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Isolation of Polyene Phosphatidylcholine and Phosphatidylethanolamine From *Euphausia superba*

937C0022C Moscow PRIKLADNAYA BIOKHIMIYA I MIKROBIOLOGIYA in Russian Vol 28 No 1, Jan-Feb 92 (manuscript received 02 Feb 90) pp 145-151

[Article by K. Yu. Gordeyev, N. N. Pridachina, V. N. Filarin, S. V. Bondarenko, and S. G. Batrakov, Scientific Research Laboratory of Biologically Active Substances from Hydrobionts, USSR Ministry of Health, Moscow; UDC 577.115:547.953]

[Abstract] This report describes three methods used to isolate in individual form the primary phospholipids of *E. superba* phosphatidylcholine and phosphatidylethanolamine with the use of ion-exchange chromatography. Results of thin-layer chromatography and high performance liquid chromatography showed that 55 percent of the lipids isolated from *E. superba* are phospholipids. Chromatography in silica gel, with its ion-exchange properties, produces a product with 95 percent purity, and these preparations are suited to many biochemical and pharmacological studies. A new method of DEAE-Spherone column chromatography is used to isolate ionogenic lipids from non-ionic compounds, carotenoids, and triacylglycerin. It produces a purity grade in the phosphatidylcholine, phosphatidylethanolamine, and lysophosphatidylcholine of approximately 99 percent, with virtually no losses in chromatography. This latter method is recommended for rapidly obtaining small (1 g) amounts of highly purified phospholipids. Tables 3; references 16: 7 Russian, 9 Western.

Construction of Rhizobium Meliloti Gene Bank

937C0081B Moscow DOKLADY AKADEMII NAUK in Russian Vol 324 No 1, May 92 (manuscript received 11 Feb 92) pp 227-228

[Article by B.R. Umarov, T.V. Ivashina, A.A. Aronshtam, A.S. Rasulov and A.G. Khalmuradov, acad., Uzbek Acad, Sci., Institute of Microbiology, Uzbek Acad. Sci., Tashkent; Institute of Bioochemistry and Physiology of Industrial Microorganisms, Russian Acad. Sci., Pushchino, Moscow Oblast; Scientific Research Institute of Agricultural Microbiology, Russian Agricultural Academy of Sciences, St. Petersburg; UDC 577.1]

[Abstract] A brief description is provided of the approach used in the construction of a gene bank for Rhizobium meliloti. The approach was based on the use of cosmid pLAFR5 bearing four to 10 fragments of the ribosomal genome, the fragmenta ranging from 20 to 30 kpb. Following transfection, 30,000 tetracyclin-resistance clones were obtained bearing recombinant cosmids representing a complete gene bank for R. meliloti. Figures 2; references 4: 2 Russian, 2 Western.

Semiconductor Biosensors: Immobilization and Properties of Urease Films

937C0046A Kiev UKRAINSKIY BIOKHIMICHESKIY ZHURNAL in Russian Vol 64 No 1, Jan 92 (manuscript received 21 May 91) pp 66-71

[Article by O.A. Bubryak, L.N. Khustochka, A.P. Soldatkin and N.F. Starodub, Institute of Molecular Biology and Genetics, Ukrainian Academy of Sciences, Kiev; UDC 577.15.086:543]

[Abstract] Trials were conducted on the immobilization of soybean urease (EC 3.5.1.5) on 0.5 x 0.5 cm silica plates coated with 0.8-1.0 μm-thick layers of SiO_2 and Si_3N_4 for preparation of semiconductor biosensors. Best results with retention of 20 percent of urease activity were obtained by immobilization of a 3:1 BSA:urease mixture with glutaraldehyde vapors for 30 min. In 1 and 5 mM phosphate buffers, pH 7.0, the immobilized urease retained 80 percent of its activity after 30 min at 65° C. In buffered 1 mM EDTA solution full activity was retained for a month at 4° C. The K_m value for the immobilized enzyme was 2.0 mM at 20° C, pH 7.0. Maximum swelling of the BSA matrix did not exceed 35 percent, indicating that this approach to urease immobilization represents a viable option for construction of enzyme biosensors. Figures 5; tables 3; references 13: 2 Russian, 11 Western.

Modulation of Mutagenic Properties of Fotrin on Murine Bone Marrow by Interferon-Inducer Ridostin

937C0162B Leningrad VOPROSY ONKOLOGII in Russian Vol 73 No 7-8, Jul-Aug 91 (manuscript received 10 Jan 91) pp 834-838

[Article by G.N. Zolotareva, N.S. Loginova, O.V. Parshina and N.N. Nosik, All-Union Scientific Center for Safety of Biologically Active Substances, Kupavna, Moscow Oblast; Institute of Virology imeni D.I. Ivanovskiy, USSR Academy of Medical Sciences, Moscow; UDC 615.015.4:575.24:611-018.46:599.323.4]

[Abstract] Analysis of bone marrow metaphases was used to confirm the fact that ridostin (5-100 mg/kg, i.p. or per os), a dsRNA interferon inducer, did not affect the rate of spontaneous mutations in 22 g male CBA x C57BL/6 mice. Accordingly, ridostatin was assessed for efficacy in modulating the mutagenicity of fotrin [as published], a Soviet antineoplastic. Administration of fotrin in an intraperitoneal dose of 20 mg/kg was found to increase the percentage of metaphases with chromosomal abnormalities to 48 percent from a control values of approximately 0.40 percent. Ridostin was found to be most effective in mitigating the effects of fotrin when administered 5 h before fotrin, reducing the count to 15 percent, a length of time which coincides with maximum interferon response (640 IU/0.1 ml of serum). These findings complement and confirm other studies pointing to the antimutagenic efficacy of endogenous interferon. Figures 1; tables 2; references 8: Russian.

Effects of Human IL-2 Synthetic Fragment on Growth and Vascularization of Sarcoma-180 in Mice

937C0162A Leningrad VOPROSY ONKOLOGII in Russian Vol 73 No 7-8, Jul-Aug 91 (manuscript received 25 Dec 90) pp 826-830

[Article by A.G. Ushmorov, L.V. Onopriyenko, B.O. Voytenkov and I.I. Mikhaylova, Order of the Red Banner of Labor Scientific Research Institute of Oncology imeni Prof. N.N. Petrov, USSR Ministry of Health, St. Petersburg; Institute of Bioorganic Chemistry imeni M.M. Shemyakin, USSR Academy of Sciences, Moscow; UDC 615.277.3:616-006.3-092.9]

[Abstract] A peptide designated C-1-6 corresponding to the middle domain of human IL-2 was synthesized for testing against sarcoma-180 in 18-22 g female SHR mice. C-1-6 (0.5, 5 or 50 μg/day q.o.d. for 4 or 5 injections, beginning 1, 3 or 4 days after injection of 2-5 x 10E+5 sarcoma-180 cells into a posterior footpad) was shown to significantly enhance tumor growth in doses of 5 and 50 μg. Additional studies demonstrated that C-1-6 significantly enhanced angiogenesis. Finally, intraperitoneal administration of supernatant derived from syngeneic macrophages incubated in vitro with C-1-6—60 days after sarcoma-180 implantation—was also shown to promote tumor growth. These findings suggest that stimulation of tumor growth by C-1-6 is predicated on release of macrophage growth factors, and that C-1-6 may have application in areas other than oncology, such as wound healing and myocardial infarction where neovascularization is crucial. Tables 3; references 10: 4 Russian, 6 Western.

Structural and Functional Hepatic Changes in Wild Rodents in Areas Affected by Chernobyl Fallout

937C0029B Moscow RADIOBIOLOGIYA in Russian Vol 32 No 1, Jan-Feb 92 (manuscript received 28 Sep 90) pp 19-30

[Article by L.N. Shishkina, L.D. Materiy, A.G. Kudyasheva, N.G. Zagorskaya and A.I. Taskayev, Institute of Chemical Physics imeni N.N. Semenov, USSR Academy of Sciences, Moscow; UDC 614.876:621.039.58]

[Abstract] Histopathologic and biochemical studies on small rodents (field mice, voles) captured in the vicinity of Chernobyl in 1987 demonstrated extensive hepatopathology. The estimated exposures of the rodents to ionizing radiation ranged from 0.02 to mR/h. The dystrophic changes were age and species dependent, consisting of marked depression of lactate dehydrogenase activity, modest elevation of succinate dehydrogenase, slight reduction in pyruvate dehydrogenase, depression of antioxidant system and concomitant rise in lipid peroxidation, lipid depletion and an increase in the phosphatidylcholine:phosphatidylethanolamine ratio. In general, a direct correlation between the level of irradiation and the degree of hepatic damage was lacking. However, a positive correlation prevailed between the number of rodents affected, degree of antioxidant depletion, and depression of lactate dehydrogenase activity. Figures 1; tables 4; references 27: 22 Russian, 5 Western.

Changes in Zooplankton Biomass in Lake Baikal

937C0081B Moscow DOKLADY AKADEMII NAUK in Russian Vol 324 No 1, May 92 (manuscript received 10 Feb 92) pp 233-236

[Article by E.L. Afanasyeva and A.V. Ignatov, Limnological Institute, Siberian Branch, Russian Acad,. Sci., Irkutsk; UDC 577.472.361]

[Abstract] Annual monitoring on zooplankton biomass in Lake Baikal conducted every September (at peak biomass) has revealed an almost two-fold drop after 1968 in comparison with the previous decade, i.e. from an average of 22.2 g/m^2 to 11.5 g/m^2. Analogous changes have afflicted phytopankton and selected fish, such as the Baikal whitefish. The reasons for these changes are being sought in a complex of factors affecting the Lake Baikal ecosystem, not the least of which is anthropogenic intervention. Figures 3; tables 1; references 6: Russian.

Assessment of Ecologically Tolerable Anthropogenic Impact

937C0081E Moscow DOKLADY AKADEMII NAUK in Russian Vol 324 No 1, May 92 (manuscript received 14 Feb 92) pp 237-239

[Article by D.G. Zamolodchikov, Moscow State University imeni M.V. Lomonosov; UDC 577.4]

[Abstract] Hydrochemical studies conducted in the 1980-1990 decade on 6 major water systems (Volga, Dnepr, Dnestr, Danube, Syrdarya, Azov basin) led to the formulation of the concept of Ecological Threshold Limits (ETL) for anthropogenic impact on ecosystems. The concept underlying ETL and appraoches to its estimation were derived in analogy to Threshold Limit Values in toxicology. Using the Sydarya River basis as an example, a table lists the ETLs for a number of chemical pollutants related to anthropogenic activity. The approach is applicable to a wide variety of aquatic and terrestial ecosystems and allows for an overall assessment of a given environment for ecologic damage. Tables 1; references 5: Russian.

Ctenophore *Mnemiopsis leidyi* in the Azov Sea

937C0105A Moscow OKEANOLOGIYA in Russian Vol 31 No 6, Nov-Dec 91 [manuscript submitted 8 Aug 90; resubmitted 28 Jan 91] pp 981-985

[Article by Ye. I. Studenikina, S. P. Volovik, I. A. Mirzoyan, G. I. Luts, Azov Scientific Research Institute of Fisheries, Rostov-na-Donu; UDC 595. 341.5]

[Abstract] A predatory species new for the plankton fauna of the Azov Sea appeared there in 1988—the ctenophore *Mnemiopsis leidyi.* The ecosystem of the Azov Sea is known to be highly polluted, a condition that prepared the way for the entry of the new ctenophore, which, only a year after it was first observed, had spread to virtually the entire sea. The biomass of zooplankton, on which the ctenophore feeds, is sharply down. The anchovy industry has been devastated by the ctenophore, whose biomass at the end of September 1989 had grown to 106 g/cu m, or 32 million tons. The kilka industry has also suffered heavily because of the ctenophore presence. The changes observed in the plankton fauna are likely to be irreversible. Figures 3, references 8: 7 Russian, 1 Western.

Emoxipin in Treatment of Primary Glaucoma

937C0114B Moscow VESTNIK OFTALMOLOGII in Russian Vol 108 No 1, Jan-Feb 92 (manuscript received 25 Mar 91) pp 14-15

[Article by Yu.S. Kramorenko, cand. biol. sci., T.A. Dobritsa, cand. med. sci., Z.A. Imanbayev and Ye.A. Yegorov, prof., Kazakh Scientific Research Institute of Eye Diseases, Alma-Ata; UDC 617.7-007.681-021.3-085.272.014.425]

[Abstract] Therapeutic trials were conducted with emoxipin—an antioxidant—in addition to conventional therapy in the management of 72 patients with closed- and open-angle glaucomas. The patients ranged in age from 37 to 79 years and were divided into three groups: (1) parabulbar injections of 0.5 ml of 1 percent emoxipin per day for 4-5 days; (2) 2 ml of 1 percent emoxipin intramuscularly per day for 8-10 days; and (3) intramuscular emoxipin + vitamin E or ayevit [as published] per

os for 10 days. Blood chemistries showed that the emoxipin + vitamin E combination was most effective in reducing serum and erythrocyte levels of lipid peroxidation products, generally by 20-50 percent. Visual improvement, including enlargement of the field of vision, was noted in 83 percent of Group I patients, 56.7 percent of Group 2 patients and in 66.8 percent of group 3 subjects. For comparison, the improvement figures for patients on vitamin E, ayevit or conventional therapy were 48, 58, and 42 percent, respectively. Consequently, emoxipin appears to be a valuable adjunct in the management of glaucoma. References 7: Russian.

Technical Bioenergetics and Ecosystem Biotechnology

937C0134A Moscow VESTNIK MOSKOVSKOGO UNIVERSITETA: BIOLOGIYA in Russian No 4, Oct-Dec 91 pp 3-13

[Article by A. V. Oleskin, V. D. Samuilov: "Technical Bioenergetics and Ecosystem Biotechnology"; UDC 573.01]

[Text] Technical bioenergetics is a component of biotechnology dealing with production of renewable fuel with the participation of living organisms. These organisms play the role of biomass suppliers and of direct participants of the production of fuel—ethanol, methane, hydrogen etc.

Ecosystem (Superorganismic) Biotechnology: An Application of Technical Bioenergetics

Pure cultures of microorganisms are used in most studies in technical bioenergetics. They are grown in special reactors (fermenters), isolated from the natural environment, where microorganisms exist as a part of associations and ecosystems. A sizable yield of the target product may be achieved in a bioreactor. For example the yield of the cells of unicellular phototrophes in fermenters is 1.5-2 times higher than in open-air water basins [11].

However, another approach based on culturing organisms of different species within ecosystems or associations has a number of advantages. Associations of microorganisms are used in technical bioenergetics to obtain methane from industrial and domestic wastes, inasmuch as pure cultures of methanogenic bacteria use a limited range of substrates and are incapable of utilizing complex organic compounds. Phototrophic organisms are cultured in open-air water basins within natural ecosystems. These include the green and brown algae, cyanobacteria and purple bacteria forming H^2, liquid hydrocarbons or raw materials for biological fuel production. Thus, organic acids synthesized by cells of the alga *Dunaliella sp.* can be converted into aliphatic hydrocarbons [11]. The biomass of algae in cyanobacteria can be fermented in alcohol or subjected to biological gasification.

Such work in technical bioenergetics pertains to a special direction of biotechnology. It is called ecosystem or superorganismic biotechnology [16]. Ecosystem biotechnology is oriented on using natural and artificial ecosystems and their components. It includes three levels: ecosystems, associations and populations.

Sokolov and Ilichev [21] use the term "ecotechnology" to mean "directed formation of ecosystems"—that is, it is similar in content to the term used here, "ecosystem biotechnology." The term "environmental biotechnology" (Umweltbiotechnologie) is used in the foreign literature, but its definition is narrow—as the rendering of industrial and domestic wastes harmless to the biosphere [31]. The global aspects of controlling natural and artificial ecosystems are generalized by the concept "engineering ecology" [25].

Let us now go on to specific projects in technical bioenergetics based on ecosystem biotechnology.

Biological Energy Conversion in Artificial Ecosystems

An ecosystem is "any unit containing within itself all jointly functioning organisms (a biological community) in a given area, and interacting with the environment in such a way that the flow of energy creates clearly determined biological structures and causes circulation of matter between living and nonliving nature" [15, p 24]. The property of the ecosystem that this definition emphasizes is circulation of matter within its bounds, which implies partial or even practically complete independence of the ecosystem from matter entering from without, that it is a closed system with respect to matter.

To one degree or another an ecosystem is likened to a self-supporting spacecraft, and it is no accident that ground rehearsals of lengthy space flights are similar to ecosystem projects. Thus, experiments with partially closed "man-algae" and "man - higher plants" systems went on for several months in Novosibirsk and Krasnoyarsk. It was demonstrated that algae: 1) regenerate completely in an atmosphere suitable for human breathing, one with a balance ratio of O_2 and CO_2; 2) regenerate drinking water, providing for 95 percent of man's need; 3) supply 30 percent of man's food (dry weight) [12]. Even fuller recirculation is achieved with a "man - higher plants" system.

Many biological developments are based on open biological systems. But they do acquire a closed nature if they are supplemented by the units that are lacking for circulation of matter. Thus, a methane-producing bacterial association does not form a closed system in relation to matter, particularly in relation to carbon. Closed circulation would be attained if the methane-producing association were to be supplemented by methylotrophic microorganisms converting CH_4 into CO_2 and partly into their own biomass, and with phototrophic organisms—for example cyanobacteria that regenerate organic compounds out of CO_2 in light. Recirculation of carbon compounds depending on light energy is accomplished in this system (Figure 1). Circulation of matter in a synthetic ecosystem would be more complete if recirculation of sulfur, nitrogen and other compounds were to be provided for by introducing the corresponding organisms into the system.

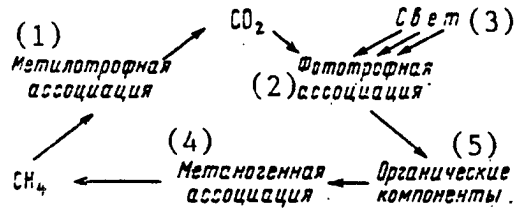


Fig. 1. A System Containing a Phototrophic, a Methane-Producing and a Methylotrophic Association of Microorganisms That Is Closed in Relation to Carbon Compounds

Key: 1. Methylotrophic association 2. Phototrophic association 3. Light 4. Methane-producing association 5. Organic components

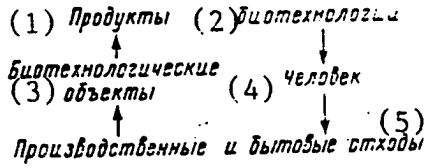


Fig. 2. Ecosystem Containing Man

Key: 1. Foodstuffs 2. Biotechnology 3. Biotechnological objects 4. Man 5. Production and domestic wastes

The ecosystem diagrammed in Figure 1 was practically realized in part in a project described by Kalyuzhnyy et al. [10]. Single celled green algae or cyanobacteria were grown in a pond under natural or artificial illumination; their biomass was allowed to settle and transform into biological gas. The CH_4 that was obtained was used as fuel. Similar projects in which photosynthesizing single-celled organisms are grown and their biomass is subsequently converted into liquid or gaseous fuel have been proposed in different countries [23]. In many of these projects, liquid wastes subject to treatment are dumped in a pond.

