

## EPIDEMIOLOGICAL, CLINICAL AND VIROLOGICAL STUDIES ON INFLUENZA MORBIDITY RATES FOR THE PERIOD APRIL 1962 — MAY 1963 IN THE CITY OF VARNA

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The epidemic process of influenza acquires various forms in its course: pandemics, epidemics and sporadic morbidity inbetween epidemics. We dispose of more precise data on its course in Bulgaria since 1952. More scanty are the data which characterize influenza epidemics in the city of Varna up to 1955 (6) which is seen on Diagr. 1. From the latter it becomes evident that influenza morbidity rates in the city of Varna run parallel to morbidity rates in the whole country, being occasionally more intensive — 1959, 1962 (1, 2, 3). The diagram reveals high level for influenza morbidity rates for the country and the city of Varna in 1956 and an epidemic peak in 1957, 1959 and 1962. The epidemic peak in 1962 is due to an influenza outbreak caused by virus  $A_2$  which started at the end of January and continued till March, the same year (2, 3).

After the epidemics a period was established, characterized by a low level of influenza morbidity rates in the city of Varna.

Stress should be laid on the fact that determination of actual levels of influenza morbidity rates inbetween epidemics is particularly difficult owing to the imperfect diagnosis and the diversity of clinical forms of influenza.

Studies were conducted in order to investigate the particularities of influenza morbidity rates during the period following the outbreak in February 1962. For that purpose statistical data were used of the local Sanitary Antiepidemic Station and the epidemiological data of the patients treated for influenza at the Clinic for Infectious Diseases of the Higher Medical Institute in Varna.

The intensity of the influenza epidemic process is reflected on Diagr. 2 and Diagr. 3. From the diagrams it is seen that from March 1962 until

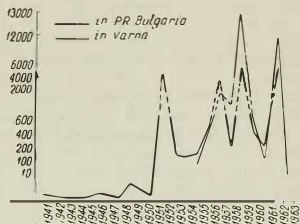


Diagram 1. Influenza morbidity rates in P. R. Bulgaria and in the city of Varna per 100,000 population for the period 1941—1963  
 ..... the city of Varna  
 — P. R. Bulgaria

the end of February 1963 only sporadic cases of influenza are recorded in Varna. The intensity of the process increased in March. It is more marked if the cases hospitalized in the Infectious Hospital are also taken into consideration.

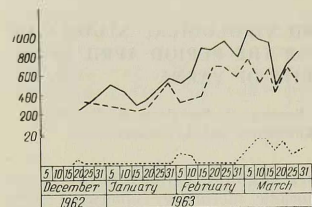


Diagram 2. Incidence rates of influenza, common cold and number of house calls for 5 days periods over the period December 1962 to March 1963

----- house calls  
 ————— common cold  
 ..... influenza

Nevertheless, influenza morbidity rates for the period after the influenza epidemic in 1962 does not exceed the usual morbidity characteristic of periods inbetween influenza epidemics i. e. the influenza epidemic process has run a course under the form of sporadic morbidity.

As far as age group distribution of the cases is concerned it should be pointed out that the group of children up to 1 year old prevails. The latter represent 47% of the registered cases, i. e. a contingent, which consists of children born after the last influenza outbreak. If we add to this group the cases in infants which at the time of the outbreak have been several months old, this percentage rises to 74.

Therefore the influenza epidemic involved primarily those groups of individuals, who have not suffered from influenza.

The clinical observations cover the more severe cases in children, admitted and treated at the Clinic for Infectious Diseases in Varna, during the months of March, April, May, 1963. The children are distributed according to age as follows: from 0—1 year — 45 and from 1 to 6 years — 34, a total of 79.

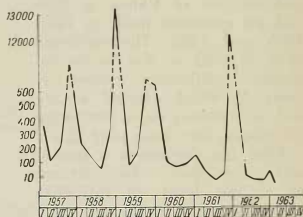


Diagram 3. Influenza morbidity rates by trimesters in Varna for the period 1957 to 1963 per 100,000 population

The clinical picture which started with an upper respiratory tract infection — with rhinopharyngitis displayed from the very beginning of the ailment some peculiarities in its course: a tendency for complications along descendant routes appearing in the first few days (tracheitis, bronchitis, bronchopneumonia) despite treatment with antibiotics as well as the markedly severe course in infants during the first few months of life. The onset of the disorder is more clear and delineated as compared to what we are accustomed to observe in ordinary nasopharyngitis. The children fell suddenly ill, the disorder rapidly progressed (in some cases mothers could even precisely check the hour of the onset of the disorder) with a rise in temperature up to  $39 - 39.5^{\circ}\text{C}$ , a dry irritant cough and marked anxiety. In two of the children the disorder started with a hyperthermic convulsion, and in 22 — with intractable vomiting. In 34 children as early as the first two days fine moist rales occurred as well as single crepitations. The toxic forms predominate (58 children). As the disease progresses the general symptoms become more marked — fever remains high —  $38.5 - 39.5^{\circ}\text{C}$  for 3—5 days. In 51 of the children acute tracheobronchitis developed and spasmodic bronchitis. Bronchopneumonia was recorded in 23 cases.

