceased patients were selected because they developed CRS and predominantly leukemia.

Presentation of patients with CRS was primarily to acquaint the Ulm RATEMA team with a clinical condition observed in the Southern Urals. Particular attention was paid to the criteria applied in the 1950s to establish the diagnosis of CRS, as well as the course of the disease and its outcomes. Two patients were presented more than once. In one case the repeated presentation was primarily caused by the complexity of the pathological process and the substantial changes in the patient's organs and body systems (Annex patient 1), and by the necessity to consult the German experts about

the treatment of progressive renal insufficiency accompanied by polyvalent allergy and agranulocytosis. The other patient (Annex patient 2) was presented for the second time to discuss the results of the treatment of nonspecific dermatitis, a frequently observed pathological condition.

The case histories of the patients with hemoblastosis were presented to discuss the up-to-date diagnostic and therapeutic methods and methods for treating patients with hematologic pathology. The presentation of a teenage patient with acute lymphoblastic leukemia was to decide about an optimal therapeutic plan. The Ulm RATEMA team gave their recommendations about the course of chemotherapy for this patient and donated the necessary medicinal preparations as humanitarian aid.

Three of the video demonstrations were to render consultative assistance by the Ulm RATEMA team to the clinicians of various medical institutions of the city of Chelyabinsk. To discuss the diagnosis and review the therapeutic regimen a patient from the Regional Oncology Dispensary who had a malignant histiocytoma was presented at one of the conferences. By the time of the videoconference the patient had developed a tumor relapse. After review of the histological preparations by the pathologist of the Ulm University the therapeutic strategy was changed. A patient from Chelyabinsk City Clinic No. 2 with a severe diabetes mellitus was also presented and recommendations given with regard to the therapy. Presentation of the patient with B<sub>12</sub>-deficiency anemia was aimed at ascertaining the diagnosis. The diagnosis was confirmed and the patient underwent a course of treatment at the clinical department of the URCRM.

The Ulm RATEMA team presented 7 case histories: 5 patients with hematological disorders, a soldier from Georgia with an acute radiation burn and having a course of treatment at an Ulm clinic, and a female patient with a Parvovirus B-19 infection of the bone marrow. The presentations focused on case histories of the patients with hematological pathology, the emphasis being made on the therapeutic protocols applied for treating patients with blood diseases and the up-to-date pharmacological preparations used in Western Europe.

The woman diagnosed with acute myeloid leukemia received two courses of anti-recurrence treatment (the first course – ATRA and 3 cycles of Cytarabine Vegetide with Daunorubicin; the second course – 2 cycles of ? ytarabin with Vepesid). The second course included allogeneic bone marrow transplantation. As a result complete remission was achieved. The presentation was accompanied by a demonstration and discussion of slides showing the bone marrow aspirate.

A patient with osteomyelofibrosis was diagnosed with a myeloproliferative disorder accompanied by an elevated level of reticuline fibers of unclear etiology. On examination a severe anemia of unknown origin was diagnosed. A differential diagnosis was made between anemia and chronic myeloid leukemia accompanied by an increased level of megakaryocytes and reticuline fibers; no specific therapy was indicated. The diagnosis was only verified two years later. Courses of anti-recurrence treatment were administered, a sustaining hormonotherapy was instituted, and splenectomy was performed. As a result of a severe megakaryocyte-blast crisis accompanied by pneumonia the patient died. The presentation of the patient's case history was illustrated by bone marrow smears and histological sections as well as

findings of the examination of the patient's organs and organ systems (chest x-ray, skeleton and bone marrow scintigram, etc.).

The case history of a patient diagnosed with chronic myeloid leukemia was presented as an example of molecular remission achieved after allogenic transplantation of bone marrow and 2 courses of Hydroxytetracaine (the second course was combined with  $\alpha$ -Interferone). The findings of the cytogenetic investigation (Ph-chromosome was identified) and cytological investigation of bone marrow were presented.

A patient observed at the Ulm University clinic with the diagnosis of chronic myelomonocytic leukemia combined with chronic lymphocytic leukemia was also presented. Therapy difficulties were found because of complications (discontinuation of Tretinoin (Vesanoid because of lymphocytosis) with the disease.