An ecosystem providing for biological water treatment that is partially closed in relation to matter has been under development in Belgium since 1978 [30]. The green alga *Hydrodictyon reticulatum* was grown in shallow water basins into which the wastes of a cattle yard and other contaminated water as well as water used to cool a nuclear reactor flowed; owing to the latter the temperature in the water basins was kept at 20-30°, which hastened algal development. The algal biomass was used as a substrate for a methane-producing association, for extraction of dyes, pharmaceutical compounds and cosmetic materials, and to fatten fish and hens.

Cultivation of algae in open water basins is an example from the field of aquaculture. Joint cultivation of phototrophes and other organisms—rotifers for example—under aquaculture conditions is planned. In China and some other countries, aquaculture of algae and cyanobacteria (*Spirulina* in Africa and Central America) has been practiced for millennia.

The following question arises: Is establishment of an ecosystem that is closed in relation to matter compatible with the fact that man continually removes the foodstuffs he needs from this system and (or) burdens it with wastes, for example with biological treatment of liquid wastes? There obviously must be a balance between that which man takes away and that which he gives to the ecosystem. In other words the production of an ecosystem that is taken away by man must be compensated by the corresponding substrate. Then we would have a "biotechnological objects - man" ecosystem dependent only on solar energy (Figure 2). Every ecosystem has compensatory mechanisms for absorption of surplus matter that threatens breakdown of the circulation of matter within it (a case of applying the unique Le Chatelier principle to an ecosystem), but this compensation does have its limits [3].

The combustion products of biological fuel and the wastes from its production—for example sugar cane bagasse in acquisition of ethanol fuel—are assimilated by ecosystems in most cases. Waste remaining after processing organic compounds into biogas is a valuable nitrogen-phosphorus fertilizer [5] or a nutrient substrate for cultivation of single-celled phototrophes. Thus, residue from processing the biomass of the alga *Hydrodictyon sp.* was used to grow another green alga—*Scenedesmus sp.*[30].

Despite biodegradation, there is the danger that wastes from production of biofuel would exceed the "throughput" of natural ecosystems. In Brazil, where vast areas were planted with sugar cane to be processed into ethanol fuel, 12-14 liters of wastes that polluted (caused eutrofication of) natural water basins were formed for every liter of alcohol. Consequently ecosystem biotechnology must reproduce multiunit circulation of matter: Ethanol production must be supplemented by biological treatment of water containing wastes from fermenting cane.

Let us now examine the energetic aspects of ecosystems. In contrast to recirculating nutrients, energy passes through an ecosystem once: It is characterized by an input and an output. Consequently every ecosystem depends on an external energy source, usually light. Phototrophic or, more rarely, chemotrophic organisms (producers), whose biomass is consumed by heterotrophes (consumers), are responsible for synthesis of organic matter out of inorganic compounds. Other heterotrophes (reducers) consume dead biomass and organic eliminations. Each of the indicated ecosystem components expends incoming energy (E) partly for accumulation of biomass (P) and partly for life-supporting processes (R):

$$E = P + R$$

P/R is the ratio of structural to energetic metabolism, and it is relatively constant for each ecosystem and each of its components. The desire to extract a maximum biomass yield at the lowest energy outlays—that is, to maximize P/R in agriculture and forestry—comes into conflict with the fact that in the course of evolution of biological systems of superorganismic rank, these ratios have established themselves at some stationary value. A

living system functions in such a way that the flow of utilized energy per unit of its mass grows in the course of evolution [18]: The intensity of energetic metabolism rises (in comparison with structural metabolism), and active behavior develops, motor activity in particular.

Thus either man must accept that ratio of biomass to the outlays of its maintenance that is characteristic of the given ecosystem, or he must reckon with the fact that artificially elevating the P/R ratio could lead to destabilization, to an imbalance in the ecosystem, which would ultimately lead (contrary to expectations) to a decrease in its productivity, and even death. A possible reserve for raising an ecosystem's productivity can be found not in attempts to surmount the stationary value of P/R but rather in a gradual shifting of the ecosystem's stationary state in the desired direction by means of its careful restructuring. For example the P/R ratio could be increased in a pond in which photosynthesizing organisms are grown by reducing the intervals of darkness (the length of night) by supplementing natural light with artificial light. The period during which phototrophes respire, expending organic compounds obtained by photosynthesis, could be reduced in this way. But this path carries the danger of disturbing the daily rhythms of the ecosystem. An ecosystem can be enriched by a new species of phototrophes that would absorb photons in a region of the spectrum inaccessible to the other phototrophes in this pond, or carry out photosynthesis at lower light intensities.

Thus creation of artificial ecosystems is determined by the possibility for establishing a balance between what man gives to biological objects and that which he takes away from them. In this case we need to consider the natural limitations on the effectiveness of energy conversion in the ecosystem.

Biotechnology and Technical Bioenergetics at the Level of Associations

An association is a component of an ecosystem. An association (community) is a group of interacting populations in a common habitat [19]. Many studies and biotechnological developments make use of not pure cultures (monocultures) but entire communities (mixed cultures), and in particular, associations of plants [12] and microorganisms [27,28,33]. Associations are capable of:

1. effectively utilizing substrates ill-suited to monocultures. A methane-producing association is an example of this;

2. producing a higher yield of valuable products (in comparison with a monoculture). Ethanol is formed more effectively out of wood shavings, initially subjected to electrolysis in order to break down lignin, by an association of anaerobic bacteria *Clostridium thermocellum* and *C. thermohydrosulfuricum* than by a pure *C. thermocellum* culture, which hydrolyzes cellulose directly [1]. Vitamin B_{12} is synthesized in larger quantities in associations of *Pseudomonas sp.* and *Proteus vulgaris* than in pure cultures of the same bacteria [6]. Extracellular polysaccharide is synthesized by *Acinetobacter sp.* in larger quantities if the bacterium *Micrococcus sp.* and the yeast *Candida tropicalis*, which supply *Acinetobacter sp.* with metabolites and stimulators of growth and polysaccharide synthesis, are added to its culture [4];

3. synthesizing products that are not formed by monocultures at all. Some amino acids are synthesized only in mixed cultures [6] many associations: One culture carries out the first stages of synthesis of a given product, while another carries out subsequent stages. A variant is also possible in which one culture does not participate directly in the biosynthesis of a product but forms chemical stimulators for another;

4. exhibiting higher resistance to infection by incidental microflora than can a monoculture.

The possibilities of joint cultivation are not limited to the world of microbes. A project of joint growth of agricultural plants is being discussed in the United States. Rejection of rye, corn, and other monocultures has been suggested [32]

Research on associations has general biological significance, because it allows us to reveal superorganismic forms of interaction that are typical of all living things. A significant role in these interactions is played by aggression—the desire to destroy, to weaken, to leave without food resources, and to place another organism in subordinate position; by isolation—attempts to avoid interacting with another organism; by cooperation—the desire to form a single system with another organism.

Types of Interrelationships Between Two Partners (Organisms or Their Groups). Partners are designated as A and B

Relationship of B to A	Relationship of A to B		
	Aggression	Isolation	Cooperation
Aggression	Antagonism; competition	Attack and passive defense	Domination and subordination; parasitism
Isolation	Attack and passive defense	No interaction	Unilateral cooperation; commensalism
Cooperation	Domination and subordination; parasitism	Unilateral cooperation; commensalism	Protocooperation; mutualism

The forms of behavior of two organisms or populations in terms of the relationships between each other are manifested in different combinations: A complex range of interrelationships arises (see table). For example when an aggressor encounters an aggressor, antagonism or a competitive struggle (indirect aggression) arises. When a cooperator meets a cooperator, protocooperation arises with sporadic contact between the partners, or mutualism arises with constant contact. The combination of aggression and isolation results in attack and passive defense. The table also gives other possible versions of interrelationships.

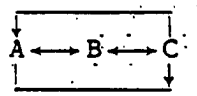
Interrelationships between organisms in nature are far from always paired:

$$(A \leftrightarrow B),$$

chains of interrelationships often form:

$$A \leftrightarrow B \leftrightarrow C$$

or



An example of such interrelationships is found in a biotechnological development aimed at protecting carnations from the pathogenic fungus *Fusarium oxysporum sp.dianthi* with the assistance of the bacterium *Bacillus subtilis*. The fungus is an aggressor in relation to the carnation (interrelationships of the parasitic form), while *B. subtilis* is an aggressor in relation to the fungus. Therefore introduction of *B. subtilis* into the soil protects the carnation from fungal infection [26].

Aggression is often nonselective. If two arbitrarily chosen forms of microorganisms are grown jointly, it is most probable that they will display aggression toward one another: A competitive struggle [18] or direct antagonism involving the use of chemical agents will begin. For example a cyanobacterium of genus *Anacystis* completely or partially inhibits growth of the green algae *Chlorella, Scenedesmus, Chlamydomonas* and *Haematococcus* [17]. The desire for isolation is also apparently a nonselective behavioral reaction. Cultivation in a Petri dish containing semiliquid medium (0.4-0.5 percent agar) produced nonmerging colonies of two bacterial species with a zone of absence of growth between them [14]. Mutual isolation of *Escherichia coli, B. subtilis* and *Vibrio alginolyticus* colonies was demonstrated when they were grown in pairs in Petri dishes in any combination. Even colonies that are progeny of bacteria of the same species do not merge when grown on semiliquid medium [14].

On the other hand relations in which cooperation dominates are usually selective; the cooperating species approach one another in lock and key fashion. In particular, interaction of a fungus with an alga or cyanobacterium in lichens is distinguished by high species specificity. Discrete, spatially separated communities of microorganisms forming compact structures—mats—were discovered in the caldera of Uzon volcano on Kamchatka [2], in hot springs of Iceland [27a] and in other habitats [11]. In this case each mat, which possesses a unique color, corresponds to a particular set of interacting species. Mats of up to four different colors are encountered in geothermal waters of Kamchatka: white (forming at water temperatures of 60-72°), olive and orange (at 45-60°) and green (below 45°). For example a green mat contains the purple bacteria *Rhodocyclus gelatinosus, Rhodopseudomonas viridis, Chromatium vinosum* and *Rhodopseudomonas palustris* and the green bacteria *Chlorobium limicola* and *Chloroflexus aurantiacus. C. aurantiacus* is a filamentous nonsulfur green bacterium, which forms the structural basis of the mat together with the filamentous cyanobacteria. In mats encountered at higher temperatures this role may also be played by filamentous sulfur bacteria of genus *Beggiatoa.*

Methane-producing associations, which convert organic substrates into biogas, consist of many species of prokaryotes and archebacteria. Archebacteria that generate methane directly—*Methanosarcina barkeri* for example—form a tissue-like substance—pseudoparenchyma—containing intercellular spaces in which other components of the microbial association are situated. Methane-producing associations appear macroscopically as dense granules with a diameter of up to 1 mm, which rise to the water surface due to the gas bubbles they form, and then sink back to the bottom when the bubbles separate from the granules [9].

Microorganisms of a methane-producing community form a single whole not only structurally but also functionally. The following are distinguished in a methane-producing association: hydrolytic microflora, which break proteins, nucleic acids, polysaccharides, lipids and other polymers down to monomers; acid-producing microflora, which carry out further decomposition of monomers down to organic acids (formic, acetic, propionic, butyric, lactic, pyruvic) and some other simple organic compounds (methanol, ethanol, butanol, acetone etc.), CO_2 and H_2; acetogenic microflora, which convert alcohols and C_3-C_5 organic acids into acetic acid, H_2 and CO_2; methane-producing microflora *per se*, which are responsible for forming CH_4 out of the mixture $CO_2 + H_2$, formic acid, acetic acid, methanol and methylamines.

A methane-producing association is an example of a metabolic (syntrophic) interrelationship. Thus, hydrolytic microflora functions effectively only if the monomeric products of hydrolysis, which inhibit hydrolytic enzymes, are continually removed from the medium. This is done by representatives of the acid-producing microflora—for example anaerobic spirochetes, which effectively absorb monomeric products and subject them to further breakdown. In turn, the function of acidogenic

microflora depends on utilization of its products—low-molecular organic compounds, as well as H_2—by acetogenic and methanogenic microorganisms. Methane-producing archebacteria supply vitamin B_{12} to components of the association [8]. To optimize biotechnological acquisition of CH_4, all types of interactions between cooperating microorganisms of the methane-producing association must be studied.

The relationship between two organisms in nature is rarely purely cooperative: Even in the case of stable, well-developed symbiosis, elements of aggression and mutual isolation may be observed. A slight change in environmental conditions or of the state of the symbiotic partners can disturb the balance between the different forms of behavior of the association's components, and lead to its disintegration.

Cooperative relations are determined in a symbiotic association of the green alga *Dunaliella maritima* and the bacterium *Pseudomonas saccharophila* by the fact that the bacterium consumes metabolites formed by the alga in light [20]. The existence of this symbiosis does not negate the presence of elements of aggression between its components. For example the alga releases antibacterial substances. The spectrum of interactions between the components of a symbiotic system, based on the data of Savelyev et al. [20], is shown in Figure 3. In the artificial conditions in which an attempt was made to reproduce the association out of its isolated components, antagonism won out over cooperation in many cases. By varying the environmental factors—the orthophosphate concentration for example—and the phases of development of the cultures at the moment they are brought together, conditions promoting restoration of a symbiotic association can be selected. Antagonism can be weakened dramatically by growing an association under the conditions of dialysis, which makes it possible to remove toxic products. This example shows that with joint cultivation, all means of interaction between partner organisms must be accounted for to the extent possible, regardless of whether a natural association is being reproduced or a new, previously nonexistent one is being constructed.

When associations are created for biotechnological purposes, it should be kept in mind that the means of interaction between partners are extremely diverse, and they are far from always limited to metabolic relationships, where the product of one partner serves as the substrate of another. Chemical communication—mutual influence by way of certain substances—is widespread. Biostimulators (aliphatic acids, pteridines, flavins, amino acids, peptides, quinoid compounds etc.) produced by one of the components of an association and favorably influencing another of its components have been isolated from some associations. Factors of opposite action exist as well—antibiotics, colicins. In some cases physical contact between the cells of interacting species is required. Thus, synthesis of oxytetracycline by joint cultivation of two strains of actinomycetes that do not form this antibiotic on their own depends on direct contact between their micelia [6].

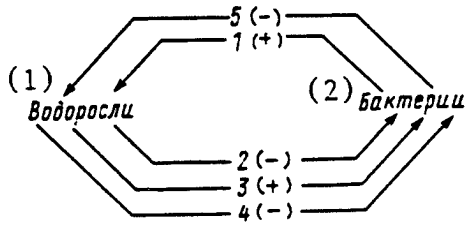


Fig. 3. Interrelationships Between Components of a *Dunaliella maritima* - *Pseudomonas saccharophila* Association, From [20]. Relationships between components: 1(+)—bacterium utilizes algal products that inhibit development of alga, 2(-)—bacterium increases the duration of the lag phase in algal growth, 3(+)—algal metabolic products stimulate bacterial development, 4(-)—the alga releases antibacterial products, 5(-)—development of the bacterium is inhibited due to reduction of the carbohydrate concentration in the medium in comparison with a pure culture; (+) and (-) signify cooperative and aggressive interactions

Key: 1. Algae 2. Bacteria

In most cases the yield of target products is increased or their spectrum is changed in a desired direction by means of cooperative interactions. An effort is made to minimize the contribution of other types of behavior. But there are examples of productive use of aggression and isolation as well. Thus, the fungus *Trichotecium roseus* synthesizes 1.7 times more trichotecin antiobiotic when the fungus *Penicillium chrysogenum* is added. Yegorov and Landau [6] believe that stimulation of the synthesis of an antiobiotic is associated with its action as a chemical agent that suppresses the undesired partner.

Developments at the Population Level

The heterogeneous nature of populations and the problem of the population-level stability of producing strains have been discussed in recent years [7], and nonlinear models of the behavior of populations have been created. In principle, the same forms of interaction typical of associations are also typical of populations—for example, competition between a biotechnologically valuable strain and a mutagen that has lost its valuable properties. Therefore in order to preserve the useful strain, conditions are created in which it would enjoy an advantage in the competitive struggle. Thus, methanol-oxidizing bacteria obtained by means of plasmid gene transfer are capable of growing at high methanol concentrations at which development of bacteria of the same species that have lost the plasmid is suppressed ([7], p 44).

In some populations, interaction between individuals is based on a combination of aggression in the direction of one partner and cooperation in the direction of another. A hierarchical structure (dominants and subdominants)

arises in such a population. It is most typical of invertebrates, among which particular types of behavior are established in individuals of a given rank. Such interrelationships also manifest themselves among single-celled organisms. The Acrasieae (myxomycetes possessing a cellular structure), particularly *Dictyostellium discoideum*, have a complex life cycle. The first phase of the cycle is characterized by cells with an ameboid form. Then these cells crawl together to form a multicelled fruiting body, in which spores mature. The spores germinate to form new ameboid cells. The factor inducing cells to crawl together is cyclic adenosine monophosphate (cAMP). The cells divide into "directors" and "performers": The former release cAMP into the environment, while the latter react to the chemical signal.

There are no projects in the literature based on the use of population hierarchy in biotechnology. Many organisms actively synthesize a target product only in a certain stage of their life cycle. If the transition to a desired stage involves chemical communication between organisms and if it appears possible and feasible to isolate the information-transmitting substance, then it could be added to the medium in order to hasten transition of the producer cells to the stages of development corresponding to biosynthesis of the target product. The green colonial alga *Botryococcus braunii* synthesizes C_{17}-C_{35} hydrocarbons in quantities reaching 75 percent of cell dry weight [24]. However, hydrocarbon synthesis by the cells is preceded by a lag phase of several days. Will isolation of an information-transmitting substance that would shorten the lag phase be successful?

Biopolitics and Its Application to Biotechnology

Concluding this survey of ecosystem biotechnology in application to technical bioenergetics, we will make a brief tour of biopolitics in order to demonstrate the possible ways of raising the effectiveness of biotechnological objects by utilizing their interrelationships in superorganismic biological structures.

Any role played by an organism in ecosystems, associations and populations (producers, consumers, reducers, aggressors, cooperators, isolates, dominants and subdominants) not only makes an impression upon its behavior but also determines preferential development of particular organs [13]. This role nullifies the individual features of the organism, but not completely. Two widely encountered situations are of interest to biotechnology.