Careful interrogation of mothers revealed that 18 of the children exhibited a state of slight discomfort, prior to the onset of influenza, with subfebrile temperature and a running nose. They have received irregular domestic treatment with penicillin. Then usually following a contact with an adult "influenzal" patient — member of the family or visitor their condition sharply deteriorated.

68% of the children were hospitalized between the first and the third day from the onset of the disease. The examination of children performed on admission to hospital usually revealed throat findings. The mucous membrane of the palate arches, the uvula and the posterior wall of the pharynx is erythematous and edematous. The tonsils are more seldom involved. Marked rhinitis at the beginning with a mucous-watery discharge, which later becomes mucous-purulent and more profuse was observed in 16 of the children. The infants were agitated, with slight perioral cyanosis and injected sclerae; in two of them marked catarrhal conjunctivitis was present. Signs of respiratory distress were recorded on admission: tachypnea, dyspnoea, nostril breathing. Auscultation of the lungs reveals fine moist rales and single disseminated crepitations on the background of a coarse vesicular breathing. Later a bronchopneumonic focus was rapidly delineated usually in the pulmonary base or axillar region. In most of the children cough is dry and hoarse at the beginning and later becomes productive; it lasts for 10—14 days. Laryngitis is not observed. This may indicate that the inflammatory process in the nasopharynx may be directly transferred over the trachea and the bronchi. X-ray examinations revealed pathological findings in the lungs of 23 children — infiltrative foci with vague delineations, which persisted for 6—8 days.

The blood picture in the observed 79 children was characterized by leucopenia with a slight shift to the left in 21 children and mild leucocytosis in 19. The remaining children had normal leucocyte counts. The ESR is markedly elevated in 59 children. Urinalysis — no pathological findings.

A more typical case is hereby presented:

D. N., aged 6 months, case history No. 452 from March 17, 1963:

Ten days prior to the onset the child suffered from rhinopharyngitis and was treated at the Pediatric Department, from where it was discharged healthy after 7 days. Four days later it suddenly fell ill with high temperature which reached 39.8°C., vomiting and laboured breathing. Two days before, friends of his brother one of whom had general discomfort and fever visited the home. The child was in contact with them. It was admitted in the Clinic in a seriously impaired general condition, febrile (38.6°C), very agitated, with dry visible mucous membranes, mild nostril breathing. The throat — darkly reddened palate arches, uvula and pharynx. Breathing — accelerated, regular, over the left pulmonary area fine moist rales, without any crepitations. The child was admitted to hospital with the following diagnosis: Rhinopharyngitis acuta. Bronchopneumonia incipiens.

Leucocytes: 12,950; of them 19% rod cells, 41% polynuclear, 33% lymphocytes, 7% monocytes, ESR — 32 min after Panchenko. Urinalysis — traces of albumin, 4-5 leucocytes, urates and much salts so uric acid. Treatment was started with penicillin and streptomycin, oxygen and vitamins. The temperature dropped on the second day to 37.7°C, but later rose again: a double peak temperature curve was recorded. The symptoms on the part of the respiratory system increased. Perioral and periungual cyanosis appeared, epigastric tirage and nostril breathing. Auscultation reveals multiple, wheezing rales over the right pulmonary area and single crepitations. X-ray examination — in the right subclavicular region a soft infiltrative shade is seen with vague markings connected with the hylum. The child also developed catarrhal otitis. On the third day resistomycin and depot-sulfamid were administered. On the seventh day after admission the temperature became subfebrile and on the 12th — normal. The child was discharged from hospital healthy on the 19th day.

The average hospital stay of the children amounted to 8 days. All were discharged healthy. Of them 11 were followed up after discharge from hospital, but no late complications were recorded.

Marked intoxication was observed mainly in the youngest children — aged up to 6 months. We observed the case of an infant aged 40 days from K. The disease ran a very rapid course, in the form of an acute infectious toxicosis, which terminated fatally.

M.Chr.J. — a big, eutrophic, breast fed infant with an uneventful past history. Since two days indisposed and tearful, with a mild cough and a low grade fever. It was treated with penicillin at home by the family physician. At home his relatives were indisposed for the last few days with mild rhinitis and lassitude. On March 24th in the night the temperature rose to 40°C; the child relaxed, convulsions occurred on its extremities. He was immediately admitted to the district hospital, but died in out-patient service in a state of clonic-tonic convulsion with severe respiratory distress and cardio-vascular failure. Postmortem examination revealed the presence of multiple punctiform hemorrhages on the pleura, the epicardium, the thymus the brain, and the intestines. The viscera were cyanotic. The lungs — oedematous.