A patient with multiple radiation skin injury was presented. The patient history revealed a case of protracted irradiation as a result of multiple exposures to a sealed  $^{137}\text{Cs}$  source. The dose received by the patient was unknown (the patient was exposed by chance: the radiation source, a container with the isotope, had been placed by somebody in the pocket of the patient's overcoat). To estimate the dose biological dosimetry was used. The dose was reconstructed based on the findings of cytogenetic studies (12 dicentrics per 500 metaphases) which corresponded to the total dose of 0.3 Gy. The diagnosis of acute radiation injury was established as late as 4 months after the onset of the disease. The patient was treated in the Department of Dermatology of the University of Ulm for about 8 months. To assess the depth of the injury to the tissues, nuclear magnetic resonance and histological studies of tissues taken from the affected area of the lower extremity were performed. Since the ulcer was infected by the aerogenic anaerobic microorganisms resistant to most antibacterial preparations, the patient was given intravenous injections of antibiotics (Tazobac). The skin ulcer in the hip was excised, the patient received corticosteroid hormone therapy, and antibiotic therapy was continued. Following the operation the patient developed arthritis and empyema of the knee-joint for which he was treated in an orthopedic ward. An intensive antibiotic therapy was administered and the joint drained. After arthroscopy, arthrotomy combined with synovioectomy was performed followed by plasty of the extensive area of the skin defect which developed after the excision of the ulcer. The patient developed myonecrosis which required another operation with a subsequent skin grafting. As a result of the treatment, a complete implantation of the graft and the restoration of the knee-joint function were achieved. The presentation was accompanied by the demonstration of the photos showing the dynamics of the inflammatory process in the wound and the development of concomitant complications (purulent gonitis). Nuclear magnetic resonance images of the affected area taken in the course of the treatment were also shown. The data presented and discussed at the conference included the dynamics of the peripheral blood parameters and immunological characteristics and findings of additional investigations of the patient.

The presentation of a patient with infection by Parvovirus included a brief description of the patient history (complaints, peripheral blood parameters in dynamics, bone marrow aspirate and biopsy) and the findings of the virological examination.

During the teleconference the discussions of various issues of a more general character were also organized, including: the use of Interferon in the treatment of hematologic patients; indications, problems and prospects of bone marrow transplantation in Germany; the application of immunologic typing in diagnosing leukemia.

## **5. Lessons learned**

### **5.1 General lessons**

The equipment chosen for the teleconsultation proved very useful for the tasks required. For the future it would be very helpful to buy equipment that already delivers digital results. It would be easier to insert the information in the multimedia database and quality loss through the process of digitalization could be avoided.

### **5.2 Special lessons**

From our experience, the communication between the two centres allowed discussions on the health status of patients and sharing of information on current methods of diagnosis and treatment of diseases (especially those with a hematologic and oncological profile), the use of new promising pharmacological preparations as well as the basic pathophysiological understanding of the underlying disease. It is also apparent that the relatively rare radiation induced health impairments require intensive discussion between the few experts in this field which are available worldwide. This allows us to share scientific information and practical experience in different fields of radiation medicine and contributes to the professional development of specialists involved in the project. The availability of a video communication link of this kind provided an opportunity to engage highly skilled specialists in giving consultations on practically any health problem. Therefore, the circle of teleconference participants is not limited to the physicians and researchers of URCRM or the University of Ulm.

Preparation for the presentation of a patient history allowed the attending physician to have a clearer notion of the patient condition, etiology and genesis of the pathological processes. Before data are entered into the database, all information on the patient's state of health should be thoroughly analyzed. Compared to the everyday hospital practice, where some aspects can be overlooked, the exacting framework of the computer database compel one to be more disciplined by requiring that the information entered should be complete and consistent. This makes one analyze the specific features of the disease course, cardinal directions of the prescribed therapy and notice one's own blunders and mistakes.

Within the framework of the RATEMA project, particular attention was drawn to the benefits gained by patient presented: rendering the necessary medical aid and recommendations on diagnosis and treatment. Our experience in teleconferencing showed that considerable time was given to a detailed examination and discussion of laboratory findings. However, the discussion indicated the need to keep a schedule fixed for the video conference. Sometimes at the end of a teleconference too little time was left for the participants to share opinions on therapeutic strategy. It is evident that, for videoconferences to be productive each should be based on a clear scenario and have a time-limit strictly adhered to.