1. Several different species and strains perform a similar role in a superorganismic structure—for example the role of the primary producer of organic matter in a fresh-water basin ecosystem. Biomass is formed at the expense of light energy by aquatic plants, algae, cyanobacteria and purple and green bacteria. Different groups dominate at different depths, but there is a zone in which three groups of producers function actively—the purple and green bacteria and cyanobacteria [11]. Presence of different species with partially coincident roles in an ecosystem is a factor that increases its stability. If for some reason one of the players of a role is taken out of the picture, another can replace it. Frequently there is also a synergistic effect that increases the productivity of the ecosystem (association, population): Different performers of the same role enter into cooperative relationships. From the standpoint of biopolitics, we can discern a clear analogy here with the increase in productivity of social labor resulting from cooperation.

There are two groups of archebacteria in a methane-producing association, one of which uses a mixture of H_2 and CO_2 while the other uses acetate as the substrate from which to form CH_4. The former group of methanogens stimulates the function of the latter [9]. Archebacteria utilizing H_2 and CO_2 reduce their concentration in the environment, eliciting so-called acetogenic restructuring of metabolism in the acidogenic components of the association. These microorganisms begin synthesizing large quantities of acetate. Development of methanogenic archebacteria consuming acetate is accelerated in this way. Consequently in the conditions of a methane tank—a reactor used to produce biogas—it would be suitable to use multicomponent associations, and not simply pairs of interacting species (fermenting anaerobe + methanogen), as in laboratory conditions [8].

2. One organism or a group of organisms plays several roles concurrently. Such a combination of roles is not possible for every organism: There are narrow and broad specialists. For example green sulfur bacteria (family Chlorobiaceae) usually perform only the role of primary producers, since they depend on sunlight as the sole source of energy accessible to them, while purple bacteria (especially of family Rhodospirillaceae) are capable of living both off of light energy and by utilizing organic compounds in the course of membrane electron transport—that is, they can play the role of producers, consumers and reducers. There are indications that ecosystems containing broad specialists function more stably and more flexibly, and that in certain situations, especially when the external conditions vary, they function more effectively. Narrow specialists are more vulnerable to changes in environmental conditions[29].

The physiologist A. M. Ugolev [22] interprets the concept "technology" from biological positions. He classifies digestion of food, movement of flagella and so on as "natural technologies." Sometimes the term "biotechnology" is used to mean "technology carried out by a living being." Such biotechnology is doubtlessly also ecosystem biotechnology, inasmuch as every living thing is organized in natural conditions into ecosystems. Following the principles of ecosystem biotechnology, we must strive for correspondence between proposed technological projects and the natural activity of living beings. Human biotechnology must become a part of natural biotechnology.

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Immune Response in Volunteer Donors Immunized With a *Pseudomonas* Vaccine

937C0122 Moscow ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII in Russian No 11, Nov 91 [manuscript submitted 8 Aug 90] pp 39-41

[Article by T. A. Makarenko, S. S. Balayan, A. I. Sergiyenko, Ye. S. Stanislavskiy, L. S. Yedvabnaya, I. A. Abramova, M. A. Krokhina, V. M. Rusanov, Scientific Research Institute of Vaccines and Sera imeni I. I. Mechnikova, USSR Academy of Medical Sciences, Moscow; Military Medical Academy imeni S. M. Kirov, Leningrad; Hematology Science Center, Moscow; UDC 615.371:579.841.11].015.46.07]

[Abstract] *Pseudomonas aeruginosa* infection is a complication observed in burn patients, cancer patients, and other surgical patients, and despite the availability of antibiotic therapy, the lethality rate associated with the infection is 60-70 percent. An earlier paper by the researchers here detailed the results of an experimental study of a pseudomonas vaccine based on soluble protein antigens of the cell wall of *P. aeruginosa.* The study established that the vaccine was not harmful to laboratory animals and that, in mice, it stimulates a protective immunity to *P. aeruginosa* infection. As an extension of that study, the work reported here tested the toxicity and immunogenicity of the vaccine on 119 volunteer donors. Rises in temperature to 37.1-37.4° C were classified as mild; rises to 37.5-37.9° C, as mid-range; rises to 38° C or higher, as strong. It was found that the vaccine induced mild responses in 15.9 percent of the volunteers and mid-range responses in 2.5 percent; the responses were gone 12-24 hours after inoculation. Only two donors exhibited a strong response, but, as with the other donors, the temperature normalized within 12-24 hours. Mild local reactions—i.e., hyperemia of the skin with a diameter of 2.5 cm or less and/or slight soreness around the injection site—were noted in 36.1 percent. Again, the reaction vanished after 12-24 hours in most volunteers, although it remained in a few volunteers for 48 hours. In 17.6 percent of the volunteers, the injection site developed into a painless, but hardened area that lasted for seven days. Blood and urine indices remained within normal ranges. The researchers concluded that the vaccine is a slightly reactogenic preparation that induced specific humoral immunity in 98 percent of the volunteers. The level of circulating anti-*P. aeruginosa*-antibodies remained high for up to five months. References 9: 7 Russian, 2 Western.

Infectious Diseases and Objectives of Medical Science and Health Care in the Prevention of Such Diseases

937C0130A Moscow ZHURNAL MIKROBIOLOGII, EPIDEMIOLOGII I IMMUNOBIOLOGII in Russian No 11, Nov 91 pp 2-7

[Article by I. N. Denisov, USSR Ministry of Health; UDC 616.9- 094:614.2(47+57); first paragraph is quote from F. F. Erisman]

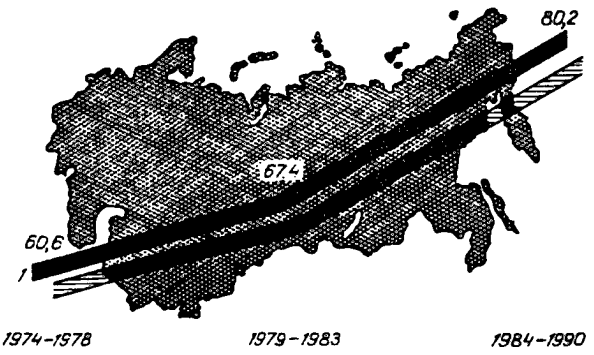

Fig. 1. Dynamics of average annual number of [cases of] infectious diseases in the USSR for the period 1974-1990 (in millions of cases)

Key: Curve 1 is the average number of cases of infectious diseases

[Text] *History gives us hope that universal education, improved social conditions, and the development of science will enable us to push farther and farther into the background our reigning epidemic diseases and, perhaps, rid the human race of them entirely.*

Our century represents the golden century of victories achieved in the struggle of physicians and the entire world community against infections. Smallpox has been eradicated. By comparison with the prevaccination year of 1957, morbidity for diphtheria has dropped almost 163-fold, poliomyelitis 156-fold, whopping cough 51-fold, and measles 16-fold. Only sporadic cases of the plague, typhus, and cholera are observed.

At the same time, without belittling the significance of the successes achieved in the struggle against a good many of the diseases that were once widespread, it would behoove us all to overcome one of the fallacies of the end of the twentieth century - - that infectious diseases have moved into the background, do not play a significant role in human pathology, and are not a pressing problem to health care.

Over the last 15 years, infectious diseases have exhibited a steady growth from annual levels of 60.9 million cases in 1974-1978 to 80.2 million cases over the last five years (Fig. 1). Direct and indirect economic losses from those cases exceed 15 billion rubles [R] a year.

Influenza and acute upper-respiratory infections account for more than 90 percent of all infections; the rest amount to only 6 million cases a year and consist mainly of intestinal and air- and water-borne infections.

There is another important trend that characterizes the epidemic situation for the country as a whole—the steady growth of infections of viral etiology, the percentage of which among all diseases except influenza and acute upper-respiratory infections has grown by 6.7 percent since 1974 and stands at 62.8 percent (Fig. 2).

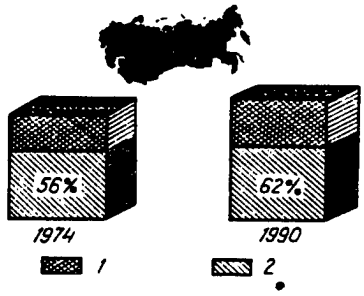

Fig. 2. Percentage of bacterial and viral infections (not counting influenza and acute upper-respiratory infections).

Key: 1—bacterial infections; 2—viral infections

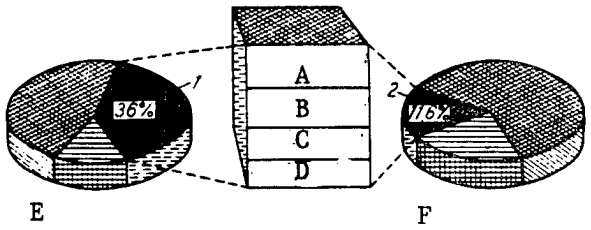

Fig. 4. Percentage represented by deaths from infectious diseases in the Central Asian republics (1986-1990).

Key: 1—percentage represented by deaths from infectious diseases; 2—percentage of the population of the Central Asian republics; A—Turkmenistan; B—Tajikistan; C—Uzbekistan; D—Kyrgyzstan; E—Deaths; F—Population

The epidemic process in the country is characterized by a marked lack of uniformity. Multiyear analysis of the infectious morbidity and mortality associated with those diseases makes it possible to separate the entire country into three groups: (1) republics with a high level of infectious morbidity—more than 1,000 cases per 100,000 population—and a mortality rate associated with the diseases of more than 40 cases per 100,000 population. This group includes all the republics of the Central Asian region—Uzbekistan, Kyrgyzstan, Turkmenistan, and Tajikistan (Fig. 3).

The population of that region accounts for 11 percent of all the country's residents, and the people in that region who die from infectious diseases account for more than 36 percent of all deaths (Fig. 4). Some 20 percent of all who die from infections in this country and some 58 percent of all who die before the age of 1 year are children born in that region. The second group (2) consists of Union republics with an average level of infectious morbidity of 500-1,000 cases per 100,000 population and a mortality rate of 15- 40 cases per 100,000—i.e., Kazakhstan, Azerbaijan, and the Russian Federation (Fig. 5). The third group (3) consists of the other Union republics, which have low levels of morbidity and mortality associated with infectious diseases—fewer than 500/100,000 and 15/100,000, respectively.

That calls for differentiated prophylactic and epidemic-control measures. To date, however, no such approach is evident in the activity of the ministry or the USSR Academy of Medical Sciences. It would seem that the development and implementation of complex regional programs for lowering the infectious morbidity could produce a quick, palpable effect.

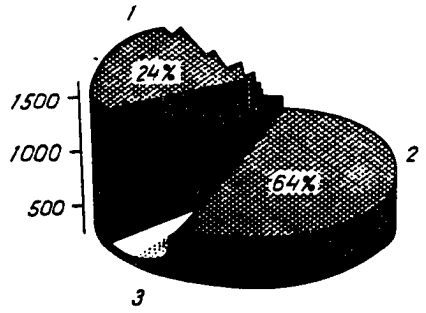

Fig. 3. Level of infectious morbidity in the USSR (in terms of average for the period 1986-1990).

Key: 1—average level of infectious morbidity in Uzbekistan, Tajikistan, and Turkmenistan (24 percent) and in the republic of Kyrgyzstan; 2—average level of infectious morbidity in Armenia, Kazakhstan, RSFSR, and Moldova (64 percent); 3—average level of infectious morbidity in Latvia, Estonia, BSSR, Georgia, Azerbaijan, Lithuania, and UkSSR.

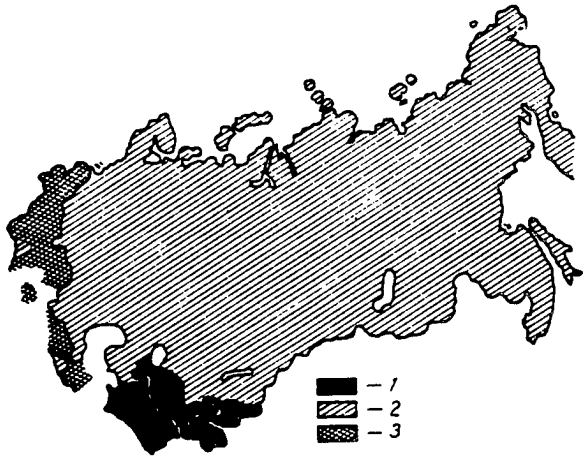

Fig. 5. Infectious morbidity in the republics of the USSR.

Key: 1—high morbidity; 2—average morbidity; 3—low morbidity.

Over the last 10 years, rates of decline have slowed considerably, and, in certain nosological—such as whooping cough, diphtheria, and poliomyelitis—morbidity has grown.

Since 1985, whooping-cough morbidity has grown almost twofold, and it stands at 13.09/100,000 population.

Morbidity for diphtheria has grown more than twofold since 1980, and its highest levels are noted in RSFSR, Latvia, and Tajikistan.

Particularly alarming symptoms of a lack of well-being are the outbreaks of diphtheria, whose incidence and intensity are growing.

If in 1988, a large outbreak affecting 58 people was recorded in Leninsk, Kazakhstan, then in 1990, an outbreak involving 688 people, 26 of whom died, was recorded in Moscow. The epidemic situation as regards diphtheria got worse in 1991 in the Ukrainian republic: in 21 of the 25 oblasts of that republic, a total of 330 cases were recorded, with 14 of them having a fatal outcome.

Regretfully, it must be said that the country that gave the world the vaccine for poliomyelitis, the country whose successes in reducing the morbidity levels of that infection inspired the physicians of many countries, is today one of the few countries in Europe in which that infection can be found.

The epidemic situation with regard to poliomyelitis became dramatically more complex in the past year (Fig. 6). A total of 312 individuals were diagnosed with it in the country, a figure that exceeds the 1989 level by more than fourfold. Morbidity has grown considerably in Azerbaijan, Armenia, Uzbekistan, and Turkmenistan.

An investigation of the outbreak in Azerbaijan revealed that more than 41 percent of the children who contracted the infection had not been inoculated, and 37 percent had had no information about inoculations.

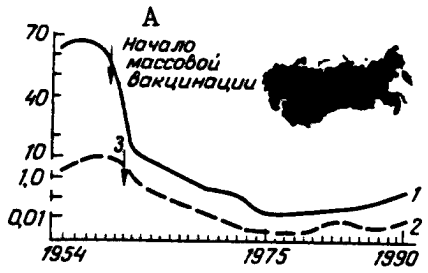

Fig. 6. Diphtheria and poliomyelitis morbidity in the USSR.

Key: Curve 1—diphtheria morbidity; Curve 2—poliomyelitis morbidity; 3—beginning of mass inoculations; A—Start of mass vaccination

Analysis indicates serious omissions in the creation of an immune interlayer of population. In 1989, only 79 percent of children under the age of 1 year were vaccinated for diphtheria in the country as a whole; only 57.5 percent were vaccinated in Uzbekistan; 61.6 percent in Kyrgyzstan; and 67.7 percent in Georgia. The situation is even worse for vaccination against whooping cough in the Russian Federation (60.3 percent), Uzbekistan (54.6 percent), and Kyrgyzstan (60.2 percent).

Only 74.6 percent of children in the country as a whole were inoculated against poliomyelitis on the proper schedule, and in the RSFSR and Uzbekistan, that figure was only at 68.6 percent and 61.2 percent, respectively.

In order to create an immune interlayer, 95 percent of the population must be inoculated.

The principal reason for the worsened situation is the unsatisfactory organization of inoculation-giving, which has become more so in recent years as a result of the worsening of the sociopolitical situation and the intensified migration of the population in the regions mentioned.

In December 1988, and then in May 1990, the board of the USSR Ministry of Health did an analysis of the status of immune-related prevention, uncovered shortcomings, and outlined a program of action.

All the measures that were outlined would be worthless if the vaccines were not of the proper quality. The production of preparations meeting the WHO requirements are a top priority and are an extremely serious problem to this day.

The last three years have seen cases—unprecedented in the entire history of immune-related preventive measures—in which the manufacture of vaccines in the country has been shut down because of the low quality of the preparations.

In December 1988, the country's only measles-vaccine production line, at the Moscow Enterprise for the Production of Bacterial Preparations, was shut down, and for five months, not a single dose of the preparation entered the health care sector. Even now, the volumes of production of the preparation have not gone back up to what they were initially. The vaccine manufactured does not meet WHO standards for thermal stability. A stabilizer for that factor, developed at the Moscow Scientific Research Institute of Viral Preparations, wasn't slated for introduction until this year.

In 1989, the manufacture of BCG vaccine was shut down at the Ministry of Medical Industry's NPO in Tashkent. The many promises to restore production are still not being kept in this, the second year since. Inoculation has been interrupted, and the current situation is already fraught with the complication of the tense epidemic situation associated with tuberculosis. Throughout the country, individuals with the latter infection number more than 500,000, and every year, nearly 100,000

people contract the disease—among them 7,000 children—and 20,000 die from various forms of tuberculosis.

The Achilles heel of our immunobiological production is that the most important vaccines—for poliomyelitis and measles—are produced by only one manufacturing enterprise. The above examples graphically illustrate the drawbacks of such a monopoly on production.

The most urgent task of the next five years is to create alternative production lines for the most important vaccines.

In the matter of the perfection of the strategy and tactics associated with immune-related preventive measures, the science center needs to develop methods accessible to practical facilities for the diagnosis of the status of the immune system, the correction of immune deficiency, and, as a result of that work, the transition to individual and regional schedules of inoculations.

In that connection, I would like to return to a conversation that took place in August 1990 at the board concerning the "development of clinical immunology." The country is creating a system of regional centers and laboratories that will study the state of the immune status of the populace as a function of ecological problems in a region and will make forecasts of immunity disruption on the individual and population levels on the basis of the data obtained. It would be best in the near future to perform a study of the state of immunity against infectious diseases and of the effect of chemical, physical, and biological factors on the state of immunity.

After 1977, when the issue of the problems and prospects of controlling infectious diseases was last discussed at a session of the USSR Academy of Medical Sciences, 20 new vaccines were developed and introduced, including seven live vaccines, 11 killed vaccines, and two subunit vaccines.

Today, up to the age of 14, a child receives 19 inoculations, including 11 parenteral administrations of six vaccines, whereas in 1977, the total number was 24. The number of renewed polio vaccinations has been cut back, and smallpox vaccinations have ceased, producing a great many complications.

More work should be done in cutting back the number of vaccine administrations through the creation of polycomponent preparations that produce longer immunity.

Success would seem to be at hand, but if we analyze how well our vaccines meet WHO standards, then we find that only 27 of the 49 that we currently manufacture meet WHO standards.

Among those that do not meet international standards are widely used vaccines such as measles vaccine and parotitis vaccine.

The tasks associated with the perfection of immunobiological preparations are divided into two independent areas. Underlying them are the perfection of existing vaccines and the development of fundamentally new vaccines (tables 1 and 2).

