

Uvodnik/Editorial

PASTEROV ZAVOD U NOVOM SADU,
90 GODINA RADA
NA PROFILAKSI BESNILA

PASTEUR INSTITUTE IN NOVI SAD,
90 YEARS OF WORK
ON RABIES PROPHYLAXIS

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Nakon osnivanja 1921. godine, Pasterov zavod u Novom Sadu neprekidno radi na besnilu do danas. Njegov doprinos preventivnoj medicini bivše Jugoslavije bio je ogroman, pre svega u proizvodnji vakcine protiv besnila. Njegov prvi direktor, dr Adolf Hempt, rođen u Novom Sadu 1874, je autor svetski poznate vakcine protiv besnila koja je nazvana po njemu i bila u upotrebi od 1925. do 1989. godine ⁽¹⁾. On je bio prvi u svetu koji je napravio potpuno inaktivnu, odnosno mrtvu vakcinu, koja je mnogo bezbednija, tako da su je mnoge evropske zemlje poput Austrije, Čehoslovačke, Nemačke i Mađarske postepeno prihvatile i to pod imenom Hemptove vakcine. Novi postupak pripreme vakcine protiv besnila i smanjenje protokola vakcinacije na samo 6 dana, dr Hempt je prvi put objavio na francuskom jeziku, koji je dobro znao, u jednom od tada najuticajnijih časopisa, *Anali Pasterovog instituta* u Parizu, 1925. godine.

Hemptonov učenik od 1926. i njegov naslednik na mestu direktora od 1946, dr Milan Nikolić (1896-1974), objavio veliki broj radova na besnilu, od kojih su neki navedeni i u savremenim udžbenicima, kao i veliku monografiju na srpskom jeziku „Besnilo ljudi i životinja“ (1955, str. 1-539), kao i manju na nemačkom („Die Tollwut“), koja je objavljena od strane jednog od najvažnijih izdavača tog vremena u svetu, Gustav Fischer Verlag, u Štuttgartu, 1961. Najcitiraniji rad Nikolića i njegovog saradnika, docenta dr

After foundation in 1921, Pasteur Institute in Novi Sad working on rabies in continuity up today. Its contribution to preventive medicine of former Yugoslavia was enormous, primarily in production of vaccine against rabies. Its first director, Dr. Adolf Hempt, born in Novi Sad in 1874, is the author of the world famous vaccine against rabies which is named after him and was in use from 1925 to 1989. ⁽¹⁾ He was the first in the world to have made a completely inactive, i.e. dead vaccine, which was much safer for use, so many European countries such as Austria, Czechoslovakia, Germany and Hungary gradually accepted it under the name of Hempt. The new procedure of preparation of vaccine against rabies and reduced protocol of vaccination in only 6 days, Dr. Hempt first published in French, which he was good at, in one of the most influential journals, *Pasteur Institute Annals* in Paris in 1925.

Hempton's student since 1926 and his successor as director since 1946, chief of staff, Dr. Milan Nikolić (1896-1974), published many works on rabies, some of which are quoted in modern textbooks, as well as a big monograph in Serbian „Human and Animal Rabies“ (1955, pp. 1-539) and a smaller one in German (*Die Tollwut*), which was published by one of the most important publishers of the time in the world, Gustav Fischer Verlag, in Stuttgart, 1961. The most quoted work of Nikolić and his associate, assistant

Zdravka Jelesića je iz 1956, u kome su bili prvi u Evropi izolovali virus besnila iz slepog miša⁽²⁾. Ovaj rad je citiran u nekoliko međunarodnih časopisa i monografija koje se bave besnilom, čak i nekoliko decenija posle njegovog objavljivanja.

U 1954. godini Nikolić je osnovao Odeljenje za humanu virusologiju, a njegov prvi šef, dr Pavle (Paul) Fenje (1915-2010.) poznat je po novoj tehnologiji za proizvodnju vakcine protiv besnila na kulturi tkiva⁽³⁾. Godine 1960, posle emigracije u Kanadu, Fenje je opisao adaptaciju soja virusa besnila „Street Alabama Dufferin“ (SAD) na rast u kulturi ćelija bubrega hrčka. Time je dao značajan doprinos u razvoju vakcine protiv besnila, ali će biti zauvek upamćen po razvoju liofilizovane vakcine protiv velikih boginja, koja je na kraju dovela do iskošenjavanja ove bolesti⁽⁴⁾.