## 6. Concluding remarks and outlook

The relevance of telemedicine in the management of rare disorders such as radiation exposure syndromes is very high, especially when the teleconsultation links are with specialists having a high knowledge and experience of these disorders. The Southern Urals is one of the most unsafe regions in the Russian Federation in terms of the general ecological situation, and radiation conditions, in particular. Environmental hazards were brought by the activities of the Mayak Production Association (MPA), a military plant for weapons grade plutonium processing. Operation of the facility has been accompanied by radioactive contamination of vast territories in the Urals and population exposures due to routine releases of radionuclides between 1949-1956, and two major radiation accidents which occurred in 1957 and 1967 affecting a large segment of the population outside the facility.

The Urals Research Centre for Radiation Medicine (URCRM) was established to deal with problems brought about by the above-mentioned accidents, is now a WHO Collaborating Centre. At present the URCRM has highly skilled researchers and experts with unique information and hands-on experience in tackling health problems among residents chronically exposed to radiation.

Having practical experience and significant scientific potential in radiation medicine, notably on the effects of chronic radiation exposure, the URCRM is striving to establish interactive cooperation with similar treatment and scientific institutions in Russia and foreign countries. This will allow the conduct of collaborative research, sharing of expertise and development of new effective methods for treating the exposed population.

Currently, the URCRM has collaborative research projects with the Russian Federation's Ministry's of Health, Emergencies, Defence and Science, as well as with foreign collaborators, such as the US Department of Energy, American universities, Commission for European Community, and research institutes and organizations in Japan, Germany, France and Sweden.

Since 1967 the Department of Clinical Physiology, Occupational and Social Medicine at the University of Ulm has devoted attention to radiation research and contributed intensively to the diagnostic and therapeutic procedures of radiation injured persons. This group has appropriate expertise to share with colleagues in Chelyabinsk. One of the most promising directions of joint activities is telemedicine and radiation medicine pathophysiology.

The "RATEMA" (the role of telemedicine in the elimination of impacts of radiation incidents) project was established as a communication channel, via satellite, to allow development of a telemedicine conference system based on the latest teleconferencing technology. The system enabled clinicians and researchers to:

- discuss the health status in patients after chronic radiation exposure (primarily patients with oncologic and hematologic diseases);
- improve the quality of medical assistance to exposed residents of the Chelyabinsk region;

- demonstrate advanced diagnostic methodology and therapeutic approaches used by specialists of both countries.

In all, 51 videoconference were conducted from January 1998 through December 1998, with a total teleconferencing time of 204 hours. 20 patients from the URCRM clinic were provided with appropriate medical advice. Some patients were discussed at more than one conference. Seven videoconferences focused on 7 German patients from the clinic of the University of Ulm.

An important factor for the application of current communication systems in public health practice is the tendency towards decreased accessibility of high quality health care to people in low population areas of Russia, and in the Urals region (Chelyabinsk, Kurgan, Sverdlovsk Regions), in particular. The vastness of the contaminated areas, large distances between the villages, inadequately developed transportation and communication systems, make the opportunities offered by telemedicine technologies promising in terms of ensuring specialized health services to the residents of the region.

The experience of the RATEMA project has clearly shown that the potential offered by telemedical consultations conducted on stationary earth stations are fairly limited. The development of an INTEMAS (Fig. 18) will ensure the accessibility of health services to exposed and sick people, and provide new possibilities for personnel training. The objectives of such a project would be to:

- develop and maintain a mobile system for conducting medical teleconferences which would allow patients the benefit of medical consultations, on the spot, without having to move them from the area of their residence;
- prepare and conduct teleconferences, develop recommendations concerning diagnoses and treatment of patients with rare diseases and victims of accidents;
- improve existing knowledge and develop new knowledge with respect to health impairments caused by toxic environmental exposures (radiation, chemicals) as a basis for new diagnostic, therapeutic and rehabilitative approaches;
- render consultative assistance to the physicians of local health organizations in the Chelyabinsk Region.