Table 1. Development of the Most Important Vaccines in the USSR and Abroad

Vaccine	Introduction abroad, year	Year of completion of development in USSR	Lag
Genetically engineered:			
hepatitis B	1986	1992	7-10 years
hepatitis A	1995	-	
rabies	1993	-	
chickenpox	1990		
cytomegalovirial	1991	-	
pertussis	1995	1995	5-10 years

Scientific research in the area of existing vaccines needs to focus on solving the following problems:

- replace multi-inoculation vaccines with single-administration vaccines
- raise the thermal stability of all vaccines
- develop vaccines that can be used soon after birth
- raise the effectiveness of vaccines, produce a long-term protective effect for vaccines against tuberculosis and whooping cough

Table 2. Development of the Most Important Vaccines in the USSR and Abroad

Vaccine	Introduction abroad, year	Completion of development in USSR		Lag
		Scientific development	Introduction into practice	
Subunit:				
pertussis	1986	1995	Not determined	10 years
intestinal	1990	1993	1995	5 years
hepatitis B	1982	1990	1993	11 years
hepatitis A	1996	1990	1995	-
meningococcal	1990	1995	Not determined	5-10 years

The next task facing the scientists of the country is the intensification of research on the creation of a new generation of vaccines.

In the growth of research in that area, there is a big lag—10 years or more.

The WHO prediction for the near future is predicated on the fact that for protection against the most widespread diseases, genetically engineered vaccines will be used, as will synthetic, subunit, liposomal, and antiidiotypical vaccines. The need for such stems primarily from the

fact that traditional vaccines do not solve the problems associated with the prevention of infections such as hepatitis and malaria.

The creation of combined vaccines is an area that holds promise.

To perfect immunization, the following problems must be solved.

There is a need for scientific substantiation of medical contraindications for preventive inoculations. And even though recently, as was mentioned above, such inoculations more than once been cut back, there is still a considerable difference between them and what WHO recommends in the matter.

Development should continue in the tactics associated with screening vaccinations of at-risk groups, with especial attention focused on the creation of specific and nonspecific agents of protection against influenza for pregnant women and newborns.

The Center for Immunoprophylaxis at the USSR Ministry of Health's Central Scientific Research Institute of Epidemiology should head that work.

Solving all the enumerated problems requires developing in the shortest time possible the consolidated state, Union-republic program Immunoprophylaxis, which includes the creation of vaccines, the organization of immunizations, specialized material-technical support and financing, and legal support that provides for the adoption of legislative acts regulating vaccine-related prophylaxis, plus public education.

As before, infections with the fecal-oral mechanism of transmission remain a representative group of human infectious diseases.

Morbidity associated with acute intestinal infections stood at 1.3 million cases in our country in 1990.

The economic losses from such infections exceed R160 million a year.

The numerous solutions and plans consisting of measures that have been adopted by councils of ministers of Union and autonomous republics and local soviets of people's deputies remain unimplemented and poorly monitored because no demands have been made, because those who are to implement the measures are irresponsible, or, sometimes, because the measures themselves are not realistic.

Organs of the state sanitary inspectorate, by focusing their attention on defining future problems and by justifying their work by levying many penalizing sanctions, have weakened the work involving hygiene education of the workers at enterprises associated with public dining, commerce, municipal services, food production, and food processing.

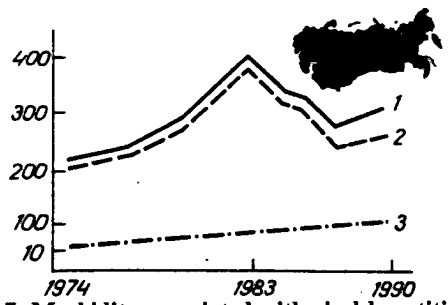

Fig. 7. Morbidity associated with viral hepatitis in the USSR.

Key: Curve 1—total of hepatitis A and B; Curve 2—hepatitis A; Curve 3—hepatitis B

Over the past five years, morbidity associated with salmonella has also exhibited a trend of growth.

The most serious problem for the country's health care sector is morbidity associated with viral hepatitis. Every year, 700,000- 900,000 cases of such infections are recorded; in 1990, morbidity exceeded that of the previous year, reaching 317 cases per 100,000 population (Fig. 7). The etiological structure of viral hepatitis within our country is represented by five forms of hepatitis that differ in nature: hepatitis A, B, C, D, and E. Viral hepatitis A accounts for 86 percent of all cases.

Hepatitis B is today a dramatic problem for our health care sector and that of the world community. Every year, throughout the world, more than 50 million people become infected with hepatitis B. Cirrhosis and primary cancer of the liver, plus chronic hepatitis are most often the result of the individual having had hepatitis B, from which more than 1 million people die every year, throughout the world.

In 1990, in our country, there were 110,000 cases of that infection.

The highest level of morbidity is in Uzbekistan, where individuals with hepatitis B constitute more than 34 percent of all hepatitis B patients in the country.

Every year in our country, more than 5,000 people die from viral hepatitis, and the overwhelming majority of them have hepatitis B.

Blood transfusions and other medical manipulations play a substantial role in the transmission of the infection at present. Genetically engineered and plasma vaccines created abroad are safe and highly effective, and some 30 million people throughout the world have already been immunized with them.

The year 1989 saw the one-time purchase of a vaccine that was sent to the Aral region and to a number of other areas with a high level of carriership. To date, 94,000 children have been immunized, and vaccination involving more than 190,000 doses will be completed in 1991.

According to estimates made by a group of technical WHO experts, massive immunization of newborns and young children is the most effective measure for preventing hepatitis B and will make it possible to eradicate that infectious disease.

The USSR Academy of Medical Sciences Institute of Virology has been developing a plasma vaccine for more than 10 years and a genetically engineered vaccine for nearly five years; both are analogous to foreign vaccines. The manufacture of commercial series has been postponed systematically over the last three years.

The situation with regard to the creation of hepatitis B vaccines is like a mirror in its reflection of our science's lag in a most important area—the development of agents for specific prevention.

Such slowness cannot satisfy our needs today. That reproach is meant not just for the scientists, but also for those who today are making decisions about the issues associated with the organization of immunizations and the production of vaccines in this country.

As the principal areas of development of the health care sector up to the year 2000, the prevention of influenza and the prevention of acute upper-respiratory infections have been defined as top priorities; economic losses of the state from such diseases are R3.5 billion.

That group of infections to date is not controllable by specific preventive agents, primarily because the etiological sources of those diseases are more than 200 viral agents, as well as a number of bacterial vectors.

Further improvement of the prevention of those infections must be carried out in the following primary areas:

- development of recombinant vaccines, and use of them in combination with immune-system stimulators
- use of special agents, including antiviral preparations for emergency prevention that raise nonspecific resistance and help to normalize the body's immune system
- prevention of seasonal hypovitaminosis and bolstering of the adaptational capabilities of the body during the period of natural decline of immunity factors through the use of vitamins and adaptogens of vegetable and animal origin

A significant place in human pathology is held by helminthiasis and other parasitic illnesses. Every year, as many as 4.5 million people are diagnosed as having enterbiosis, ascaridosis, trichocephalosis, and other forms of helminthiasis.

The number of those invaded is equal to—and in some years exceeds by 1.5-fold—the number of individuals contracting infectious diseases, not counting those with influenza or acute upper-respiratory infections. The economic loss from helminthiasis is as high as R1.7 billion a year.

The situation with regard to malaria has worsened in recent years, and active foci continue to exist in Tajikistan, Uzbekistan, and Azerbaijan, where 300-400 cases a year are diagnosed.

The true number of cases of parasitic diseases within the country is, according the expert estimates, more than 40 million.

Invasion with parasites is accompanied by permanent toxic action on the human body, manifesting itself as allergies, suppressed immune system, retardation of the mental and physical development of children, avitaminosis, and damage to the cardiovascular system, pulmonary organs, and digestive-tract organs.

The development of new agents for the prevention and treatment of parasitic diseases is being performed with little effectiveness, and the financing of that research is inadequate.

The Ye. I. Martsinovskiy Institute of Medical Parasitology and Tropical Medicine is not doing all the science it could on that important segment of the work.

To eliminate those deficiencies, the Complex Program of Scientific Research on the Diagnostics, Treatment, and Prevention of Parasitic Diseases Among the Populace Up to the Year 1995 has been created.

A complete surprise to the world community was the discovery in 1979 of the HIV infection, better known to a broad segment of the public by its extreme manifestation—acquired immune deficiency syndrome (AIDS)—which at present is the object of serious concern among the governments and people of all countries. A great many special publications have been devoted to that problem in recent years, which is why I will not spend any time on that topic here.

On the increase is the number of diseases—as well as the percentage they represent among diseases of infectious pathology—that are caused by conventionally pathogenic microorganisms that are responsible for more than 100 nosological forms of pyoinflammatory diseases.

The extent of such diseases and the immense damage they do to the health of the populace and to the country's economy can be classified among the top-priority problems associated with the battle being waged by medical science and the practicing health care sector.

In the United States, for example, more people die from sepsis alone than from all the other infectious and parasitic diseases taken together that must be recorded.

Every year, 70 million people—primarily middle-aged and elderly—are hospitalized in our country's treatment facilities. Some 5 million of them develop hospital-acquired infections, half of them in the postop period. The length of hospital stays grew to 23 million bed-days, and the losses from the lack of production of additional product is R800 million.

The level of hospital-acquired infections is the most important indicator of the quality of medical care provided the populace. Solving that problem requires immense material expenses and radical improvement of the material-technical base of facilities. At the same time, it needs to be emphasized that even under the existing conditions, painstaking performance of traditional measures can reduce that morbidity level by at least twofold.

At present, a distinct group of infections with a transplacental, or vertical (mother-fetus), route of transmission has been formed.

Congenital rubella is one of the infections that is to be eradicated by the year 2000. Every year, some 400,000 cases of that disease are recorded in our country, primarily among young children. In addition, as selected tests show, 18 percent of women of childbearing age do not have any immunity to that infection. The broad circulation of the virus puts unborn children at high risk, forming in them congenital defects and having a large effect on the level of infant mortality.

The only means of specific prevention of rubella is vaccination.

The RSFSR Ministry of Health's Pasteur Leningrad Scientific Research Institute is doing work to prepare a vaccine for release. Doing everything possible to introduce the vaccine as quickly as possible is the task of scientists and workers of the practical sector.

Cytomegaloviral infection causes serious pathology in the fetus. An examination of 236 women afflicted with that infection showed that in 5.5 percent of cases, the babies born were ill; in 31.5 percent, spontaneous abortions took place; in 7 percent, there were stillbirths; and in 56 percent, nonviable babies were born, among them children with damage to the central nervous system and cirrhosis of the liver.

The growth in the role of cytomegaloviral pathology is helped along by disruptions in the ecological balance, immunodepressive therapy, and the spread of HIV infection.

Of course, those figures are far from the true dimensions of the extent of the infection, and in most cases, diagnosis is made very late.

Scientific research in the prevention of infectious and parasitic disease is being performed by 43 research institutes at which 16 academicians and 21 corresponding members work.

In the last five-year plan alone, in the field of epidemiology, virology, and microbiology, 27 doctoral dissertations and 185 candidate dissertations were defended, 57 monographs were published, and nine textbooks for institutions of higher learning were published.

At the same time, we cannot be satisfied with the state of affairs in epidemiological science. In the early part of the century, it underwent rapid growth and was on the leading edge. And it is indisputable today that it was our country that took the initiative in the eradication of smallpox, that our country took an active part subsequently in performing the program adopted by the world community and so successfully completed.

Without claiming to know the absolute truth, I would think it advisable to note the error in the notion that epidemiology must involve itself primarily with infectious diseases. As foreign practice shows, the use of epidemiological methods in the study of noninfectious pathology has enriched classical epidemiology.

The number of scientific publications in the field of epidemiology has declined markedly. There are no epidemiological schools, and young scientists do not consider it prestigious to be involved in epidemiology, preferring more private areas to it.

All the epidemiological research institute of both the USSR Academy of Medical Sciences and the ministry that are involved in solving a problem that is responsible for losses that, according to the most conservative estimates, amount to R20 billion a year are maintained on a total of R27 million a year.

While it must be said that not everything is being done that could be done to create a legal basis for giving the science groups more independence and giving the research new forms and methods, one still can't help but reproach the directors of the institutes for the fact that enough small joint ventures, for example, which hold such promise for the achievement of the end result, have been introduced into practice.

We are working at present in a situation in which all spheres of activity of society—economics, politics, and administration—are undergoing profound changes and in which the notions and stereotypes that have come about and have turned out to be unstable are changing. In this generally positive process, one must not disperse everything that is positive, everything that was brought about by our ancestors and teachers and achieved by the country's health care sector and the world community.

Health Assessment of Protective Coveralls

937C0120A Moscow GIGIYENA I SANITARIYA in Russian No 11, Nov 91 (manuscript received 21 Aug 90) pp 35-38

[Article by P.V. Dubiley, G.G. Zhilyayev, G.P. Sharnin, V.A. Kachalkin, I.A. Bolshakov and B.M. Chernov, Kazan Chemical Scientific Research Institute; UDC 614.895.5-07]

[Abstract] The physiologic status of 22-40 year old male volunteers was the key criterion used in evaluation of chemically protective coveralls under controlled conditions (air temperature 26 or 40° C; ambient temperature 30 or 46° C; relative humidity 20 or 55 percent). Work was simulated by physical exertion equivalent to 1340 kJ/h with the test terminated in 4 h or when sublingual temperature reached 38.5° C and heart rate 170 beats/min. The end point of the study was correlation of the physical characteristics of the coveralls (number of layers, transpiration and pervaporation rates, air pemeability) with health-acceptable duration of job performance. The resultant data led to derivation of empirical equations for projecting length of work possible in a given type of coverall. Figures 1; tables 3; references 8: Russian.

Health Safety Regulations for Transdermal Agents

937C0120B Moscow GIGIYENA I SANITARIYA in Russian No 10, Oct 91 (manuscript received 17 Jul 90) pp 6-8

[Article by V.A. Kondrashov, Scientific Research Institute of Hygiene and Occupational Diseases, USSR Ministry of Health, Leningrad; UDC 613.632:615.91.032.77]-07]

[Abstract] A comprehensive assessment is provided of the rationale underlying determination of maximum permissible levels for cutaneous exposure to chemicals. The discussion covers conventional toxicologic approaches, including animal studies, applied to the special situation posed by skin and other surfaces. The resultant findings were used to classify chemicals in their various states (solid, liquid, gaseous) as to toxicity in acute and chronic exposures. As a result, the concept of maximum permissible levels for cutaneous exposure has received wide acceptance and is undergoing further refinement. Tables 2; references 2: Russian.

U.S.-Russian Cooperation in Cardiosurgery

937C0146A Moscow NEZAVISIMAYA GAZETA in Russian 27 Aug 92 p 6

[Article by Dmitriy Frolov: "Capital's Cardiosurgeons at World Level: Something You Can't Say About the State of This Sector in the Country"]

[Text] The epithet "unique," which is generously used for some reason as a compliment each time the discussion turns to the accomplishments of Soviet medicine, may be attributed to the full extent to the department of emergency surgery and intensive therapy for children in their first year of life with congenital heart defects, under the Cardiovascular Surgery Institute imeni Bakulev. The department is truly unique, which is exactly what the problem is: Each year in the CIS 40,000 youngsters are born who, according to the idea, should become its patients, with almost half of them being Russian. Seventy percent of these children die without living out the year, although had they been born anywhere in Western Europe or North America, such a fate would have awaited only 15 percent of them. Cruel as it may sound, it is nonetheless entirely obvious that the situation will not change in the immediate future: Pediatric cardiac surgery is simply beyond our pocketbooks.

To persuade oneself of this, it would be sufficient to simply take a peek at the ward, where the window latches are just about the only thing manufactured in this country. Everything else, be it a heart monitor, a metering unit or a child's bed, was manufactured outside this sixth of the terrestrial world, and has no acceptable analogues in our country. The same can also be said for pharmaceuticals and disposable instruments and materials, the cost of which totals $1,200 for a single operation. The operation itself costs the patient $80,000-120,000 in the United States. In our country it was of course free of charge until recent times, but now this pertains only to Russian citizens, while residents of the so-called near frontier must pay for the care. The tentative price of the operation is up to R86,000. It may be possible that this money might somehow influence the wages of medical personnel, but it will clearly make no changes in the status of materials and medicines. Consequently the idea of collecting payment in hard currency has already been raised on several occasions; as far as Russians from other cities are concerned, money for treatment at the capital used to be provided either by them or by rayon health departments having jurisdiction over their place of residence, in compliance with the well known resolution of the Moscow government. But judging from everything, the transition to insured health care will not promise a flow of money to cardiosurgeons: According to the present version of the law, these operations will be paid for out of public health funds, which will hardly be much larger than the current medical budget.

In the meantime the Bakulev Institute is solving the problem in a way that has become traditional in the country—through donations from well-to-do sponsors. For example owing to the help of the Troitsk Institute of Innovative Thermonuclear Research and the European office of the American firm GORE and Associates, which provided adhesive compound and plastic materials to the surgeons, the institute has managed to introduce a new type of operation to correct one of the most severe and frequently encountered congenital heart defects, one meaning certain death of the child.

The reference here is to so-called transposition of major vessels, where as a result of disturbed development of the fetus the aorta and the pulmonary artery in a sense trade places, thus disturbing the entire circulation: Rather than oxygen-enriched blood, the heart pumps dark venous blood through the arteries. Up until now, this defect has been corrected in our country by surgical treatment that changes the "architecture" of the atrium. However, 10-20 years later almost half of the patients that undergo this operation begin suffering arrhythmia and breathing difficulty, and progressive limitation of mobility arises. On the other hand the new method of surgical correction, which is already well known in the world, has been inaccessible because it requires transplantation of coronary vessels, which actually restores the heart's normal anatomy.

Specialists of the Bakulev Institute were able to solve this problem, and now their center possesses practically the entire modern arsenal of surgical correction, and it is not inferior in its possibilities to the world's leading clinics. And although we can only dream about providing the same volume of such expensive forms of health care that are provided in the West, patriots of Russian medicine have now received a truly flattering confirmation that the rumors of its death were greatly exaggerated.

