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The role of air temperature in the dynamics of respiratory infection incidence in a megalopolis

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Abstract — The results of statistical analysis of data related to the morbidity of respiratory infections in Moscow in the period of 1959–1988 are described. A decrease in morbidity in the winter epidemic period and its growth in the summer interepidemic period are pointed out. The analysis shows that the regularities of the spread of respiratory infections do not depend on the season, but the parameters of the epidemic process essentially change at the beginning of the school year and in the period of Christmas holidays. The respiratory infection morbidity in the interepidemic period linearly grows with decreasing air temperature, but the beginning of an epidemic does not depend on air temperature. A mathematical model taking into account the dependence of the intensity of a respiratory infection on air temperature is constructed.

Respiratory tract infections are the most widespread diseases in developed countries. On the average, an adult person falls ill with an acute respiratory disease (ARD) 2.5 times a year and children under 4 years fall ill 4.5 times a year [9]. The respiratory infection death rate is 1–2%. The risk of unfavorable outcome is maximal for infants, aged people, and people with immunodeficiency [3].

The high morbidity leads to a considerable economic burden at the national level [4] and to a faster deterioration of the immune system of an organism [5].

The term 'acute respiratory disease' combines more than 200 aetiologically separate diseases, which have the following three common factors: the way of transmission of the causative agents (droplet, contact), the localization of the main pathologic process (in respiratory tracts), and the clinical symptoms.

The main pathogens of respiratory tract diseases are viruses: rhinoviruses, coronaviruses, viruses of influenza A, influenza B, parainfluenza, and adenoviruses. Different types of viruses have different seasonal patterns. For example, the influenza virus A causes the most intense epidemic in winter months. The beginning of a school year in educational institutions is annually accompanied with outbreaks of infection caused by parainfluenza viruses of types I and II. Parainfluenza viruses of type III are the cause of ARD in summer and at the end of spring [6].

The ARD viruses quickly loose their infectious activity in the ambient environment, therefore, a high population concentration is necessary for epidemic development. The infection probability increases in prolonged contacts, for instance, in

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public transport or in recreational and educational institutions. Another condition for epidemic development is the population size. The fact is that a sick person releases viruses only for a few days and then his immune system eliminates the virus and forms the immune memory against this virus. During the infection period a single person can infect several other persons and then after some infection cycles the population gets a sufficient number of sick persons, and we may speak on an epidemic. If the population is separated into several parts, the epidemic picture is distorted due to delays in the causative agent transmission and to some local variations, for example, in weather. Therefore, it is most convenient to study the course of the epidemic using the example of a certain city.

The laws of epidemic development are well studied [2], but from the viewpoint of the general theory a causative agent has to appear, for which there is no immunity in a considerable part of the population. However, this does not explain the regular ARD incidence in winter periods, which is not always connected with the appearance of a new causative agent. A possible explanation of the winter increases in the disease incidence, is the assumption that a low temperature impairs the resistance of the immune system and increases the population crowding, because people spend much time indoors. Yet there are no studies with a quantitative estimation of the role of climatic factors in the dynamics of the ARD incidence, and the correlation of these factors with the level of specific and nonspecific resistance of the population.

The population of Moscow in 1960 – 80ies is a convenient sample for the study of epidemic processes. The population of 8 millions was served by the state health care system. Migration processes were strictly controlled and had a limited influence on the population and the morbidity. The diagnostics standards for ARD remained practically the same within the whole period. The cases of diseases were accounted in medical certificates with diagnoses. The data for the whole city were summarized for the estimation of the epidemic situation. The long-term array of comparable data was thus formed for the ARD incidence in the population of the known size. Note that Moscow has several permanently working weather stations on its territory, which allows one to obtain a continuous series of observations and compare them to the morbidity data.

1. ARD morbidity in Moscow during the period of 1959 – 1988

The data are the records of the number of medical certificates with the ARD diagnosis issued by Moscow medical centers per week. The considered time series exhibits seasonal fluctuations and long-term trends.