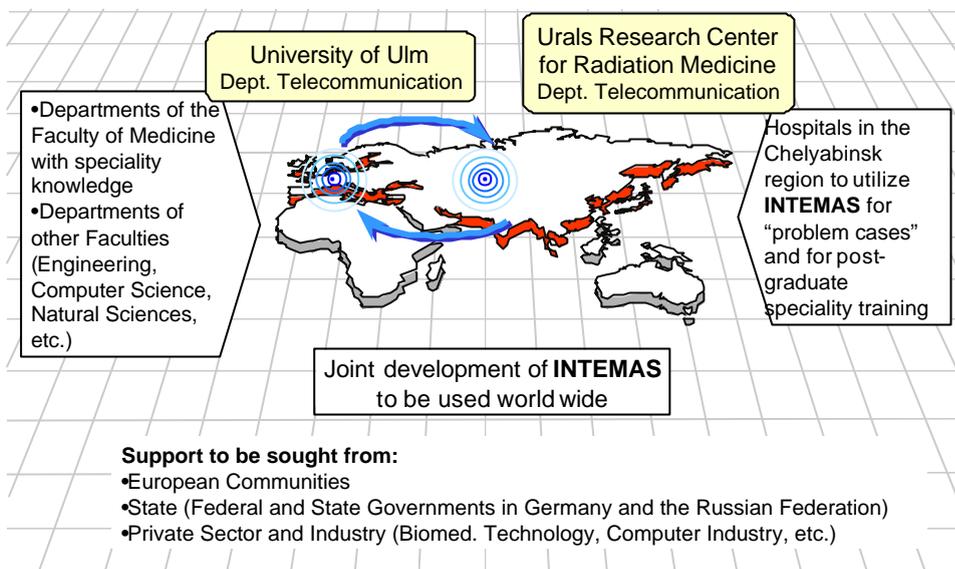


Fig. 18: Concept and implementation of **INTEMAS**: Interactive (and mobile) Tele-medicine Assistance System in health care delivery and advanced training

Within this Project a multimedia reference system can be developed which could be of use in cases when help is needed in emergency situations (radiation accidents, thermal or mechanical injuries, toxic conditions). This would provide timely information support to decision-making about issues related to organization and delivery of emergency help to victims of accidents.

The application of multimedia informational technologies may become an important component of the Project to provide an opportunity for advanced training to medical specialists working at the health institutions in the Chelyabinsk Region.

Clearly the University of Ulm would be an ideal partner for entering such an INTEMAS project. The University of Ulm with its faculties in medicine, natural sciences, engineering and computer technology has the entire technical background to be a substantial partner in such an endeavor. Furthermore, in Ulm an International Centre for Advanced Studies in the Health Sciences and Services is being established to offer courses for "teaching of teachers" in these new areas of telemedicine.

## **7. Annexes: Case histories of 2 patients discussed at RATEMA telemedicineconsultations**

### **Annex 1**

#### **Presentation of a patient with the identification number 2.2**

The first presentation of patient (identification number 2.2) took place on December 21, 1997. The patient was born on March 21, 1941, in the village of Kurmanovo located on the Techa River within of 87 km of the release site from the Mayak plant (Fig. 13). She lived in Kurmanovo until the evacuation of 1960. The family lived in a wooden house without conveniences, which stood at a distance of 100 m from the water edge. They used river water for all their domestic and agricultural needs (drinking, cooking, laundry, washing, cattle maintenance). No other water was available.

The patient has been regularly followed-up at the URCRM clinical department since 1955 and estimated to have a total dose to red bone marrow of 656 mSv, mainly from internal exposure (the external dose was estimated to be 76 mSv). The maximum dose rate in the period 1950 through 1952 was 130 mSv/yr (the diagram showing dose accumulation dynamics is demonstrated - Fig. 14). As of 1975 the patient's Sr-90 body content measured in the WBC SICH 9.1 was 605 nCi.

In 1955 the patient was diagnosed with chronic radiation sickness, 2nd degree of severity on the basis of the patient's complaints of asthemia (weakness, rapid fatigue, headache, reduced appetite), ostealgic syndromy, and moderate leukocytopenia in the peripheral blood (up to  $2.0 \cdot 10^9/l$ ). The patient was referred to the Clinic of Biophysics Institute in Moscow for further examination and treatment. The patient was hospitalized for 5 months (12/1955-05/1956). An examination found the presence of leucopenia and neutropenia, endocrine insufficiency, infantilism of sex organs, symptoms of vegetative dysfunction (a slight tremor of the eyelids, increased tendon and periosteal reflexes in the extremities), and stage 4 trachoma. The patient was receiving symptomatic treatment when her condition deteriorated dramatically, and she developed temperature elevations up to  $39.5^\circ \text{C}$ , acute lacunar tonsillitis accompanied by hepatomegaly. The leucocyte count in the peripheral blood decreased to  $0.4 \cdot 10^9$  cells/l, and aganulocytosis was noted. Bone marrow preparations were typical of agranulocytosis: extreme paucity of granulocytes, granulopoiesis became arrested at the promyelocyte stage (agarnulocytes), and relatively numerous lymphocytes. The patient received antibiotics, 5 transfusions of packed leukocytes, 2 transfusions of fresh blood and injections of vitamins. This therapy resulted in an improvement at day 12 of hospitalization: the temperature and the symptoms of tonsillitis subsided, the leucocyte count increased up to  $1.5 \cdot 10^9$  cells/l, and neutrophilic granulocytes were observed ( $1.1 \cdot 10^9$  cells/l).