Ukrainian Health Minister Approves Autovaccination

937C0146B Kiev VECHERNIY KIYEV in Russian 15 May 92 p 2

[Article by Nikolay Zakrevskiy: "Your Microbes—Your Cure"]

[Text] **The Kiev Autovaccination Center cures chronic ailments against which traditional healing methods are powerless.**

The stories below have something in common with bedtime stories. The kind that carry the secret hope of universal sorcerer-healers and the universal miracle of healing. A woman from Kiev—an elderly teacher—underwent a simple operation followed by a course of therapy. But the wounds did not heal—the focus of inflammation transformed into a persistent suppurative process, which soon engulfed nearby portions of the body, including the ribs and part of the sternum. Osteomyelitis, the doctors asserted, attempting to stop the disease with antibiotics and antiseptics. But when even this didn't help, the surgical knife was placed into motion: operations, anesthesia, injections.... However,

the ailment would not let up, and the disease progressed. There is no way of telling how much suffering the woman would have had to undergo, had doctors of a specialized autovaccination center not come to her assistance. Her illness, which would not yield to the tested methods of medical practice, backed off after a course of vaccinations.

And then there was Nastenka, a 16-year-old girl who could get no respite from angina and from chronic influenza. Trips to polyclinics and visits to doctors helped to reduce the severity of illness, but alas, they did nothing to do away with the continually recurring tonsillitis. An autovaccine administered to the young girl at the center became an insurmountable obstacle to the former ailments.

When I visited the center and acquainted myself with the healing practice of its specialists, I learned of other heart-warming stories: Two courses of vaccinations were found to be sufficient for a certain instructor at a Kiev VUZ to rid himself of chronic prostatitis of 15 years' duration. Just a single course of treatment with autovaccine provided salvation in a struggle against many years of chronic bronchitis suffered by a certain day-care provider.

In the year that the center has been in existence, it has received a total of over 2,000 patients. Note that this is with six permanent associates. People come to it from different cities in all of Ukraine and from countries adjacent to it. And this is understandable, since after all, a center like the one in Kiev simply doesn't exist in the CIS countries today.

"Vaccination is not a new method in medicine," said V. V. Sologub, the scientific director of the autovaccination center.

"Specifically, it has its origins in the times of Louis Pasteur, and it has been in use since the beginning of the present century. The methods of making and using autovaccines are of course changing. In our opinion we selected the most effective, and we are using a special solution that helps to render harmless the microbial agents that are responsible for chronic disease and simultaneously promotes effective stimulation of immunity. On the whole, our method has been tested out, and it has been permitted for use in general clinical practice by the Ukrainian Ministry of Health."

The explanation of the therapeutic properties of autovaccine is rather simple. An autovaccine is an individual immunological preparation (from the word auto, meaning one's own in Latin). It is made from microorganisms isolated from a focus of inflammation in a specific patient. And it is used to stimulate active immunity against agents of the inflammatory disease in the same patient. Medicine made to order, so to speak.

Understandably the process of making the autovaccine is labor-intensive, which means that it is more expensive than assembly line production of the same antibiotics. This is one of the reasons why widespread manufacture of individual vaccines has not become part of our medical practice. Except, as medical workers and microbiologists say, in cases where the health of the powers that be or of persons of close kin to leading medical luminaries has been concerned.

No, a "golden middle" was found in medicine, predominantly foreign—so-called polycomponent vaccines were developed. Each such healing agent is capable of destroying microbes of a single species, which of course makes it universal but not always effective. In the same way that people differ from one another, microorganisms sometimes differ, despite their overall similarity. They differ in their deleterious effect upon the human body. It took the scientific enthusiasm and, if you will, the medical honor of Kiev doctors—M. L. Rozhavin, I. Yu. Mikityuk, V. A. Nudga, V. V. Sologub (sufficiently competent specialists in clinical microbiology having experience in medical practice and scientific research)—in order to not only revive the old, forgotten methods, but also to initiate discussion of them as a new, important, promising direction of medicine.

Chronic suppurative-inflammatory illnesses are among the most serious medical problems today. Antibiotics and other chemical therapeutic preparations are traditionally paid homage to in the treatment of persons with such recurring illnesses. However, the treatment results often boil down not to the patient's complete recovery but only to suppression of aggravated symptoms. This is precisely where the autovaccine came to the rescue. Experience of the center's work shows that autovaccine makes it possible to deal successfully with chronic diseases such as furunculosis, otitis, cystitis, urethritis, vaginitis, trophic ulcers, erysipelas, chronic pulmonary diseases, asthma and a number of others. Dealing with them successfully, let me note, after traditional medicines and treatment methods, tried out on patients over a period of a number of years, had not resulted in the desired recovery.

It would seem that this fact alone should attract the attention of the leadership of the Ukrainian Ministry of Health to the work of the Kiev Autovaccination Center. There are also other facts that shouldn't be ignored either: the decrease in effectiveness of antibiotics and other chemical preparations in the treatment of chronic illnesses owing to the body's habituation to them; the body's chemical overload, evoking negative side effects; the decrease in immunity of people, especially in areas affected by the accident at the Chernobyl Nuclear Power Plant and, finally, the increase in the number of cases of infections contracted within the hospital, which have become the scourge of hospitals and polyclinics. All of this essentially makes use of the autovaccination method proposed by Kiev medical personnel not only promising but also to some degree a salvation.

"By utilizing the principles of designing autovaccines," Viktor Vladimirovich continued, "out of hospital strains

isolated in, let us say, the last half year within a particular department of a hospital, we can manufacture a polyautovaccine—a preparation for preventive immunization of patients that are to undergo treatment in a surgical hospital."

In other words, it would be possible to reduce the risk of contracting an infection while in the hospital to naught.

Of course, this is as yet only a dream of Viktor Vladimirovich, although it is a sufficiently grounded one, if we carefully read the items and divisions of the scientific-practical program of this center. The one unfortunate thing is that expansion of the volume of therapeutic care (each month the center presently receives 100-150 outpatients) and research are being held back by the absence of material resources. The program, by the way, is written for a 3 year period, and it foresees creation of the same kind of polyautovaccine to treat some of the most widespread forms of chronic diseases. Consequently wouldn't it make sense to try to make the dream a reality? This idea looks good not just from a medical standpoint alone; it looks good even from a purely economic standpoint.

Just the most approximate calculations regarding the functions of city hospitals show that the expenses of treating and maintaining patients with infections that they contracted while in the hospital, which, as we know, significantly worsen the state of patients and lengthen their stay in medical institutions, such that the outlays on their treatment naturally grow—this pertains primarily to burn, obstetric, urological and traumatological hospitals—are several times more expensive to the state than making the polyautovaccine and conducting immunizations.

By the way, certain preconditions already exist for solving the problem of financing the scientific program of the autovaccination center, such that a microbiological and an immunological laboratory could operate with modern equipment and a staff of qualified specialists. For example, it is currently an accepted practice to subject surgical clinics to bacteriological and epidemiological examination. All that remains to be done is to use the isolated and identified strains of bacteria to make preventive polyautovaccines.

"Nor will we discount the fact," said V. V. Sologub, "that part of the money needed to carry out the scientific research program could be returned through the sale of autovaccines by the vaccination center, and in the future, as the program is implemented, through the sale of licenses on the preparations developed here and through income obtained from their sale."

I hold in my hands some comments from well known medical scientists regarding the use of autovaccine. "Introduction of this highly effective method into medical institutions of different profiles in the republic will promote successful treatment of patients...," believes Professor L. L. Gromashevskaya of the Kiev Scientific Research Institute of Epidemiology and Infectious Diseases imeni L. V. Gromashevskiy. "I feel that use of autovaccine combined with basic therapy is one of the promising methods of treating patients suffering chronic inflammatory diseases"—this is the opinion of A. V. Rudenko, director of the microbiology laboratory of the Kiev Scientific Research Institute of Urology and Nephrology.

Well, medical specialists have voiced their opinions. Now it's the turn of the leadership of the Ukrainian Ministry of Health to act.

Belgorod Vitamin Products Meet GMP Standard

937C0146C Moscow IZVESTIYA in Russian 3 Sep 92 p 3

[Article by Yevgeniya Manucharova: "Belgorod Begins Producing New Pharmaceuticals Against New Diseases"]

[Text] **The Belgorod Vitamin Combine has introduced production of pharmaceuticals at the GMP level—that is, at a level satisfying world standards. The first lot of preparations that had formerly come only from Holland will reach the pharmacies in September.**

Beta-carotene. De Nol. What does the ordinary inhabitant of Russia and the CIS know of these pharmaceuticals? It is precisely he, after all, that needs them right now. Every foreign visitor stocks up with them before crossing our border. And there is good reason why beta-carotene is added even to popular beverages (such as, for example, to the citrus drink Tampico, which is sold in our country).

Beta-carotene is a derivative of vitamin A. It is characteristic that this is a vitamin. Substances of this series have been raised by medicine from the class of general fortifying compounds to the rank of potent therapeutic ones. Their effectiveness has turned out to be so high that pharmacology is currently enjoying a real vitamin boom. The range of use of vitamins is extremely wide: from helping infertile men (vitamin C) to treatment of ischemia (vitamin E). Derivatives of vitamin A eliminate radionuclides from the body.

And the latter are unfortunately being accumulated by all of us, without our knowing it. Including by inhabitants of those regions about which official statistics report: The radiation background does not exceed normal. The problem, you see, is that people don't stay put. Everything might be normal in a person's home, but then he might travel somewhere else (to work for example) where the background is different. And even if the amount by which the norm is exceeded is not great, radionuclides do accumulate. They have to be actively eliminated from the body, which is why everyone needs beta-carotene.

Despite this, our pharmacological industry does not produce it. It is only planning to do so (as is obvious

from the specific-purpose program to eliminate the consequences of the Chernobyl disaster). The country purchases it with hard currency for severely exposed people. Even one of our leaders in vitamin production—the Belgorod combine, which produces vitamin A, has only been able to experimentally produce 5 kilograms of beta-carotene thus far. It is not in a position to initiate industrial production—that would take a lot of money. Completely new modern procedures and a new level of production are required, inasmuch as our industry is now obligated (by new agreements) to satisfy the stiff requirements of an international standard—GMP. Until this time, our standards had been totally different.

Had the Belgorod combine possessed the possibility other countries typically have for obtaining hard-currency loans, the matter would be simply solved: Go out and buy the "know-how." And it wouldn't take long for the combine to pay off the loan. Pharmaceutical production is an extremely profitable venture. It is surpassed in profitability in the world only by diamond mining and the drug trade. Pharmaceuticals are expensive in the international market. (An American, for example, is compelled to give up a month's wages for them yearly).

Western pharmacological firms are very much interested in what the Belgorod Vitamin Combine produces. England offered to buy up all of its ascorbic acid—vitamin C (the quality of this preparation satisfies the foreign purchaser). There are also many wishing to obtain vitamin A, even if it doesn't satisfy the GMP standard. The preparation turned out to be so greatly needed and profitable for the big Slovakofarma that the Czechs are cooperating with the Belgorod combine in vitamin production.

This was one of the economic maneuvers by Belgorod aimed at attaining the GMP level in relation to the most important pharmaceuticals. The plant actively opted for cooperation with Dutch pharmacologists as well (Brocades-Steethman & Pharmacia) in order to produce De Nol—a preparation which the inhabitants of Russia and other CIS states need no less than beta-carotene. The fact is that the quality of the diet has decreased dramatically in the former USSR, and consequently the number of people suffering from gastric ulcers and their precursor, gastritis, has increased. There are not enough pharmaceuticals for such patients. Even in better times the demand for them was only 20 percent satisfied.

The state-run Farmindustriya Corporation and the vitamin combine signed an agreement with Brocades-Steethman & Pharmacia. The Netherlands have already imported the necessary equipment, materials and substances into Belgorod to produce the preparation. The agreement foresees that in the future, De Nol will be produced out of our own raw and other materials. This is why Kursk has been included in the project—it will supply the raw materials.

The equipment was installed, and it is operating. But the raw materials still have to be purchased with hard currency. And so the combine is asking that it be allocated a certain part of the money that we pay out today on imported De Nol. With this money, it will obtain the preparation in a cheaper variant—unpackaged—from the Dutch. This will allow the country to economize $3.3 million on each million packages.

The important first stage is now beginning: Automatic machines in Belgorod will begin stamping out blisters containing De Nol tablets and packaging them in boxes bearing the brand of the vitamin combine and Brocades. In September, 40,000 packages will reach Russia's pharmacies. Is the director of the combine, Leonid Afanasyevich Gorbach, pleased with this? No, not yet: The orders for De Nol coming from pharmacies of the CIS states require many times more.

The state-run Farmindustriya Corporation is organizing training in the use of De Nol for practicing physicians together with Brocades. The training will begin with a scientific seminar, which will be attended by public health organizers of different regions of the CIS.

'Peptos' Director Describes Center's Peptide Products

937C0146D Moscow ROSSIYSKAYA GAZETA in Russian 29 Oct 92 p 4

[Interview with Vladislav Isaakovich Deygin, general director of the Peptos engineering center for peptide preparations, by correspondent Mariya Nikolayeva; place and date not given: "Pharmacy Shelves in the Next Century"]

[Text] It is no accident that allergies and AIDS are called the diseases of the 20th century. We breathe poisoned air, we eat contaminated food, and we find ourselves in stressful situations from one day to the next. This is what creates breaches in our immune system.

There are many pharmaceuticals in the West capable of plugging these holes to one degree or another. But what hope is there for us? This was the topic of correspondent Mariya Nikolayeva's discussion with Vladislav Deygin, general director of the Peptos Engineering Center for Peptide Preparations of the Russian Academy of Sciences and an adviser to the Russian Supreme Soviet on medical matters.

[Nikolayeva] Vladislav Isaakovich, you are now working on the creation of a group of preparations under the intriguing name "Pharmaceuticals of the 21st Century." What sort of pharmaceuticals are these, and for whom are they intended?

[Deygin] The preparations our center produces are a completely new generation of pharmaceuticals of biological origin. They are needed by each of us for the body to exist normally in these difficult days. As an example

Timogen not only improves the body's defensive properties but also relieves allergic reactions, and helps against most skin diseases and does in fact increase life span.

When we know for certain that a disturbance of the work of the immune system is associated with its overall depression or the action of radiation, we can boldly prescribe a course of treatment with Timogen. It is being used on a permanent basis by personnel involved in disaster relief efforts at the Chernobyl Nuclear Power Plant and by workers of nuclear power plants and the main conveyer of the Volga Motor Vehicle Plant.

Another preparation, Dalargin, is a unique ulcer treating agent. Gastric and duodenal ulcers heal quickly.

[Nikolayeva] Many believe that the appearance of biostimulators and the spread of natural medicinal drugs, used in particular in Eastern medicine, will sharply reduce the need for resorting to chemotherapy.

[Deygin] My attitude toward chemotherapy is more on the positive side.

Many chemical pharmaceuticals possess extremely high effectiveness, and they act usefully. However, some of them do have side effects. Our drugs have a milder action. For example the only problem with the peptide preparation Dalargin is that it reduces arterial pressure.

[Nikolayeva] With what sort of medicines will our home medicine cabinets be filled in the immediate future?

[Deygin] Besides preparations that keep the internal system "under observation," we need antistress drugs that would help us adapt better to modern conditions. It's no secret to anyone that psychological discomfort is precisely what leads to alcoholism and drug addiction. A new preparation we have developed (its development name is Opilong) is intended precisely to quench any "interest" that may arise in narcotic substances before it's too late.

Russian-Danish Pharmaceutical Joint Venture Planned

937C0146E St. Petersburg SMENA in Russian 3 Oct 92 p 3

[Article: "There Will Be No Problem With Insulin"]

[Text] Bent Dzhensen [transliteration], a representative of the Danish firm Novo Nordisk, reached agreement yesterday at a meeting of the mayor's committee on social problems to establish a joint venture with the St. Petersburg Farmatseya Association. Association general director Angelina Bystrova expressed her readiness to create an insulin production line at her enterprise. Incidentally a consignment of insulin was recently sent free of charge to St. Petersburg by the Danish government.

Novel Russian Cancer Therapy Receives U.S. Patent

937C0146F Moscow TRUD in Russian 13 Nov 92 p 2

[Article by political reviewer Vitaliy Golovachev: "...For a Report to the Russian President: The Fate of a New Cancer Treatment Method to Be Decided"]

[Text] A new ray of hope recently appeared in the struggle with cancer, one of this century's terrible diseases. Hundreds of people with diagnoses of sarcomas, melanomas and carcinomas (different forms of cancer) were saved in Russia owing to a new, extremely promising treatment method. Its authors include inventor and scientist V. F. Gudov, Professor V. P. Kharchenko, director of the Scientific Research Institute of Diagnosis and Surgery, the Nizhegorod Professor N. Ye. Yakhontov, and a number of other specialists. U.S. patent No. 5067952 was awarded in November of last year to the new method, which is being used successfully by Russian doctors. TRUD explained all of this to readers in a series of articles (6, 9, 11, 16, 30 June, 2 July, 8 September). Let us recall how a therapeutic effect is achieved. Microparticles of iron (sometimes invisible to the unaided eye) are injected into the tumor. These particles make it possible to heat the neoplasm with a high-frequency field uniformly, with a precision of tenths of a degree. At a temperature of 43.5 degrees up to 100 percent of the cancer cells within the heating zone die.

These are of course only the first steps, and although such treatment has been carried out for several years already, it might be too early to make any far-reaching conclusions. But even these first steps prove the research to be promising.

The articles elicited a wide response in our country and abroad. At the request of readers the editor's office established a public fund to support the new cancer treatment method, and collection of money, the absence of which is holding back large-scale research and practical therapy based on ferromagnetic hyperthermia, was announced. The public fund already has over half a million rubles in its account, but unfortunately this is not enough to establish a specialized clinic.

A certain American businessman expressed his readiness to use his own money to build our country's first private Russian-American clinic that would make wide use of the new cancer treatment method. We would hope that the government will meet him half-way, and support this interesting initiative.

There are many other proposals as well. Here for example is a letter we just received from Australia written by Nikolay Kovalenko, an Australian citizen of Russian descent. "I read your article '289 Given the Gift of Life'," he writes, "with delight and the hope that a possibility has finally appeared for helping people suffering cancer. I decided not to limit myself to just delight and hope, and try to do something practical. I made copies of the article. I intend to organize its translation

into English, distribute it to local newspapers and send it to doctors in hospitals. The next step will be an attempt to organize an international public fund to support the new method in Australia. We need to establish an international organization with branches in all countries. And draw up a charter. We can create an international joint-stock company. In this case 55 percent of the controlling capital should be in Russian hands, the Russian state and private individuals, without the right of sale of Russian shares outside of Russia. In the future we could organize trips to Russia for cancer patients for treatment at a hospital built with money from the international joint-stock company. May God aid you in your effort."

It's a good thing that foreigners responded with such great interest to the highly promising developments of Russian specialists. Understandably the cancer problem troubles all people on Earth. But what is being done to widen the use of the new method in our country? Things are moving forward, though not very quickly. In the latter part of October V. Kotelnikov, a Russian people's deputy and a member of the Supreme Soviet Committee for Science and Public Education, sent a letter to Russian Federation President Boris Yeltsin. The letter asked for support for the new direction, which is a significant national achievement. "All tests have been conducted on the method," writes V. Kotelnikov, "but there are probably influential opponents to the effective treatment method, which might explain the red tape in adopting a program to widely introduce the innovation." The letter also reports that "recently bandits set fire to the home of the author of the new cancer treatment method, V. Gudov."