Clinically it was difficult to make etiologic diagnosis. Differential diagnosis included influenza, viral infections, other respiratory infections and bacterial rhinopharyngitis. The exact diagnosis of influenza was made after the results of the virologic examinations were received.

Nasopharyngeal washings were used for virologic examinations. They were obtained and treated after the generally accepted methods by contamination of 11 day chicken embryos which were incubated at 35° C (5). To prove the presence of influenza virus in the allantoic fluid the hemagglutination test was performed using a 1% suspension of chicken erythrocytes. Typing of isolated influenza strains was performed by means of the hemagglutination inhibition test (H.I.T.) with type specific antiinfluenza sera.

47 double sera specimens from the patients were used for serologic investigations. They were provided from Varna and several surrounding villages at the onset and on the 14th day of the disease. Sera were examined by means of H.I.T. after the generally accepted method with standard diagnostic sera, production of NIEM (Research Institute for Epidemiology and Microbiology). The role of influenza virus A<sub>2</sub> and B as etiologic agents in the influenza epidemics in 1963 was established.

A total of 59 specimens of individual nasopharyngeal washings were virologically investigated, from which 7 strains of influenza virus were isolated. Typing revealed that influenza virus A<sub>2</sub> is concerned. No type B influenza virus was isolated, although its spread in some villages in the district was proved serologically by means of the hemagglutination inhibition test (H.I.T.). The strains adapted to chicken embryos comparatively easily and as early as the 2nd — 3rd passages the titre reached from 1:64 up to 1:256, and toward the 5th—6th passages — from 1:256 to 1:512.

The infectious titre of the strains (1, 3, 6, 15, 24) was 10<sup>-8</sup>. The same strains appear nontoxic for rabbits and mice.

Nasopharyngeal washings were examined also in tissue cultures and in newborn mice. No viral agents were detected in the inoculated tissue cultures and newborn mice.

### Conclusions

The influenza epidemic process developed under the form of sporadic influenza morbidity and involved mainly groups of population who have not suffered from influenza during the last epidemic in 1962.

Seven strains of type A<sub>2</sub> of influenza virus were isolated.

By means of hemagglutination inhibition test (H.I.T.) and on 47 double serum specimens a rise in antibody titres against type A<sub>2</sub> and type B was established.

The acute onset of the disease, with rapid and early toxemia and a more severe course differentiate the disease from common cold and the remaining upper respiratory tract diseases. One is impressed by the tendency toward rapid development of descendant respiratory complications — tracheitis, tracheobronchitis, spasmodiobronchitis with bronchopneumonia. The addition of influenza to existing rhinitis, rhinopharyngitis and bronchitis of other etiology severely complicates the clinical picture and demands rapid measures and a serious attitude toward the ill child. During influenzal outbreaks not every rhinitis and cough in children should be regarded as influenza. For that reason children with such symptoms should be isolated from adult members of the family, suffering from influenza.

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### ЭПИДЕМИОЛОГИЧЕСКИЕ, ВИРУСОЛОГИЧЕСКИЕ И КЛИНИЧЕСКИЕ ИССЛЕДОВАНИЯ ЗАБОЛЕВШИХ ГРИППОМ В ТЕЧЕНИЕ ПЕРИОДА ОТ АПРЕЛЯ 1962 ГОДА ДО АПРЕЛЯ 1963 ГОДА В ГОРОДЕ ВАРНА

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#### РЕЗЮМЕ

Гриппозный эпидемический процесс протек в виде спорадической гриппной заболеваемости и охватил преимущественно контингенты неболевших гриппом.

Вирусологически были исследованы 59 индивидуальных проб — смывов, среди которых были изолированы 7 штаммов гриппозного вируса типа А<sub>2</sub>.

Посредством РЗХА 47 двойных сывороточных проб было установлено заболевание гриппным вирусом типа А<sub>2</sub> и типа В.

Острое начало, быстро наступающая ранняя интоксикация и более тяжелое течение отличают заболевание от банальных ринофарингитов и остальных катаров верхних воздухоносных путей. Бросается в глаза склонность к быстрому развитию осложнений — трахеобронхитов, бронхитов со спастической компонентой и бронхопневмоний. Прибавление гриппа к существующим ринитам, ринофарингитам и бронхитам с иной этиологией, очень утяжеляют клиническую картину и требуют быстрых мер и серьезного отношения к заболевшему ребенку.