Nedavno, mi smo upotrebili BHK 21 C13 kulturu ćelija za proizvodnju humane vakcine protiv besnila, u vreme kada uvozna vakcina nije bila dostupna. Rezultati dobijeni u ovom istraživanju ukazuju da BHK 21 C13 ćelije omogućavaju proizvodnju efikasne i bezbedne vakcine protiv besnila za humanu upotrebu⁽⁵⁾.

Primena imunoglobulina je obavezan deo profilakse besnila kod svih teških, transdermalnih ozleda od besnih životinja. Od 1990. godine, u saradnji sa Institutom za transfuziju krvi u Beogradu, Pasterov zavod učestvuje u proizvodnji antirabičnog imunoglobulina (HRIG). Bez nacionalne proizvodnje, ne bi se mogle obezbediti dovoljne količine ovog preparata, jer je njegova cena na svetskom tržištu prilično visoka, preko 1.000 \$ po pacijentu⁽⁶⁾.

professor, Dr. Zdravko Jelesić is the one from 1956, in which they were the first in Europe to isolate bat rabies virus⁽²⁾. This work was quoted in several international journals and monographs which deal with rabies, several decades after its publication.

In 1954 Nikolić founded Department for Human Virusology and his the first head, Dr. Pavle (Paul) Fenje (1915-2010) introduced a new technology for rabies vaccine production on tissue culture⁽³⁾. In 1960, after emigration in Canada, Paul Fenje described the adaptation of the Street Alabama Dufferin (SAD) strain of rabies virus to grow in hamster kidney cell cultures. He made important contributions to the development of rabies vaccines but will be forever remembered for his development of a freeze-dried smallpox vaccine, which ultimately led to the eradication of this disease⁽⁴⁾.

Recently, we used BHK 21 C13 cell culture for human rabies vaccine production, in time when imported vaccine was not available. Results obtained in this study indicate that BHK 21 cells offer the possibility of producing an efficacious and safe cell-culture rabies vaccine for human use⁽⁵⁾.

Application of the rabies immunoglobuline is a compulsory part of the prophylaxis of rabies in all severe, transdermal lesions caused by rabies infected animals. From 1990 in cooperation of Institute of Blood Transfusion in Belgrade and Pasteur Institute in Novi Sad, we produced human rabies immunoglobulin (HRIG). Without national production, sufficient quantities of human rabies immunoglobuline could not be provided, since the price on the world market is rather high (over \$1000 per patient)⁽⁶⁾.

REFERENCE

1. Lalosevic D. Dr. Adolf Hempt i osnivanje Pasterovog zavoda u Novom Sadu. Medicinski fakultet Novi Sad, Monograph. No.74,2008,1-120.

2. Nikolic M, Jelesic Z. Isolation of rabies virus from insectivorous bats in Yugoslavia. Bull World Health Organ. 1956;14(4):801-4.

3. Fenje P. A rabies vaccine from hamster kidney tissue cultures: preparation and evaluation in animals. Can J Microbiol 1960,6:605-609.

4. Fenje P. [Development of medical virology] Med Pregl. 1998;51 Suppl 1:69-70.

5. Lalosevic D, Lalosevic V, Lazarevic-Ivanc Lj, Knezevic I. BHK-21 cell culture rabies vaccine: immunogenicity of a candidate

vaccine for humans. Dev Biol (Basel). 2008;131:421-9.

6. Romić M, Tomović O, Medić P, Pelević S, Sindić M, Popović M, Gligorović V, Bogdanović G, Mitrović M, Petrović M, Stankov S, Lazarević-Ivanc L, Lalosević V, Lalosević D. [10 years' of production and use of human rabies immunoglobulin in Yugoslavia] Med Pregl. 2001;54 Suppl 1:33-7.