Within just a few days this letter was sent from the office of the president to the Russian Federation's vice prime minister for science, the higher school and technical policy, B. G. Saltykov, with the following instructions: "Please look into the question of wide introduction of the national achievement in the treatment of oncological diseases and AIDS referred to in the appeal to the president of the Russian Federation by Russian People's Deputy V. Kotelnikov, and prepare a briefing on it. Communicate the results to the author and to the office of the president so that a report to B. N. Yeltsin could be written." It was signed by V. Semenchenko, the director of the office of the Russian president. The deadline was 20 November.

Vice prime minister B. Saltykov communicated instructions to the Ministry of Health and the Academy of Medical Sciences. A separate note was sent to the procurator and the Ministry of Internal Affairs in connection with the burning and destruction of the inventor's dacha.

As with any progressive thing, the new treatment method has its proponents and opponents. Still, we would wish to believe that a broad avenue will be opened for the new method of healing patients with the terrible ailment in the very near future. Human life is precious. In the name of saving human lives, doctors must abandon all intrigues and ambitions, and work together. We must not forget the hundreds of thousands of tragedies—the premature deaths of people due to cancer.

Russian Health Minister Approves Photodynamic Cancer Therapy

937C0146G Moscow IZVESTIYA in Russian 20 Nov 92 p 7

[Article by Svetlana Tutorskaya: "Treatment of Cancer—Hopeful Results: Russian Health Ministry Gave OK to Clinical Testing of a New Method"]

[Text] **The method assimilated by the Scientific Research Institute of Laser Medicine in Moscow entails introducing a special substance into the blood of the cancer patient—a sensitizer that is absorbed primarily by cancer cells. This substance makes the cells sensitive to low intensity red laser radiation. Forty-eight hours after injection the area invaded by the tumor is irradiated with this light. Sick cells disintegrate, and soon healthy tissue grows in their place.**

This method had been tested previously only on mice. The difficulty lay in obtaining a pure sensitizer—one that was nonallergenic and did not cause inflammation.

Such a sensitizer has now been found, tested by the Pharmacological Committee and approved. It is made from donor blood. It consists of hematoporphyrin and its derivatives. It is manufactured by the Moscow Institute of Precision Chemical Technology.

The first results of clinical use are encouraging, though unfortunately the patients that are sent to the Institute of Laser Medicine have not the initial but later stages of cancer. There was a patient with an enormous tumor of the mouth and pharynx: Because of the deformity caused by the malignant growth he was unable to open his mouth normally. After treatment the tumor went away, and mouth function recovered. A neglected breast tumor in a certain woman was reduced considerably in size, and she began to feel better.

The method proved itself well in treating skin cancer. I was told by Doctor of Medical Sciences Ye. Stranadko, Moscow's chief oncologist, that thought was being given to treating certain genital neoplasms in women and treating a number of cases of lung cancer.

The institute sent letters to cancer dispensaries and oncologists warning them that a fee would be collected for treating persons from other cities and the residents of other CIS countries. The institute has no beds for this type of treatment, which does hardly anything to make its associates optimistic. The inflow of patients is already high in comparison with the size of the scientific research institute. Beds may have to be leased. A single dose of hematoporphyrin injected into the patient costs R3,500. Such that in order to develop the method, the Institute of Laser Medicine must introduce elements of paid treatment. Doctors in Germany, Italy, India and

China have shown interest in the new procedure. And in the near frontier, Lithuanian colleagues have displayed an interest in the innovation.

Photodynamic treatment may become a great help to those patients who are unable to endure operations and radiation therapy. But it is also fully possible to use the new method in conjunction with traditional ones.

New Burn Treatment Compound

937C0146H Moscow SOVETSKAYA ROSSIYA in Russian 10 Dec 92 p 2

[Article: "Effective Innovation"]

[Text] A new burn-healing organic composition that accelerates recovery by a factor of 3-5 was developed by scientists from the Institute of Surgery imeni A. V. Vishnevskiy. Russian specialists are using a biological culture—so-called fibroblasts, which are contained in human subdermal tissue.

"Such tissue can be grown in the laboratory in just 20 hours," Vladimir Tumanov, the director of the laboratory of tissue culture at the burn center of the Institute of Surgery told this ITAR-TASS correspondent. "When injured portions of skin are covered with this composition, the wounds in a sense acquire a 'new skin,' which is also bactericidal."

Ukrainian Test for Rapid Diagnosis of Cancer

937C0146I Kiev VECHERNIY KIEV in Russian 16 Nov 92 p 2

[Article by Nikolay Zakrevskiy: "Cancer Test Sends Cancer Packing: Kiev Scientists Who Created a Quick Method for Diagnosing Cancer That Makes the Fight Against This Extremely Serious Ailment Possible in 95 Percent of Patients Are Prepared To Bring It Up Before Bureaucratic Indifference"]

[Text] It borders on the miraculous: A drop of human blood is applied to a slide (exactly the same kind used when blood is taken from the fingertip for general analysis), after which it is exposed to special reagents, and two hours later the doctor already knows whether cancer has begun its insidious attack upon the body, or if it is in hiding, awaiting its moment, or if, as they say, God was merciful.

"This is a drop of blood from a cancer patient who knows nothing yet, and is experiencing no bodily discomfort," Professor K. A. Galakhin, director of the pathological anatomy department of the Ukrainian Scientific Research Institute of Oncology and Radiology of the Ukrainian Ministry of Health, handed me a narrow transparent glass slide with a brown spot of dried blood the size of a kopeck coin. I compared it with an exactly identical sample but from a healthy person. The visual difference is huge: Asymmetrical rays of a darker color could clearly be seen jutting out from the former, while in the latter case the light brown color was even and uniform in tone around the entire circumference of the drop.

"Our diagnostic method has come to be called the oncotest," explained Konstantin Aleksandrovich, who is by the way a member of the International Academy of Pathologists. "It was under development for around 15 years. Today it is officially recognized. An inventor's certificate was obtained. Professor Yevgeniy Ivanovich Suslov, a department director at the Ukrainian Scientific Research Institute of Physiatrics and Pulmonology, with whom I've worked for many years, is rightfully considered to be the method's founder. It was through this effort that we arrived at the invention."

As we know, there are many means of diagnosing oncological diseases today—from traditional X-ray analysis to recently introduced computer tomography. But among these methods, the oncotest is unique. Why? It allows us to reveal illness in its initial stage, before there is either a malignant tumor or pronounced clinical manifestations.

There is no need to go into what advantage this provides. According to the statistics one out of every three cancer patients dies before living out the year. The main reason for the unsatisfactory treatment results is late diagnosis of the tumor. And it is not all that easy to determine the presence of disease. In breast cancer, for example, the asymptomatic period of disease may last from 10 to 15 years.

"The oncotest doesn't tell us where in the body the malignant tumor is," continued V. A. Vladimirov, a department director of the same institute. "It reveals that disease exists. Moreover it does so long before it can be detected by means of ultramodern medical apparatus."

Let me note in passing that contemporary clinical analysis does not allow for sufficiently broad inspection of an organ—the liver for example. And even nuclear magnetic resonance or computer-assisted tomography cannot yet guarantee detection of cancer in its initial stage. On the other hand the oncotest makes it possible to detect the ailment, as they say, in its embryonic form. Herein lies its advantage.

A person with a positive reaction is put on record, he is tested periodically, and naturally he takes the necessary drugs and medicines for preventive purposes. But if the tumor continues to grow, treatment is started on the patient. And the success of a cure in the initial stage is 95 percent according to medical personnel.

In the words of Vitaliy Aleksandrovich, one out of every two of the persons tested with the initial form of cancer at the small business he heads, Edemvita, has already become practically healthy. Healthy without surgical intervention, or chemical or radiation therapy—the treatment methods that are used in later stages of disease. The method makes it possible not only to keep the

particular vitally important organ undamaged, but it also avoids the additional radiation load created by X-ray analysis.

Another important thing is that X-ray diagnosis, the most widely employed method, does have its limit: It is unable to reveal a tumor if it is less than 0.5 cm^3 while the oncotest reveals its presence without error.

All of this should make us happy. Except for the fact that this happiness is balanced by an equal measure of bitterness. Each year around 160,000 new cases of malignant neoplasms are registered in Ukraine, and more than 100,000 persons die of this serious ailment. In Kiev, the corresponding figures are around 8,000 and 5,500 persons. If we consider the post-Chernobyl tendency for universal increase in cancer (by an average of 3-5 times for some types), the oncotest is quite simply becoming Ukraine's saving grace. Still....

The small business Edemvita can carry out 30-40 laboratory analyses a day. By the way, this enterprise is the only one serving all of Ukraine's 53 million population. For the method to assume assembly line proportions—in other words, for any treating physician to be able to conduct the test independently, in the words of the subjects of my interviews the methods requires industrial development. Economists estimate that R500,000 a year would be sufficient for this. Just half a million to produce a direct economic impact of hundreds of millions: After all, diagnosis, treatment and maintenance of cancer patients consume truly astronomical sums. This is from an economist's point of view. But who has calculated the moral or human loss, which can never be replaced?!

The diagnostic method developed in our country was examined by the State Committee for Science and Technology in spring of this year. It was unanimously approved. But nothing more—financing was not initiated. All of the hopes are on the Ministry of Health, but even it is holding its silence.

In the meantime Western specialists, who applauded the invention of Kiev scientists, proposed investing our "know-how" and placing it on an industrial footing in their own countries. For example at a recent September international conference on tumor markers (substances that are generated by tumors—author's note) in Australia, the report by the Kiev scientists evoked a real commotion: Business proposals rained down from representatives of Sweden, Italy, the United States and other countries.

We could of course sell our invention, and then purchase the finished product for hard currency, which is something we often do successfully. On the other hand we could take an approach that would be better for the state—exporting something that has no analogues in world medical practice. Of course, after first injecting the necessary amounts of money into industrial development of the oncotest.

Ideally, it would look like this: A doctor conducting a preventive examination or an ordinary check-up would use an oncotest kit and establish whether or not disease is present. It would be appropriate to note that last year, only 14 percent of the total number of cancer patients were revealed during preventive examinations. Not because the medical personnel worked unconscientiously, but because a simple, inexpensive and effective diagnostic method was unavailable. Now that it exists and now that the number of cancer patients is increasing geometrically in the republic, is it right to ignore something that could preserve and lengthen the life of people?

* * *

P.S. The small business Edemvita is taking orders for examination of labor collectives, plants, factories, and institutions by telephone: 266-01-98. The address is: Edemvita, Yanvarskoye Vostaniye Street, 2.

Mucor 12M - Promising Source of γ-Linolenic Acid

937C0022B Moscow PRIKLADNAYA BIOKHIMIYA I MIKROBIOLOGIYA in Russian Vol 28 No 1, Jan-Feb 92 (manuscript received 25 May 90) pp 140-144

[Article by N. S. Funtikova, S. N. Kulakova, F. A. Medvedev, I. V. Konova, and M. M. Levachev, Microbiology Institute, Russian Academy of Sciences, Moscow; Nutrition Institute, USSR Academy of Medical Sciences, Moscow; UDC 582.281.212.0,13:577.115.3]

[Abstract] The fatty acid composition of Mucor 12M, which was experimentally produced as a result of ultraviolet radiation exposure, was studied and the structure of the isomer of linolenic acid in lipids of this strain was researched using modern methods. The Mucor 12M strain was shown to accumulate biomass two times faster than the original strain. Analysis of the fatty acid composition of the Mucor 12M fungus lipids revealed myristic, palmitic, palmitolic, stearic, oleic, and linoleic acids, and insignificant amounts of acids with chains of C_{20} or more. This analysis revealed the presence in its lipids of γ-linolenic acid in significant amounts with the complete absence of the α-isomer and a high content of oleic acid 18:1ω9. The content of γ-linolenic acid and monoene 18:1ω9 acids in Mucor 12M lipids to a large degree depends on the culture conditions. In conclusion, the possibility of using physiological factors to control lipogenesis processes in fungi makes this source of lipids even more promising for use in medical practice. Figures 3; tables 1; references 13: 2 Russian, 11 Western.

Prospects for Scientific Investigations Into the Improvement of the Activity of the Medical Services During Accidents and Catastrophes

(Review of the Literature)

937C0088A Moscow VOYENNO-MEDITSINSKY ZHURNAL, in Russian No 3, Mar 92 pp 4-8

[Article by V. M. Manik, Major General of the Medical Service; E. G. Zhilyaev, Candidate of Medical Sciences, Colonel of the Medical Service; A. V. Ivanchenko, Doctor of Medical Sciences, Lieutenant-Colonel of the Medical Service; UDC 614.2:001.89]:614.8.028.4]

[Text] Dozens of natural calamities and catastrophes take place in the world annually with the deaths of 100 or more individuals. Occurrences with a smaller number of victims and with fewer material losses are observed almost daily in the large countries.[22] The probability of technogenic catastrophes associated with the increase in the density of population, urbanization, and the concentration of production is growing.[17, 27] The medical consequences of these events, as well as interethnically based conflictual situations which are capable of leading to losses of lives, as a rule require the provision of emergency medical assistance.[18, 27] The aggregate of medical measures in such situations corresponds to the concept of "catastrophic medicine", the main principle of which is the rendering of emergency aid to victims under complex conditions and in the presence of a disparity between the scopes of the sanitary losses to the available medical forces and resources.[16, 17, 26, 27]

We have presented a brief analysis of the literature of recent years which reflects the advances of contemporary medicine and the promising concepts in the field of the rendering of early (mainly prehospital) medical assistance to the injured in cases in which they arrive en masse. An attempt is made in the course of the analysis to evaluate the orientations of the experimental and clinical investigations directed toward a search for new or the improvement of existing resources and methods of treatment of victims with pathology characteristic for accidents and catastrophes.[1]

The specific aspects of the pathology itself and the conditions of its development affect the essence of these resources and methods. As is well known, catastrophes are characterized by suddenness, brevity, massiveness of material and human losses, the polyetiological character and diversity of the injuries, the need for emergency rendering of medical assistance, and not infrequently its limitations (lateness).[15, 17, 19, 22, 26, 27] The principle which states that a stream of individuals with severe injuries, having the prospect of survival given emergency (immediate) rendering of medical assistance, is segregated from the total number of victims, has priority status in catastrophic medicine. This assistance includes a complex of treatment and diagnostic techniques directed toward the most rapid identification of pathology and the creation at the prehospital stage of conditions for a favorable outcome. This stage is regarded as the initial stage in the conduct of intensive therapy which will be prolonged under other conditions (the hospital) and in greater scope.[17] The time during which such aid must be rendered is 6-8 hours.[15, 17] The prognosis for the life of victim depends to a substantial degree precisely on the timeliness and completeness of the rendering of emergency medical assistance.

The planning of medical assistance in relation to the consequences of earthquakes, floods, explosions of solid explosive materials and compressed gases (voluminous explosions) in populated centers, and air and rail catastrophes is urgent; this is attested to, for example, by well-known tragic events of the last decade in the USSR and in a number of foreign countries.[1, 2, 13, 15, 17, 27] Mechanical injuries to the musculoskeletal apparatus, chest and abdomen, the prolonged compression syndrome [crush syndrome] (PCS), nerve traumas, blast contusion and indirect injuries by airshock, thermal and associated and combined traumas, shock, purulent-septic complications, and the intoxication syndrome are the most important pathologies in such catastrophes.[1, 4, 9, 13, 15, 17, 19, 20, 23, 26, 27] Radiation accidents at NPS [nuclear power stations] and plants of the nuclear fuel cycle and of nuclear power installations may bring in their wake acute radiation injuries, including associated injuries (such as occur through the incorporation of radionuclides), as well as the irradiation of the large number of individuals (the population and participants in the elimination of the after-effects of an accident) in relatively small doses, which do not lead to acute injuries and do not immediately threaten life or the development of illness, but which induce clinically definable syndromes and remote sequelae, such as cancerogenic and genetic as well as stochastic effects.[3, 5, 6, 7, 8, 11, 14, 21, 26, 27, 28, 29] Under the conditions obtaining when victims arrive en masse, effective aid may be secured only through the use of special sorting, and on the basis of the standardization (unification) of the complex of medical procedures.[10, 12, 15, 17, 27] Regardless of the localization of traumas, the following are essential elements of early medical assistance which are included in the protocols of[10]: the administration of tetanus antitoxin, antibiotics, agents improving the functional state of the cardiovascular system, preparations traditionally used for the treatment of acute radiation illness, infusion and transfusion therapy, temporary immobilization, and analgesia. In the case of mechanical traumas, surgical treatment is the main item in the rendering of initial physician and paramedical assistance; conservative treatment (bandaging, analgesics, infusion therapy, etc.) are the main item in the case of thermal burns. A generally acknowledged principle of the rendering of medical assistance in combined radiation injuries consists in the combined use of methods and agents traditionally employed in military field surgery and radiology in the treatment of victims with corresponding isolated injuries. In catastrophes in which individuals with severe traumas predominate in the structure of the victims, priority is assigned to surgical and resuscitative aid.[10, 15] The actual practice of elimination of the after-effects of

the accident at the Chernobyl NPS (1986-1989), of the Armenian earthquake (1988), of the gas explosions at the all-product line in Bashkiriya (1989) and of explosive materials at the Arzamas-1 stations and the Sverdlovsk humpyard (1988), of the railway catastrophe on the Oktyabrskaya railroad (1988), and others, demonstrated the merits and inadequacies of the agents and methods of anesthesia, infusion, detoxification, and antibacterial therapy used at present time, and confirmed the necessity of improving methods of tissue microcirculation and radiological assistance. The character, localization, and severity of injuries, the level of professional training of personnel, and the supply of temporary medical units with the appropriate equipment and pharmaceuticals influence the choice of method of anesthesia during surgical operations under the conditions obtaining when victims arrive en masse. In any case, alleviation of pain should be effective, accessible, simple, safe, and inexpensive.[24, 26] According to generalized published data, [17, 26, 24, 27] regional anesthesia, which is most effective in operations on the extremities, as well as intravenous anesthesia using calypsol (ketamine), including its use in combination with tranquilizers of the benzodiazepine series, neuroleptanalgesic agents and sodium oxybutyrate were the methods of choice in the surgical interventions in 44 percent of cases in Armenia.[1, 17] The use of ketamine prove to be very expedient in the case of the en masse arrival of victims with burns.[1] The alpha stereoisomer of ketamine, as well as moradol, tramal, the new narcotic nabbufin, which has a number of advantages over traditional narcotic analgesics,[27] the use of which in the conditions of catastrophes is undesirable, especially in victims with traumas of the head, chest, abdomen, and with burns of the upper respiratory passages, are promising.[17, 26, 27]

The high frequency of shock,[15] the main causes of which were pain, massive blood loss, dehydration, and severe intoxication, [15, 26, 27] requires the earliest possible correction of hypovolemia through infusion therapy, and the prescription of comprehensive pharmaceutical treatment.[15, 27] In the rendering of assistance in such cases, standardized protocols of the administration of colloidal and salt solutions have been used, depending upon the severity of shock. Rheopolyglukin, polyglucin, hemodez, plasma, blood, and albumin have been used.[1, 29] The replacement of high molecular weight dextrans of the polyglucin type by new preparations, such as volecam and oxyamal, and derivatives of hydroxyethyl amylopectin starch, is promising, since they are capable not only of performing a replacement function, but of being assimilated in the organism and participating in energy metabolism. It is necessary to increase the relative proportion of protein preparations in the structure of infusion therapy carried out for the purposes of the pharmacological correction of the state of the organism.[1, 15]

Autointoxication and sepsis represent a serious threat to the life of wounded and burned individuals. Detoxification therapy takes on a special significance in the case of the PCS.[15, 20] Conservative methods have been demonstrated in the early period of toxemia with maintained diuresis (hemodilution, the correction of the ABS [acid-base status] and water and electrolyte balance, and forced diuresis). Therapeutic diarrhea, enterosorption, and hyperbaric oxygenation (HBO) can be used.[17, 26] Infusion therapy directed toward the restoration of the volume of circulating plasma, the increasing of diuresis, and the improvement of the rheological properties of the blood must be considered the most effective measures eliminating endotoxemia in the PCS, and in the prophylaxis and treatment of acute renal insufficiency. Approximately 10 percent of victims require the use of methods of extracorporeal detoxification, namely, hemodialysis and hemosorption.[26] Sodium thiosulfate, the so-called "hepatic protective therapy", vitamins B6, B12, C, Essentiale, Liv-52, the intravenous administration of solutions of glucose, novocaine, contrical (trasylol, gordox), rheopolyglukin, hemodez, and polyvisoline, are indicated in the acute period of PCS.[1, 17] These measures, as is the case with the extracorporeal methods of detoxification, should be included in the complex of the therapy carried out as early as possible, since the duration of the circulation of the products of proteolysis in the blood and their concentration in traumas and burns in many respects determine the degree of secondary disturbances of the functions of organs and systems.