Analysis of morbidity trends. Consider the variation of morbidity in this 30-year period. The annual morbidity grows at the rate of 0.1 cases per 1000 people per year, from about 8 to 11 cases in 30 years. Figure 1 shows that this growth is typical for the minimal level of the morbidity; in other seasons the dynamics is not obvious. In order to estimate the variation of morbidity depending on the season, we

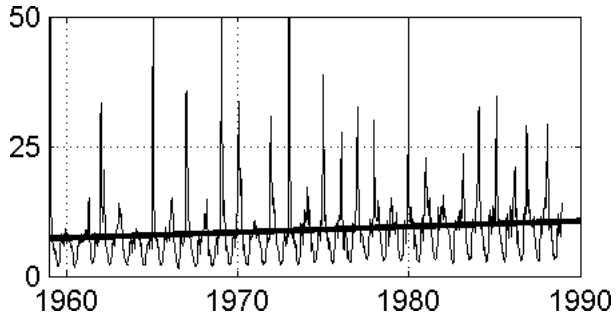


Figure 1. Thin line represents the ARD morbidity in Moscow from 1959 to 1989 (the number of new cases per 1000 per week). The long-term trend is represented by the thick line: the morbidity grows at the rate of 0.1 cases per 1000 persons per year.

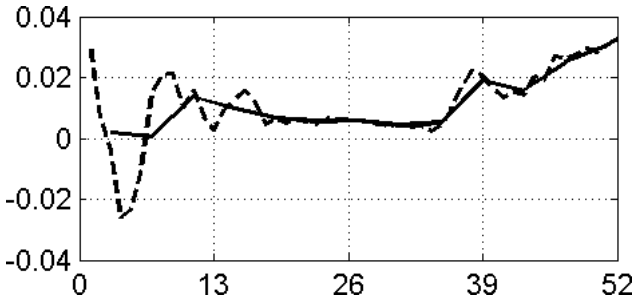


Figure 2. The coefficients of the trend line slope versus the week number (1 corresponds to the first week of January). The solid line represents the mean values of the coefficients for the corresponding month, the dashed line represents the same for the week.

estimate the slope of the trend line for each week and each month (see Fig. 2). It is seen that the growth of the annual morbidity is caused by the growth of the autumn morbidity and in a lesser degree by the spring morbidity. The morbidity dynamics in the epidemic period (January, February) is characterized by the growth at the beginning and in the end of the epidemic rise and a decrease in the peak morbidity.

Analysis of correlations of morbidity levels. As was already noted, the probability and the rate of the epidemic spread and its end greatly depend on the level of the immune protection of the population from the causative agent. The fraction of the individuals with the immune memory characterizes the level of immune protection of the population. The immune memory is formed after the recovery from an infection caused by that agent. Therefore, the level of the current morbidity has to depend on the morbidity in the previous time period. The level of the immune memory decreases in time, and it is assumed that after several years it does not provide protection from infections. In order to study the relations of ARD morbidity levels in different time intervals, we use the autocorrelation and the correlation functions.

The autocorrelation function (ACF) characterizes the relationship between a time series and the same series shifted by some time interval (time lag). For the

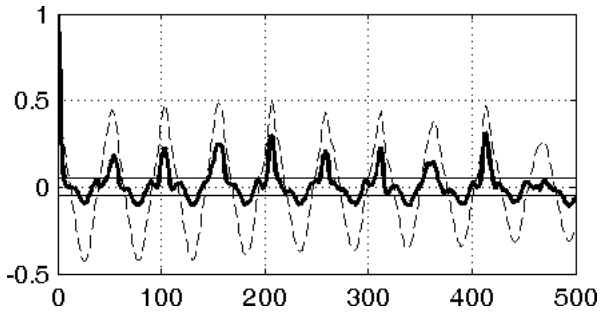


Figure 3. Autocorrelation function versus lags in weeks. The dotted line represents the ACF for weekly data on ARD incidence. Thin horizontal lines represent the boundaries of 95% confidence intervals. The thick line represents the ACF of the series obtained from the original one by removing the linear dependence on air temperature.

time series $X_1, X_2, \ldots, X_n$ of length n the ACF is calculated by the formula

$$R(k) = \frac{1}{(n-k)\sigma^2} \sum_{t=1}^{n-k} [X_t - \mu][X_{t+k} - \mu]$$

where $k < n$, σ^2 and μ are the variance and the mean value of the series, respectively.