On May 8, 1956, surgery for acute appendicitis was performed. Her post-operative period was uneventful. The patient was discharged from the clinic of the Biophysics Institute (Moscow) with signs of neutropenia and leukopenia which were interpreted as an effect of chronic radiation exposure. Later the patient remained under the observation by URCRM clinicians.

On admission to the URCRM clinic in 1959 and 1964 recurrent agranulocytic reactions were noted (a picture is shown). An association between the occurrence of agranulocytosis and administration of analgesics was established and confirmed (in 1964) by a skin test for that drug. In the subsequent years of follow-up antibodies were found in the patient's blood. Due to this it became impossible to administer blood transfusions. Since it was difficult to find a suitable donor, the patient's blood was shipped to Moscow to be studied at the Institute for Hematology and Blood Transfusions. It was concluded that the patient's serum contained incomplete anti-Rhesus antibodies and incomplete antibodies of another specificity.

In July 1971 the patient developed severe agranulocytic crisis caused by the administration of a medicinal preparation containing analgin. The patient was admitted to the URCRM clinic in poor condition with temperature elevations of up to 40° C, chills, extensive necrosis of oral and anal mucosa. A complete absence of granulocytes in the peripheral blood persisted for 9 days. An attempt to obtain a bone marrow sample for analysis resulted in failure. Intensive treatment with antibiotics, corticosteroids and preparations stimulating leukopoiesis led to the resumption of granulocyte production in the peripheral blood. However, later the patient developed a septic condition which persisted for 7 months: a dramatic temperature elevation, necrotizing angina, periostitis of the lower jaw, adnexitis, pyelonephritis. There was the presence in the peripheral blood and bone marrow of mobile Gram-positive rods resembling *Listeria* in terms of cultural and biochemical properties. The patient's septic symptoms were accompanied by severe ostealgia: pains in the sacral and pelvic bones and coxofemoral joints; increased rigidity and stiffness were noted in the same bones. A favorable curative effect was achieved by the administration of levomycetin. However, long-term use of this preparation was precluded due to its toxic effect on hemopoiesis.

X-ray examination of the skeleton revealed diffuse foci of osteoporosis. Chondrolysis was noted and prevailed in the clinical picture of the disease. A deformity of the patient's nose, destructive changes in the cartilage of the coxofemoral joints, pubic symphysis and intervertebral disks were manifest. From 1971 to 1972 the patient's height decreased by 6 cm. The pathologic changes listed above were attributed to an insidious septic process that developed in the patient with impaired allergic reactivity and recurrent agranulocytosis. At age 31 years, in June 1972, after a course of treatment at the orthopedic department, her health status was defined as a disability. Subsequent agranulocytic crises were observed in 1973, 1977, 1980, 1986. It was impossible to establish a direct association between the patient's agranulocytosis and administration of preparations containing analgin since allergic reactions were triggered by different preparations; the patient developed polyvalent drug allergy. No agranulocytic crises were observed after 1989. The patient was repeatedly examined and treated at the URCRM clinic for pyelonephritis, cholecystitis, ankylosing osteoarthritis of the spine and coxofemoral joints for functional disturbances.

In 1989 the patient developed erysipelas on the right shin and accompanying lymphostasis which recurs annually. Also, in the past 5 years (since 1991) she has been treated for iron-deficiency anemia. Each year the patient is treated at the URCRM for disorders of the osteo-muscular system and chronic infectious processes in the kidneys and gallbladder. It is known from the patient's past history that in addition to the diseases

listed above she suffered focal pulmonary tuberculosis (1955), and bacterial pneumonia of the right lung (1969).