The general strategy of detoxification therapy developed for application to combined radiation-thermal injuries can be used with success in other conditions as well. Inhibitors of proteinases are used in order to decrease the formation of toxic products in the organism; this is one of the initial factors in the prophylaxis of endogenous intoxication in the acute period of injury. It is possible to limit the influence of toxins on tissues using membrane-protectors, antioxidants (tocopherol, olefine). Inhibitors of the synthesis of metabolites of arachidonic acid are used in order to stabilize the lysosomal membranes in macrophages, and nonsteroidal anti-inflammatory preparations are used to suppress the activity of cyclooxygenase and thromboxane synthetase and to restore blood flow into internal organs in the presence of endotoxemia. Intravenously administered washed erythrocytes absorb a significant amount of medium-molecular weight peptides on their surface. Gamma globulin and preparations with antibacterial action, inhibitors of toxic oligopeptides isolated from the blood of donors, monoclonal immunoglobulins M, which in small quantities protect cell structures from the influence of practically all gram-negative bacteria and endotoxemia are used for the purpose of reducing the functional activity of toxins. An increase in the rate of excretion of toxins from the organism (efferent therapy) is achieved by the fractional intravenous administration of hemodez and by the use of various types of sorption detoxification, hemo- and enterosorption, and by the use of application sorbents as well. The expedience of the use of cholestyramine, kaopectate, kaolin (for the binding of

the intraintestinal pool of endotoxins), lactulose (acidification of the milieu in the bowel is achieved), histamine H_2 receptor blockers, and antagonists of serotonin and antiadrenergic preparations (elimination of ischemic injuries of the bowel and influence on the rate of translocation of endotoxins) has been proven in model experiments.

It has been proven that such factors as psychoemotional stress, the combined character and severity of injuries, injuries to the CNS, and massive infection of wounds exert an influence on the immune system. In this connection the necessity of developing and introducing express methods which permit immunomonitoring and immunocorrection at the stages of evacuation arises. Immunocorrective methods and agents should stimulate the central link of immunity and actively influence the general mechanisms of direct adaptation (effector mechanisms).[1, 26] The preparations thymalin and thymogen correct the cellular link of immunity and increase the content of T lymphocytes in victims with PCS. The wide use of HBO, UV irradiation of the blood, comprehensive antibacterial and general health-improving therapy.[20] have a favorable influence on the results of treatment. In the case of the crush syndrome and other injuries, antibiotics and antiseptics (brulamycin, gentamycin, dioxidine, metradzhil), antistaphylococcal and anti-blue pus plasma, leukocytic mass, bacteriophage, T-activin [1, 17, 23] are used for the purpose of the prevention of infectious complications and immunodeficiency. It is advantageous to use ointments on a water-soluble base of the levosin type in the wound process for the prophylaxis of purulent-septic complications.[20] Immunomodulating therapy of burned individuals also includes levamisole, thymalin, and T-activin.[1]

In the case of combined radiation injuries (CRI), the following are promising for experimental development: agents to accelerate the proliferation of hematopoietic stem cells and committed precursors of the granulocytic-macrophage line; agents normalizing the suppressed rate of proliferation of the precursors of T cells and promoting the differentiation of thymocytes; "replacement" therapy by means of humoral opsonizing factors; agents and methods of the directed regulation of the secretory activity of tissue macrophages, including through the liberation of humoral mediators of macrophages which increase the resistance of the organism (colony-stimulating factor, interferon, lysozyme, etc.), with the simultaneous suppression of secretion of alteration effectors, procoagulants, proteases, interleukin-1, tumor necrosis factor. The effectiveness of lithium carbonate, thymotropin, and interleukin-2 in CRI with a sublethal radiation component has been demonstrated experimentally. Loads placed on a traumatized organ are decreased in order to improve the microcirculation in damaged tissues (immobilization, etc.); measures are carried out to reduce energy expenditures and oxygen consumption (local cooling, the use of antihypoxic agents); and infusions of agents promoting the normalization of blood supply in an injured area (preparations improving the rheological properties of the blood, spasmolytics, small doses of heparin) are prescribed.[23, 26] Analogs of the enkephalins, in particular dalargin which increases tolerance to hypoxia (including hypoxia in blood loss conditions), improves the microcirculation in acutely evolving processes,[25, 30] and eases the course of the respiratory distress syndrome,[26] are of great interest as anti-ischemic agents. The use of dalargin in massive injuries for the prevention and treatment of shock of varying etiologies is promising.[26, 29]

Parenteral nutrition has an important place in the therapy of injured patients. Amino acid mixtures are used in rendering aid to large contingents of burned victims: those of domestic manufacture such as poliamin, and imported mixtures such as alvesin, syntamin, levamin, protinutril, as well as fatty emulsions, lipofundin, etc.[1]

Emergency measures of skilled therapeutic assistance were carried out in the Chernobyl NPS accident for all injured victims with acute radiation illness who arrived at medical-sanitary units. Repeated injections of metoclopramide (cerucal) or of dimetpramide were prescribed in the case of intractable vomiting; infusions of hypertonic sodium chloride solution were used in the presence of hypochloremia, and "Trisol" and glucose solutions in the presence of dehydration. Haloperidol, droperidol, and aminazine can be used in such cases, with monitoring of arterial pressure. Plasmapheresis and/or hemosorption, for the purpose of arresting the DIC [disseminated intravascular coagulation] syndrome, transfusions of fresh-frozen plasma, heparin, inhibitors of proteolysis and plasmapheresis are indicated in the presence of an extremely severe primary reaction with marked intoxication and disseminated radiation burns. The dosed administration of solutions, including rheopolyglukin, glucose, hemodez, polydez, salt solutions and sympathomimetics are prescribed in the presence of circulatory collapse.[27]

Riboxin as a "mild" action radioprotector, suitable for repeated administration, including in the case of relatively low doses and low dose rate of ionizing radiation, should be numbered among the promising antiradiation agents.[29] It has been established experimentally that melanin (the natural pigment) decreases the frequency of all types of mutations radio-induced in sex cells in the case of remote radiation effects.[29]

The condition of the rescuers and medical personnel participating in the elimination of the consequences of a catastrophe indirectly influences the effectiveness of the rendering of early medical aid to victims. The rational use of tranquilizers and actoprotectors (bemityl), especially in combination with piracetam, riboxin, and preparations containing amino acids, vitamins, macro- and microelements (panangin, glutamevit, etc.),[30] bemityl in combination with psychostimulants, namely derivatives of aminoadamantane,[30] may promote an increase in work capacity.

Thus, a review of the problems associated with the rendering of medical aid in catastrophes at the prehospital stage has made it possible to come to a number of conclusions. The study of the mechanisms of the development of the principal syndromes in mechanical, thermal, and radiation injuries requiring the earliest carrying out of a complex of emergent measures, the selection and the assessment of agents which are capable at the advanced stages of treatment of preventing the development of irreversible changes in homeostasis in victims under the conditions of the lateness (delay) of skilled aid, are the most urgent. The development of rational standardized protocols for the use of agents and of emergency aid methods, and the search for effective pharmaceuticals and methods of conservative therapy directed toward the early prophylaxis of toxic-infectious and other complications of traumas, burns, and radiation and combined injuries, as well as for agents suitable for the prevention and treatment of pathological states induced by radiation in low doses, are required.

Footnote

1. Accidents at chemical plants are not considered here, nor are the psychiatric aspects of catastrophes, due to the specificity of the pathology and treatment of this category of victims.

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Mobile Search and Evacuation Complexes

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[Article by V. P. Spichev, Candidate of Medical Sciences; Major General of the Medical Service; UDC 614.8.028.4:614.882/.883]

[Text] A tendency toward an increase in the number and scales of catastrophes was manifested especially noticeably in recent years. In the 20 years just past of about three million people died and about a billion suffered severe sequelae of natural disasters as a result of natural cataclysms. It is well known that the extent of these losses has fluctuated over a wide range depending upon a number of conditions, in particular, the character of the catastrophe, the intensity of the effect of injurious factors, the type of building in the zone of the catastrophe, the density of the population and the degree to which it was protected, the time of day, etc. For example, in an earthquake from 22 to 55 percent of the traumas occur as a result of the effect of the falling structures of buildings and 55 percent as a result of the incorrect behavior of individuals (panic, failure to know how to take cover, etc.).

Craniocerebral trauma occupies first place in frequency and the structure of losses. Injuries to the extremities and soft tissue wounds usually share second and third places. As a rule, multiple and combined traumas (more than 70 percent) constitute a high relative proportion. These injuries are frequently complicated by hemorrhage, shock, and purulent infection. About half of the injured require treatment in hospital conditions. Traumas incompatible with life occupy first place among the causes of death; traumatic shock the second place; and acute blood loss, the third place. Lethality in traumatic shock reaches is 12.5 percent (P. K. Dyachenko, 1989). This number is increased up to 30 percent in a case of combined trauma of the femur and organs of the abdominal or thoracic cavity. During the earthquake in Tang Xian (China, 1976), the ratio of the dead and injured was 3:2; in the case of the earthquake in Armenia, it was 5:2.

Analysis shows that a significant proportion of the injured die as a result of rendering tardy medical assistance, although the trauma sustained was not lethal. Therefore, the role of its first stage is immeasurably increased in the system of the staged rendering of medical aid. Shortening the times and improving the quality of medical aid at this stage substantially increases the effectiveness of subsequent treatment-evacuation measures and decreases lethality and disability among victims. Mobile medical complexes, capable of rendering pre-physician and primary medical assistance in them, both to victims and to rescuers, serve these aims in many respects. The organization of the interaction of medical formations (complexes) with the rescue services of various ministries and departments which provide for the extraction of victims from ruins, their evacuation from danger zones, and their delivery in a number of instances to medical aid stations takes on special significance under the conditions in question. The experience involved in eliminating the consequences of the earthquake in Armenia showed that it is not expedient to draw off specialists-rescuers for the delivery of victims to medical aid stations or to treatment institutions. First, this distracts rescuers from the performance of their primary tasks; second, the quality of the primary medical assistance rendered by them is, as a rule, low, and the delivery of victims is accomplished on incidental transport, which aggravates their condition. In the final analysis all of this has an influence on the results and outcomes of treatment. According the data of Yu. G. Shaposhnikov (1989), during the evacuation of victims to treatment institutions by means of incidental transport, lethality among them was up to two-thirds of their total number; transport by means of the first aid line [non-specialized] brigades, up to 40 percent; and by brigades of specialists of the Institute of Traumatology and Orthopedics, up to 16 percent. Of course, it is not possible to count on medical aid being rendered to all victims in a catastrophe zone by highly qualified specialists.

The occurrence of numerous human victims during catastrophe imposes a sharp disparity between the volume of required medical assistance and the presence of the forces and means necessary to render it. Therefore, the rapidity of the delivery of specialized medical formations or mobile complexes to a focus of destruction will have a substantial influence on the effectiveness of the treatment-evacuation measures. Complexes for these purposes should include mobile medical installations, which are interconnected functionally and technologically and which ensure an autonomous mode of operation on the first day.

It is expedient to form mobile search and evacuation complexes (MSEC) as the forces and means of the first

echelon. These should be made up of search and evacuation transporters with the capacity to render primary medical and pre-physician assistance in them, vehicles for the rendering of primary physician assistance, and medical evacuation transporters (motorized vehicles). It is expedient to use the MSEC in the destruction zone together with combat-engineer and fire subdivisions carrying on the search for and extraction of victims, and the clearing of ruins and evacuation routes.

Their use in combination with the search and evacuation helicopter, furnished with equipment for the remote detection of victims and with means of communication should be provided for the purposeful operation of the complexes in search regions. A helicopter can also evacuate gravely injured victims while rendering them medical assistance on board. The MI-8 ("Bissektrisa" [Bissector]) helicopter provides for the carrying out of this task.

The universal principle of the use of the system in peace and war time and the necessity of reducing expenditures for the development and production of means of transport for the equipping of medical subdivisions for extreme conditions determine the advisability of the use of military armored medical automobiles, proposed for development, as the basic vehicles. The possibility of forming MSEC using available GT-MU and MT-LB transporters whose relatively great capacities for cross-country travel make it possible to use them as search and evacuation transporters, will come about in a very near future. The motorized dressing ward (AP-2), which is designed for rendering of primary medical assistance and the AS-66 MP vehicle, with a system of secondary springing of stretchers provide for sparing evacuation of victims to treatment institutions. However, inadequate capability of traveling cross country and vulnerability to mechanical influences limit the possibility of their use in zones of destruction, contagion, and flooding. In this connection, it is expedient to use the wheel-based armored medical vehicles which are being developed, as well as the medical evacuation bus AME-42031 (on a KamAZ-4310 automobile chassis) as sanitary transporters and primary medical assistance vehicles.

It may also be possible in the future to use the chassis of the infantry fighting vehicle for these purposes. The armored medical vehicles (AMV) being developed by the Military Institute of Medical Technology can be delivered to the region of a catastrophe by all means of transport and if necessary move from unloading points on their own, overcoming obstacles, water, barriers, and areas of contagion. A further increase in the mobility and efficiency of the delivery of forces and means of medical support directly to the region of a catastrophe may be realized through airborne landings and by parachute. It appears expedient to develop highly mobile landing *divisions of medical-diagnostic complexes* on the basis of armored vehicles, vehicles for the rendering of primary medical assistance and for the deployment of medical operating theaters, in combination with medical evacuation transporters. The use of armored medical vehicles, in combination with the collective defense systems available on them, firefighting equipment, night vision instruments, means of communication, and powerful searchlights in combination with search systems, will increase the mobility and effectiveness of medical subdivisions, accelerate the process of their formation, and decrease expenditures for the development, production, operation, and repair of these vehicles. Thus, the conception of emergency medical aid to the population which presumes the creation of a two-stage system of treatment-evacuation measures, should be built on a basis of the formation of the forces and means of increased mobility and efficient preparedness, using the advances of science and practice.

The universal principle of the use of this system in peace and war-time envisages the priority of the first stage of the treatment-evacuation measures in regions of destruction and foci of contagion. Mobile search and evacuation complexes are a means for realization of these principles during the accomplishment of the tasks of the first stage: the search for and extraction of people from ruins, their evacuation from the regions of destruction and flooding, from foci of contagion, etc., as well as the rendering of primary medical, pre-physician, and primary physician assistance based on emergent indications, and evacuation to treatment institutions. These subdivisions should be in the first echelon of forces and means arriving at regions of a catastrophe for the purpose of efficient actions and the creation of conditions for the operation of treatment institutions of the second echelon.

Conclusions

1. The increase in requirements for the effectiveness of functioning of the first stage of the system of treatment and evacuation measures in extreme situations determines the necessity of the high-priority equipping of medical formations with promising types of mobile military medical technology.

2. It is advisable in order to fulfill these requirements to have mobile search and evacuation complexes based on armored medical vehicles, motor vehicles of primary physician assistance and medical evacuation, in the first echelon of the forces and means which are to be moved to a region of catastrophe or natural calamity.

3. The comprehensive approach to the formation of the forces and means of the first echelon, using basic armored vehicles with their systems of life-support, protection, and communication, will substantially increase the efficiency of the system of treatment-evacuation measures overall and will reduce expenditures for the development and production of armored medical vehicles.

Use of Low-Intensity Millimeter Range Electromagnetic Waves in Medicine

937C0086B Moscow MEDITSINSKAYA RADIOLOGIYA in Russian Vol 37 No 3-4, Mar-Apr 92 pp 53-54

[Article by O. V. Betskiy, Moscow; UDC 616-002.582-073.916]

[Abstract] The most surprising property of millimeter wave VHF-radiation, which is non-ionizing, is that its biological (therapeutic) effect is mediated (the positive effect is noted in organs that are unattainable for electromagnetic waves). An important property of VHF millimeter waves is their powerful absorption by water or aqueous solutions. Hence, the radiation is virtually completely absorbed in the epidermis and dermis layers. VHF radiation is currently being used with success in the treatment of coronary heart disease, hypertension, cancer, traumatology, etc. Possible mechanisms by which VHF millimeter waves operate are discussed.