The ACF for weekly ARD data has the form of an oscillating curve with the period of 52 weeks, or one year (see Fig. 3). The shape of the curve indicates the regularity of the seasonal cycles of morbidity. That is, if we compare the morbidity for any weeks distant from each other by a particular time interval, the maximal correlation is observed for the intervals of one year, two years, etc. Therefore, the seasonal climate variation essentially influences the ARD incidence. Figure 3 shows that the ACF has the local maximum 0.52 ($p < 10^{-4}$) for the lag value of 4 years (207 weeks), this value is by 15% greater than that for the lag of 1 year and by 9% greater than that for the lag of 2 years. This strengthening of the positive correlation between ARD morbidity levels, as the time interval increases, is most likely caused by deterioration of the immune memory. The correlation increases after the removal of the linear dependence on air temperature (see below). Thus, the calculation of the ACF has confirmed the effect of climatic factors on ARD morbidity and a sufficiently fast decrease of the immune memory against ARD causative agents. But the method of ACF gives an average estimate for this dependence over a year and does not allow us to study the specific correlations between morbidity levels typical for different seasons.

It is known that respiratory infections are caused by different pathogens in different seasons, and it is useful to study how the correlation coefficients between ARD morbidity levels for adjacent weeks depend on the season. This will reveal the seasonal peculiarities in the morbidity dynamics. To do that, we construct a matrix from the elements of the time series of ARD morbidity levels $X_1, X_2, \ldots, X_n$, where the ith row contains the morbidity for the ith year from the 1st to the 52nd week,

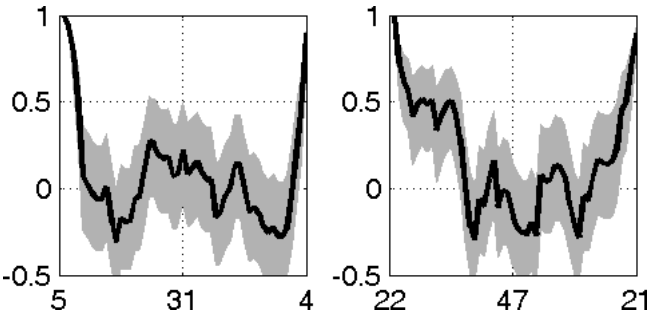


Figure 4. Example of analysis of intrinsic relationship. On the left: the sequence of correlation coefficients for the morbidity of the 5th week with that for the next weeks. The grey area corresponds to 90% confidence intervals. On the right: the same for the 22nd week.

and the jth column contains the morbidity for the jth week in each year:

$$\begin{array}{cccc} Y_{1,1} & Y_{1,2} & \dots & Y_{1,52} \\ Y_{2,1} & Y_{2,2} & \dots & Y_{2,52} \\ \dots & \dots & \dots & \dots \\ Y_{m,1} & Y_{m,2} & \dots & Y_{m,52}. \end{array}$$

For each column of the matrix we construct the sequence of correlation coefficients with other matrix columns. Figure 4 shows the curves describing the sequences of correlation coefficients for the 5th (February) and 22nd (May) weeks. It is seen that morbidity for the 22nd week has a high correlation with that for the following 15 – 20 weeks. The morbidity for the 5th week has significant correlation coefficients only for the next 5 weeks. The presence of a positive correlation indicates either the presence of a factor synchronizing variations of morbidity levels, or a dependence between those levels in successive time periods. The weather could be such synchronizing factor, but it is known that a significant correlation between weather characteristics holds not longer than 5 days.

It is more probable that this correlation is caused by the fact that sick people infect sensitive individuals, who fall ill later. Therefore, the more sick people we have at a current moment, the more there will be in the next observation period. Such positive correlation holds, while a considerable part of the population has no immunity to the causative agent. The duration of the positive correlation period depends on the morbidity level, and the lower the morbidity is, the longer is the period with a big share of sensitive individuals in the population. When the portion of sensitive individuals becomes small, the spread of the causative agent slows down and the correlation between the morbidity at the beginning and in the phase of the population immunity formation becomes negative. The results presented in Fig. 4 are in good agreement with this interpretation. In fact, the duration of winter epidemics does not exceed 1 – 1.5 months.