Admission to the URCRM clinic in December 1996 resulted when the patient's condition deteriorated: complaints of pains along the spine, in humeral and coxo-femoral joints, aching pains in the epigastric area and right hypochondrium. Loss of mobility in the coxofemoral joints caused difficulty in walking unaided (a video sequence is demonstrated). The patient was overweight, with a pronounced waddling gait and used a walking stick. Her skin and mucous membranes were pale, nose disfigured and the dorsum nasi sunken. A diffuse enlargement of the thyroid was noted, and a node was palpable in the right lobe. Palpation of the abdomen revealed tenderness in the epigastric area and the right hypochondrium. Limited movement in the left humeral joint, thoracic and lumbar-sacral parts of the spine, and a complete absence of mobility in the coxo-femoral joints was observed. The right lower extremity was taut and swollen. No soft tissue indentation occurred with pressure (compared to the left leg).

The state of the patient's hemopoiesis was demonstrated (a microscopic picture of the leucoconcentrate shown in the figure). The findings included: leucopenia of  $3.7 \cdot 10^9$  cells/l and neutropenia of  $2.1 \cdot 10^9$  cells/l.

X-rays of the spine and coxo-femoral joints showed changes between the years 1971-1972 and 1996. All interarticular spaces and intervertebral disks were still visible in the X-ray film of the spine in 1971, though the chondrolysis had already begun. In 1972 the intervertebral spaces (D10-D12) appeared sharply narrowed; and sclerosis of adjacent surfaces was noted. Similar changes were observed in vertebrae L3-L4. The x-ray film of 1996 showed a complete block of the above-listed articulations; there were manifest degenerative-dystrophic changes in the disks.

The x-ray of the patient's coxofemoral joints taken in 1971 showed destruction of the articular cartilage. In 1972 changes include a narrowing of the articular cavity of the right coxofemoral joint, a blurred picture of the articular surface of the acetabulum; dilation and deformation of the upper and lower parts of the articular cavity of the left coxofemoral joint due to the destruction of the articular cartilage and subchondrous bone tissue; overgrowth of bone tissue at the edges of the "roof" of the coxofemoral joint; flattening of the head of the left thigh, rarefaction of its edges measuring 2.5 cm in length; and development of arthrosis of the coxo-femoral joints was also observed. The x-ray of 1996 showed manifest degenerative-dystrophic changes in the coxofemoral joints.

The patient's clinical diagnosis was defined as ankylosing arthrosis of the coxo-femoral joints, pelvic bones, left humeral joint and spine caused by agranulocytosis complicated by sepsis in a patient already suffering from stage 2 chronic radiation sickness; stage 3 functional insufficiency of joints; iron-deficiency anemia; recurrent agranulocytosis, in remission; leukopenia; chronic gastritis, in remission; chronic cholecystitis, in remission; chronic pyelonephritis, latent inflammatory stage; chronic renal insufficiency; chronic erysipelas of the right shin, in remission; lymphostasis; diffuse goiter of 3rd degree; multiple-nodular goiter with cystic degeneration, without clinically manifest dysfunction; disturbance of fat metabolism; and 2nd degree exogenous-constitutional obesity.

The patient received the following treatment: iron preparations, enzyme preparations, spasmolytic drugs, hepatoprotectors (cholagogical drugs), hormone therapy and physiotherapeutic applications.

Demonstration of this patient at a video conference had a dual purpose:

1. To demonstrate a patient with agranulocytosis chronically exposed to radiation; the patient's disease was characterized by chronic, recurrent and progressive clinical course; in addition, the patient developed an ankylosing osteoarthritis of the coxo-femoral joints and spine; this disease caused the patient's disability at a young age.
2. To discuss with German colleagues the prospects for further treatment of the patient, and, in particular, ways to improve the motor function of the lower extremities (by using a coxo-femoral joint prosthesis and reducing the lymphostasis).

**A repeat demonstration of the patient (October 9, 1998).** In 1997 the patient was treated at the clinic of the URCRM for a recurrent episode of erysipelas of the right shin, chronic pyelonephritis accompanied by amyeloidosis, generalized osteoarthritis of the coxo-femoral joints and the spine.

The nature of her complaints changed over the period: she noted weight loss (lost about 10 kg), pains in the epigastric area and right hypochondrium, in addition she suffered from headaches and noise in the head; pains in the bones and joints persisted. To rule out a malignant growth, an oncological examination was conducted, but no oncological pathology was revealed. No agranulocytic crisis was previously noted. No changes were noted in the state of the patient's osteo-muscular system.