Embryotoxicity of Mycotoxin Vomitoxin (Deoxynilvalenol) in Rats

937C0120C Moscow GIGIYENA I SANITARIYA in Russian No 10, Oct 91 (manuscript received 14 Aug 89) pp 49-51

[Article by V.A. Tutelyan, N.A. Krinitskaya, L.I. Avrenyeva, E.Ye. Kuzmina, A.B. Levitskaya and L.V. Kravchenko, Institute of Nutrition, USSR Academy of Medical Sciences, Moscow; UDC 616.992.28-022.38-055.26.07:616-053.1]-092.9]

[Abstract] In view of grain crop contamination by the mycotoxin vomitoxin, its potential for embryotoxicity was tested on female Wistar rats, weighing 200-250 g at the start of the trials. Intragastric administration of 0.2 to 10 mg/kg of vomitoxin during the 7-15th day of gestation demonstrated that 0.2 mg/kg was the maximum dose that was innocuous for the pregnant females and lacking embryotoxicity and teratogenicity. Higher doses had an adverse impact on ossification and induced fetal wastage, as well as on weight gain in the females and on their hematologic findings. Tables 3; references 14: 8 Russian, 6 Western.

Influence of Cytochalasin D, Diphtheria Toxin and Ricin on Localization of Eukaryotic Elongation Factor-2 Along Actin Bundles in Fibroblasts

937C0081A Moscow DOKLADY AKADEMII NAUK in Russian Vol 324 No 1, May 92 (manuscript received 25 Feb 92) pp 196-199

[Article by Ye.A. Shestakova and L.P. Gavrilova, Institute of Proteins, Russian Acad. Sci., Pushchino, Moscow Oblast; UDC 576.3]

[Abstract] Indirect immunofluorescent studies were used to demonstrate adherence of elongation factor-2 (EF-2) along actin bundles in both mouse embryobic fibroblasts and human diploid fibroblasts. Incubation of the murine preparations with cytochalasin D resulted in reversible disorganization of the EF-2 strands, indicating that the strand-like organization of EF-2 depends on the actin cytoskeleton. EF-2 inactivator diphtheria toxin and ribosome disorganizer ricin had no effect on EF-2 distribution along actin bundles in the human system, nor did EF-2 bind to isolated polymerized actin. These observations were interpreted to suggest the existence of special molecules or factors (adaptors) which facilitate attachment of EF-2 to actin strands, but that EF-2 per se does not bind to actin. Figures 2; tables 1; references 15: Western.

Invertors: Genome-Controlled Intracellular Regulators of Plasma Membrane

937C0081C Moscow DOKLADY AKADEMII NAUK in Russian Vol 324 No 1, May 92 (manuscript received 03 Feb 92) pp 229-232

[Article by V.V. Frolkis, academician, Ukrainian Acad. Sci., Institute of Gerontology, Kiev; UDC 612.014.3:575.1:615.27]

[Abstract] Extensive biochemical, electrophysiological, and physiological studies have indicated the existence of a class of molecules or factors designated invertors: a class of signal proteins that transmit information from the genome to the plasma membrane. As such, they determine metabolic activity and regulate cellular functions. Depending on the system under study, invertors have been shown to either activate Na^+-K^+-ATPase, open potassium channels, or inhibit adenylate cyclase. To date, invertors have been identified in heart cells, hepatocytes, adrenocortical cells, and neurons. Invertors are at the heart of a membrane-genome feedback mechanism with profound implications for cellular homeostasis. Figures 4; references 9: 2 Russian, 7 Western.

Modulation of Growth of Experimental Mammary Neoplasms by Low-Frequency Electromagnetic Fields

937C0162C Leningrad VOPROSY ONKOLOGII in Russian Vol 73 No 9-10, Sep-Oct 91 (manuscript received 25 Feb 91) pp 937-941

[Article by D.Sh. Beniashvili, V.G. Bilanishvili and M.Z. Menabde, Oncological Scientific Center, Georgian Ministry of Health, Tbilisi; UDC 612.014.42:618.19-006-021.6-092.9]

[Abstract] Effects of exposure to alternating (50 Hz) and permanent (0.2 oersted) electromagnetic fields (EMF; 0.5-3 h/day) on nitrosomethylurea (NMU)-induced (50 mg/kg. i.v.) mammary neoplasms were evaluated in 55-60 day old female rats. The results showed a significant increase in mammary tumors as well as a shorter latent times in animals exposed to both type of EMF for three hours per day. In addition, three hours per day exposures to EMF alone served to induce tumors in the absence of NMU, with alternating EMF shown to be the more hazardous factor both in terms of incidence and time of onset ($P < 0.05$). In some animals combined exposure also led to appearance of tumors at other sites, with the mechanism of action of EMF explained in terms of their impact on the pineal gland and reduction in body levels of melatonin which, in turn, predisposes to elevated estrogen levels. Figures 1; tables 1; references 12: 3 Russian, 9 Western.

Pharmacologic Manipulation of Cholinergic System in Nucleus Accumbens and Sound Differentiation in Dogs

937C0167A Moscow ZHURNAL VYSSHEY NERVNOY DEYALTELNOSTI IMENI I.P. PAVLOVA in Russian Vol 42 No 5, Sep-Oct 92 (manuscript received 13 Nov 91; in final form 11 Jan 92) pp 919-929

[Article by K.B. Shapovalova and Ye.V. Pominova, Institute of Physiology imeni I.P. Pavlov, Russian Academy of Sciences, St. Petersburg; UDC 615.78+612.825.55+612.821.6]

[Abstract] An analysis of the involvement of cholinergic mechanisms of nucleus accumbens (NA) in acoustic signal differentiation was conducted on five outbred dogs with an established avoidance reflex. Microinjections of 0.05-0.1 μg of carbacholine into NA and analysis of behavioral changes and of EMG patterns of the m. rectus femoris and semitendinous muscle revealed, in most cases, improved differentiation between meaningful and nonmeaningful metronome signals. This was evident in greater response efficiency and was attributed to greater attentiveness to meaningful stimuli. Ipsi- and contralateral injections found to be equipotent. The effects were long-lasting and underscore the importance of sensory mechanisms in NA in initiation and implementation of conditioned responses. Figures 4; tables 3; references 26: 5 Russian, 21 Western.

Modulation of Conditioned Behavior and Nigro-Striatal Exchange in Rats by Chronic Activation and Blockage of Neostriatal Dopamine- and Enkephalinergic Systems

937C0167B Moscow ZHURNAL VYSSHEY NERVNOY DEYALTELNOSTI IMENI I.P. PAVLOVA in Russian Vol 42 No 5, Sep-Oct 92 (manuscript received 28 Oct 91; in final form 18 Mar 92) pp 930-935

[Article by A.F. Yakimovskiy and I.V. Karpova, Institute of Physiology imeni I.P. Pavlov, Russian Academy of Sciences, St. Petersburg; UDC 612.821.6+615.78]

[Abstract] Trials on 180-200 g male Wistar rats were conducted to determine the effects of prolonged stimulation and inhibition of neostriatal dopaminergic mechanisms on conditioned avoidance behavior. The study involved daily injections of 45 μg amphetamine, 5 μg haloperidol, 5 μg naloxone, 15 μg leu-enkephalin or 15 μg leu-enkephalin tetrapeptide analog (LETA) into the rostral neostriatum for 14 days. The results demonstrated that chronic activation of dopaminergic mechanisms faciliated the conditioned response, whereas antagonism of these mechanisms retarded performance. In both situations neostriatal levels of dopamine were depressed while those of its metabolites—HVA and DOPAC—were elevated. Although naloxone was without a telling impact and leu-enkephalin induced only a short term (2-3 days) depression of the conditioned response, LETA administration induced a cataleptic state with plastic rigidity and concomitant elevation of neostriatal dopamine levels without, however, changes in the concentrations of HVA or DOPAC. The latter findings were reminiscent of schizophrenia and further confirm the complex interaction of dopaminergic and opiate systems in its pathogenesis. Figures 2; references 17: 10 Russian, 7 Western.

Cholinergic Modulation of Spontaneous Hippocampal Activity

937C0167C Moscow ZHURNAL VYSSHEY NERVNOY DEYALTELNOSTI IMENI I.P. PAVLOVA in Russian Vol 42 No 5, Sep-Oct 92 (manuscript received 17 May 91; in final form 17 Jul 91) pp 944-954

[Article by Ye.S. Brazhnik, O.S. Vinogradova, V.S. Stafekhina and V.F. Kichigina, Institute of Theoretical and Experimental Biophysics, Russian Academy of Sciences, Pushchino; UDC 612.822.3+615.78]

[Abstract] Evaluation of cholinergic mechanisms in hippocampal electrical activity involved intravenous administration of physostigmine (0.1 mg/kg) followed, in some cases, by scopolamine (0.3-1.0 mg/kg, i.v.) 30-40 min later in wakeful rabbits. The electrophysiological studies on delta and theta modulation in intact rabbits and those with resected afferent paths to the hippocampus showed that the frequency of overall discharge was not affected by either agent. Accordingly, the latter parameter appears not to be under cholinergic control. However, the decrease in discharge activity of high-frequency neurons (> 25 spikes per second) and an increase in the activity of low-frequency neurons (< 25 spikes per second) indicated that septal cholinergic influences do affect the pattern—although not the level—of hippocampal activity. Figures 4; tables 1; references 31: 5 Russian, 26 Western.

Modulation of Cerebral Electrical Activity by DSIP and DSIP-Congeners in Rats

937C0167D Moscow ZHURNAL VYSSHEY NERVNOY DEYALTELNOSTI IMENI I.P. PAVLOVA in Russian Vol 42 No 5, Sep-Oct 92 (manuscript received 21 Nov 91; in final form 18 Mar 92) pp 977-985

[Article by V.V. Vorobyev, N.V. Shibayev, I.A. Prudchenko and I.I. Mikhaleva, Institutes of Cellular Biophysics, Pushchino, and of Bioorganic Chemistry, Moscow, Russian Academy of Sciences; UDC 612.822.3+612.821.7+615.78]

[Abstract] The frequency spectra of electrical discharges in the cerebral cortex, striatum, hypothalamus and hippocampus were evaluated in 300-350 g male Wistar rats treated intraperitoneally (160 μg/kg) or intraventricularly (1 μg/kg) with DSIP or two of its analogs (differing in amino acid at position 2). Studies conducted in autumn showed that intraperitoneal DSIP injection led to initial inhibition of high frequencies (20-26 Hz) within 20 min, followed by 30 min of marked activation. The congeners induced either attenuation or activation. Analogous results were observed in the spring-summer season, except for the lack of the initial inhibitory stage with DSIP. In addition, only the striatum showed delta-frequency activation, reflecting the unusual susceptibility of this formation to DSIP. On intraventricular administration the most pronounced effects were noted in the cortex, with DSIP activating the 14-16 Hz band and the analog peptides the 9.6-11 Hz band. Figures 1; tables 3; references 25: 13 Russian, 12 Western.

Modulation of Active Avoidance in Rats by 8-Azaguanine and Leu-Enkephalin

937C0167E Moscow ZHURNAL VYSSHEY NERVNOY DEYALTELNOSTI IMENI I.P. PAVLOVA in Russian Vol 42 No 5, Sep-Oct 92 (manuscript received 02 Jul 91; in final form 20 May 92) pp 1031-1033

[Article by Yu.N. Samko, Institute of Normal Physiology imeni P.K. Anokhin, Russian Academy of Medical Sciences, Moscow; UDC 612.821.6+615.78]

[Abstract] An analysis was conducted on the impact of 8-azaguanine (8-AG) and/or leu-enkephalin (LE) administration into lateral ventricles on acquisition of active avoidance responses in 150-200 g male Wistar rats. The basic results were that administration of 5 μg of 8-AG 24 hours before training inhibited acquisition of the conditioned response. Administration of LE (20 μg) immediately before training facilitated acquisition, and combination of both factors partially reversed the inhibitory effects of 8-AG. Since 8-AG inhibits protein synthesis and since LE facilitated acquisition and reversed the adverse effects of 8-AG, LE is evidently one of the peptides involved in mediation of this type of conditioned behavior. Tables 1; references 4: 3 Russian, 1 Western.

Pharmacies Decentralized

937C0108B Moscow DELOVOY MIR in Russian
3 Sep 92 p 12

[Article by Ekaterina Sokolovskaya: "Pharmacies and the Market"]

[Text] Moscow pharmacies recently became independent. Until now, only the Central Pharmacy was a legal person. Starting July 1, all of the city's pharmacies obtained the right to open their own account, to conclude contracts, to pay for deliveries of products, i.e., to carry out their affairs independently. In Zelenograd, the "first swallow", the commercial joint-stock pharmacy, "Vitafarm", has already become the founder of four joint-stock enterprises of the closed type, comprising an association of joint-stock pharmacies. Supply problems were the main cause of the necessity of associating for Zelenograd, an administrative district located at a distance from Moscow. Pharmaceuticals are products with rigidly limited shelf lives and sales periods; therefore, it is often impossible to store a large amount of medications in one pharmacy, and disadvantageous as well. At the same time, suppliers, by contrast, are interested in selling large consignments of goods. In addition, it is much more convenient over all in carrying out general bookkeeping and in solving their problems. However, the accounts, expenditures, and profits of each enterprise are undoubtedly its own, just as concerns about how to become competitive, to increase revenues, and to attract buyers remain its own.

"Vitafarm" is already able to share its first results. The assortment of goods which this pharmacy is offering customers is unusually wide for us. This includes infant food and cosmetics, eyeglasses and homeopathic agents, therapeutic and decorative cosmetics, medicinal herbs, and ancillary goods. The quality of these products is guaranteed by the excellent reputation and considerable repute of the companies supplying them. "Vitafarm" has concluded a contract with the "Farmatseya" association which is engaged in hard-currency purchases and in the supply of hard-currency pharmacies, and sells these preparations for rubles. They are quite expensive for the purchaser, but nevertheless cheaper than for hard currency. And, in light of the fact that many of these are produced only abroad and could be acquired previously only for dollars, the services of this commercial pharmacy are indispensable for many people. The pharmacy offers a large selection of children's cosmetics of the American company "Johnson and Johnson", all sorts of creams and lotions, shampoos and balms, lacquers and hair sprays of the German company, "Nivea". The eyewear at "Vitafarm" is of joint Anglo-Indian manufacture. An entire well-known collection of homeopathic agents, about 400 items in all, and much much more, are offered. The pharmacy's daily turnover of goods reaches 30 thousand rubles.

"So far we are far from accomplishing that was planned," states Nadezhda Suvorova, director of the Central Joint-Stock Pharmacy of Zelenograd, the founder of "Vitafarm". "The wages of our workers are not high enough. It is necessary to invest a large part of the assets in the business. At the initial stage we were able to get by without debts and without getting credits at a bank. Work was organized and contracts concluded. However it may turn out that tomorrow there won't be any contracts, and it will be necessary to turn to the commodities exchange. Therefore is necessary to carry a certain reserve of money. It required a good deal of effort to convert the Zelenograd pharmacies to a joint-stock basis. The organizational stage was very tense. On the contrary it was much easier to solve these problems in the pharmacies which became municipal pharmacies in the Moscow administrative districts. We also set up two such pharmacies. We also had the idea of selling pharmacies through an auction to private owners. But how this might turn out for patients requiring pharmaceuticals is unpredictable. It obvious that the pharmacy business requires professional knowledge since it affects people's lives, and the errors of amateurs in this field are not correctable. In any case, a service must exist which carries out licensing, the certification of pharmacy workers and their assignment to qualifications categories, monitoring the maintenance of sanitary codes for the storage of pharmaceuticals and monitoring the condition of pharmacies. This is especially important now that pharmacies, while shifting to new forms of property, are beginning to compete with one another, and that the goods whose sale is giving them the possibility of achieving success include narcotic, psychotropic, anabolic, and other agents which are dangerous in unskilled or impure hands. Let us hope that the recently created Moscow Chamber of Pharmacies will take care of this problem.

"Well, we are doing everything we can to hold on to our good reputation, and this is so above all because even before we could not work in any other way, and now that pharmacy work has become a business for us, we are convinced that an honest attitude toward our work will be profitable as well."

International Virology Conference in St. Petersburg

937C0108A Moscow NEZAVISIMAYA GAZETA, in Russian 15 Sep 92 p 6

[Article by "Severo-Zapad" Information Agency: "Virologists of the World Meet in Saint Petersburg"]

[Text] The international symposium "One Hundred Years of Virology" will take place from September 21 through September 25 in Saint Petersburg, the World Health Organization, UNESCO, the Russian Academies of Science, Medical Science and Agricultural Science have acted as its organizers. More than 500 scientists from the United States, England, France, Germany and Japan will participate in the work of the symposium.

Pharmacies Decentralized

937C0108B Moscow DELOVOY MIR in Russian 3 Sep 92 p 12

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UK-Russian Cooperation in Drug Manufacture

937C0108C Moscow IZVESTIYA in Russian 9 Sep 92 p 7

[Article by Lidiya Ivchenko: "A New Approach to the Importing of Pharmaceuticals; It Is Not Only Supporting Public Health, But Stimulating Domestic Industry"]

[Text] Paracetamol in sweet syrup, an effective pain-relieving and temperature-lowering agent, one of the most popular medications, which probably not a single family with children in Europe can get along without, will soon appear in our pharmacies. It is now produced by the English company "Wellcome", but in time the Kursk Pharmaceutical Combine will begin to produce it; the English will transfer technology, the trademark of its product, various types of equipment, etc. to this combine, as an agreement of the recently created joint Russian-English joint-stock company stipulates. "Such cooperative collaboration is one of the paths to the support and development of our own pharmaceutical industry," states the RF [Russian Federation] Deputy Minister of Health, Chairman of the Committee on the Medical Industry, A. Vilken. "The fact is that we will not get along without purchases of pharmaceuticals abroad anyway; we have to import 30-40 percent of preparations, since we do not produce some of them at all. So we have worked out a new approach to these purchases. Companies that wish to cooperate with us are obtain a guaranteed order for consignments of finished pharmaceuticals, which they immediately deliver to our country. For this they pass along to us within the agreed period the know-how and partial equipment for the production of these preparations, and train the enterprises' workers; in a word, they participate in the organization of production in Russian enterprises. That is, now we are not simply buying, but are gaining access to the newest technologies and modern training methods, which is undoubtedly stimulating our industry. In particular, the 'Wellcome' company is contributing 60 percent of the assets paid to it for paracetamol in the form of equipment for the Kursk Pharmaceutical Combine, its partner." Aleksey Vilken emphasized that collaboration of this kind also yields a not inconsiderable gain in time. At the "Akrikhin" enterprise, for example, which is close to Moscow, the production of the cardiovascular agent, capoten, which is already half as expensive as it would be if bought in finished form, has been set up in this manner. As our raw materials are adapted to foreign technology, the "currency" component of raw materials will be excluded more and more. The production of the anti-ulcerative preparation, venter, has also been mastered; only some components for its manufacture are being purchased abroad. Cytotec, which are also anti-ulcerative tablets produced by the Moscow production association, "Moskhimfarmpreparaty", jointly with the American company, "Searle", has been sold in pharmacies for several months now.

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