An epidemic cycle typical for some pathogen is a period when the morbidity is interdependent. Thus, the duration of the epidemic cycle for the 5th week of the

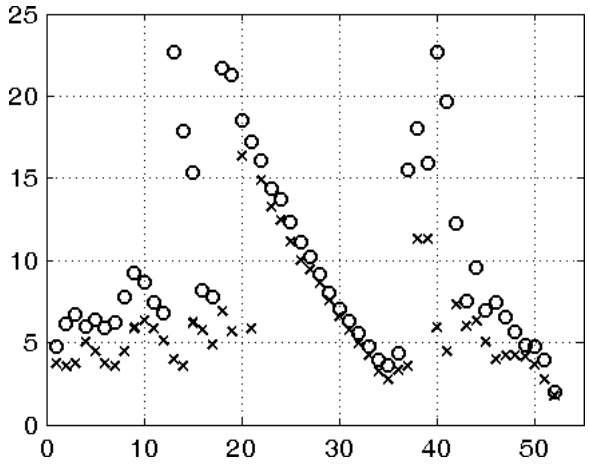


Figure 5. Duration of the epidemic cycle in weeks versus the number of the week. The time interval when the correlation coefficients for the morbidity in the *i*th week and in the following weeks are greater than zero is denoted by circles. The crosses denote the time intervals when the correlation coefficients are distinct from zero with 95% probability.

year is $4-5$ weeks, and for the 22nd week it is $17-19$ weeks. Draw the graph of the dependence of the duration of the epidemic cycle on the number of the week (see Fig. 5). There are two periods of monotone decrease of the epidemic cycle duration in Fig. 5: the summer and winter ones. We may suppose that the natural course of epidemic processes related to the propagation of viruses with various pathogenicity is broken by a sharp change in the pathogene transmission rates at the beginning of the school year and during the Christmas holidays.

2. Influence of air temperature on ARD morbidity level

Within the studied period the population of Moscow increased from 6 millions to 9 millions of people. Naturally, the epidemic threshold was also changed. We assume that the epidemic threshold for respiratory infections equals 15 cases per 1000 people per week. The analysis of air temperature data in Moscow for this period shows that in the interepidemic period the ARD incidence linearly grows under a decreasing air temperature (see Fig. 6).

3. Influence of air temperature on influenza epidemic development

Recent works in influenza epidemiology have showed that all influenza epidemics are caused by new antigenic variants of viruses, which first appear in East and South-East Asia and then spread over the world within a year: in the first $6-9$ moths the new strain affects the population of Oceania, North America, and Europe, and then the countries of South America [12]. It is interesting that epidemics evolve on different continents and in different climatic zones (including the tropics) with

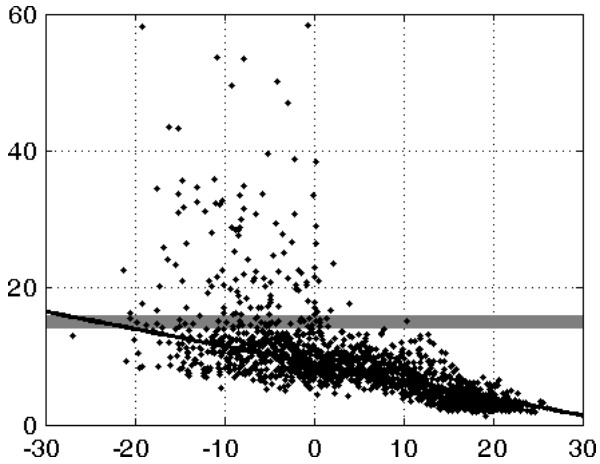
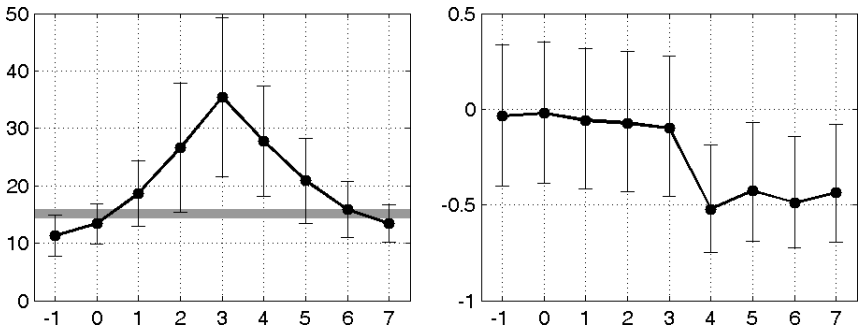