In 1997 the patient developed renal amyeloidosis. Urinalyses were indicative of persistent albuminuria, leucocyturia, bacteriuria. The patient's chronic renal insufficiency was progressing; she had developed a nephrotic syndrome (tables showing the findings of urinalyses are shown). Treatment antibacterial preparations resulted in improvement of her general condition and diminished symptoms of chronic renal insufficiency.

The purpose of the second presentation was to discuss the possibility of conservative management of progressive chronic renal insufficiency, given the presence of polyvalent drug allergy and exacerbation of chronic pyelonephritis. It appeared that amyeloidosis developed as a result of administration of nephrotoxic preparations for the patient's chronic purulent infection.

The patient's bone marrow preparation, taken in April 1968, was demonstrated and commented on by the physician of the clinical laboratory. The sample was obtained by sternum puncture and had abundant cellular elements. Hyperplasia of the erythroid series was noted: erythrocyte precursors made up 48.4%, but mature forms predominated. There was up to 22% juvenile cells (promyelocytes, myelocytes, metamyelocytes) and up to 18.2% mature neutrophils. Pathological mitoses were present in both erythrocytic and granulocytic cells. A leukocyte sample taken in September 1998 showed no abnormalities in the peripheral blood.

Changes in the patient's immune status were observed since 1979, and indicated an increase in the oxidation-reduction potential of phagotyzing cells and lack of reserve; manifest antigen stimulation of B-system lymphocytes; periodically occurring

pathogenic immune complexes; dysimmunoglobulinemia; a characteristic sign: and impaired T-cell population ratio (decreased CD4+/CD8+ ratio).

Cytogenetic studies over four examinations, with the first examination in 1970 showed, of 65 metaphases analyzed, 18% were hypodiploid and contained 44 or 45 chromosomes from the groups C, D, G. There was 1 chromosome fragment and 1 metaphase had several chromatid fragments. An examination conducted in 1975 yielded 2 metaphases of the 40 metaphases studied contained 45 chromosomes and 1 metaphase had 1 chromatid fragment. A cytogenetic study of 1983 of 40 metaphases revealed 5.5% were hypodiploid, 1 dicentric was found, 3 chromosome fragments, and 1 chromatid fragment. In 1998: 52 metaphases were stained by conventional methods, and 15 were studied using differential staining. No structural or numerical aberrations were revealed.

## **Annex 2**

### **Presentation of a patient with the identification number 103.2**

Patient 103.2 was born in 1935 in the village of Muslyumovo and lived there up to 1954. The village is located on the bank of the Techa River at a distance of 78 km from the site of discharge of radionuclides (a schematic map of the position of the village relative to the river is shown - Fig. 13). The patient lived in a wooden house, without modern conveniences, which stood within 20 m of the water edge. The family did not use well water; river water was used for domestic needs (drinking water, cooking, laundry, bathing, irrigation of kitchen-gardens, etc.).

Since 1956 the patient was regularly observed at the clinical department of the URCRM. The total dose to red bone marrow amounted to 671 mSv, the major contribution being from internal exposure (the external dose was estimated as 110 mSv). The maximum dose rate in the period 1950 through 1952 was 130 mSv/year (a diagram describing the dynamics of dose accumulation is shown).

In 1956 the patient was diagnosed with chronic radiation sickness (CRS) of 1st degree severity. Diagnosis was based on the patient's complaints of general weakness, rapid tiredness on regular effort, malaise, limpness, apathy, irritability, tearfulness, pains in tubular bones (humeral and tibial), muscular pains, dizziness on sharp turn or inclination of the head, headache, somnolence in the day time, sleep disturbances at night; changes in peripheral blood parameters: neutropenia up to  $2.1 \cdot 10^9/l$ , increased count of neutrophilic band granulocytes, anemia (hemoglobin 95 g/l), thrombocytopenia ( $159-176 \cdot 10^9/l$ ), monocytosis, and accelerated ESR. A neurological examination revealed a decreased muscle tone, increased tendon reflexes of the upper and lower extremities, tremor of the hands and hyperhidrosis were noted. In addition, dysmenorrhea, alopecia and increased brittleness of nails were observed.

Over the entire period of observation at the URCRM clinic she was noted to have disorders of the central nervous system and cerebral blood vessels (early symptoms of atherosclerosis), respiratory organs, (pulmonary tuberculosis, chronic obstructive bronchitis), cardio-vascular system (ischemic heart disease), gastro-intestinal tract (chronic hyperacidic gastritis, ulcerative disease of the duodenum, chronic pancreatitis, chronic cholecystitis), urogenital organs (dysmenorrhea), locomotor system (diffuse osteochondrosis of the spine, sub-acute deforming osteoarthritis of

the upper and lower extremities). Besides, the patient exhibited a polyvalent allergy (to medicinal preparations and foodstuffs), manifested by skin eruption. The patient was repeatedly treated at the URCRM clinic. The major pathologic disorders are presented over time in the table.

The patient was first demonstrated at a videoconference in March 1998. There had been a dramatic deterioration in the patient's condition and the patient was admitted to the clinical department of the URCRM. Without apparent cause, there was polymorphous vesiculo-pustulous eruption all over the patient's body accompanied by permanent severe itching causing sleep disturbance. The vesicles showed a tendency to fusion and ulceration. In addition, at the time of hospitalization the patient manifested the following pathological signs: morphological changes in the gastrointestinal tract (chronic cholecysto-pancreatitis in remission, ulcerative diseases of the duodenum); immune system disorders (a sharp increase in the number of circulating pathogenic immune complexes), and changes in the electrocardiographic findings (of a sclerotic nature). The purpose of the patient demonstration was to ascertain a diagnosis and develop a common therapeutic strategy. A diagnosis of autoimmune neurodermatitis was made and it was decided to continue treatment with dexamethasone (tablets) at the dose of 8 mg/day; the patient tolerated the preparation well.

In April 1998 the patient was again examined at a teleconference by the dermatologist Prof. Peter (the videosequence of April 1998 was played). It was noted that the therapy proposed proved effective: no new rashes appeared and itching subsided. As a result it was decided to continue the administration of corticosteroids (tablets of prednisolone at daily dose of 20.0 mg).

From March through October 1998 the patient was on dexamethasone with a gradual reduction in the dose to 0.25 mg/day. Six months after commencement of the treatment, the patient decided to stop taking the preparation because of pains in the epigastric area and because her skin condition became normal. Two to three days after the preparation was discontinued the patient began to suffer from skin itching during day and night, and 2 days later she developed vesiculo-pustulous eruptions in the area of the fossa poplitea and flexura ulnaris. The patient resumed taking dexamethasone at the dose of 8 mg/day: within a week the patient's condition improved, the rash on the skin disappeared. Over the period of observation the patient followed a strict diet and took additional medication protecting the mucous membrane of the stomach and the duodenum.

Presently the patient regards her condition as satisfactory: her itching has subsided, her appetite and sleep are normal. A significant positive change in the patient's condition was noted (the video sequence of October 22 is run). Skin elasticity has been restored completely, no new eruptions were observed, only areas of hyperpigmentation at sites where vesicles were formerly observed.

The clinical diagnosis was defined as follows: autoimmune neurodermatitis; polyvalent allergy; ischemic heart disease; atherosclerotic cardiosclerosis with transient disturbances of the rhythm; sclerosis of the cerebral vessels and the aorta; ulcer of the duodenum in remission; chronic cholecysto-hepatitis in remission; chronic obstructive bronchitis; diffuse pneumofibrosis; pulmonary emphysema;

primary deforming osteoarthritis of the upper and lower extremities; diffuse osteochondrosis of the spine.

X-ray films were demonstrated: intensified lung pattern with signs of fibrotic changes; the joints (hands, shoulders, knees) showed degenerative-dystrophic changes represented by non-uniform consolidation of the bone tissue and contraction of the arthral opening.

Since 1977 the patient has not experienced any hemopoietic system disorders. A peripheral blood preparation was shown by the laboratory physician of the URCRM clinical laboratory: no pathologic findings can be observed. Changes in the immune system were demonstrated with the initial immunogram indicative of intensive oxydation-reduction reaction in neutrophilic granulocytes, and lack of reserve potentials in them. A repeat immunological examination, performed at the height of the skin eruption revealed a sharp decrease in the number of circulating pathogenic immune complexes.

The patient's current condition is satisfactory, voicing no complaints. Her skin is a normal color and elasticity, tissue turgor is normal, and no skin dryness. A small papulous eruption can be seen on the lateral surface of the knee joint. The visible mucous membranes are a normal color. Examination of the inner organs revealed no pathologic findings.

**Conclusion:** The objective of the repeat demonstration of patient D-va was achieved: a clinical diagnosis was established, adequate therapy administered resulting in a significant improvement in the patient's general condition.

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