Figure 6. Morbidity versus mean air temperature for the corresponding week in the period from 1959 to 1989 (black points). For the morbidity lower than the epidemic threshold (grey line) the coefficient of correlation with the temperature equals -0.78, $[-0.760.8]$.

a certain shift in time. This shift is mainly caused by the approach of a colder and rainy season [2]. It has been shown that the source of new influenza virus A strains is a region with a developed transportation network. Epidemics in different countries of this region often overlap, which causes a long circulation of viruses at a high epidemic level. This provides favorable conditions for the formation and spread of new virus strains.

In this paper we assume that an ARD epidemic occurs in some particular period if even for one week the morbidity exceeds 15 people per 1000. This value is called the epidemic threshold. Generally speaking, the epidemic threshold is a standard determined annually by the sanitary-epidemiological authorities based on analysis of the epidemiological situation. The epidemic threshold for influenza and acute respiratory virus infections for present-day Moscow is $31-32$ thousands cases a day. If the number of cases exceeds the threshold for three–four days, one says that an epidemic begins. Sometimes such a sharp excess of the threshold is followed by a similarly sharp decrease in the morbidity in one or two days. Such phenomenon is not classified as an epidemic. For the period from 1959 to 1988, the ARD incidence exceeded epidemic threshold for 129 weeks, which is 8.6% of the total observation period and includes 22 epidemics. Note that 82% of the epidemics occurred in the period from the middle of December to the middle of February. The mean duration of an epidemic was 5.6 weeks, the most prolonged excess of the epidemic threshold was observed in the winter of $1969-1970$ and lasted 12 weeks.

Figure 7a presents the averaged dynamics of morbidity during an epidemic. Figure 7b presents the correlation coefficients for morbidity and air temperature for each week of the epidemic. It is easy to see that the morbidity level does not depend on air temperature either before and or during the first three weeks of the epidemic. Starting from the fourth week, the morbidity has a significant negative correlation



(a) (b)

Figure 7. (a) The dynamics of ARD incidence in the epidemic period. The black points denote the mean morbidity. The thick grey line indicates the epidemic threshold. (b) Correlation coefficients for morbidity and air temperature for the corresponding week of the epidemic. For the fourth, sixth, and seventh weeks $p < 0.05$, for the fifth week $p = 0.054$. Ordinate axis: morbidity; abscissa: the duration of the epidemic in weeks.

with air temperature. One may come to the conclusion that the evolution of the epidemic does not depend on air temperature, but in the case of a low air temperature the morbidity level decreases more slowly and the epidemic lasts longer.

4. The mathematical model of the influence of air temperature on the prevalence of respiratory infections

The specific feature of the ARD epidemiology is the fact that a considerable part of infected individuals have no clinical symptoms and do not release the pathogens into the environment. In this case they form the immunity to this pathogen. This feature explains the results of epidemiological studies showing that after an epidemic caused by a new influenza virus about 90% of population have antibodies to this virus, although only $5-10\%$ of the population have had a disease with clinical symptoms. The next peculiarity of the ARD epidemiology is that the appearance of clinical symptoms and the degree of sickness depend on the ambient temperature. This relates to the fact that respiratory viruses effectively propagate in the bronchi epithelium within some particular temperature ranges. As a rule, this temperature is greater than the air temperature, but lower than the body temperature. The temperature of the epithelium of the respiratory tract and the area of the corresponding part of bronchi walls increase approaching the deeper lung parts. As the result, a decrease in temperature leads to the situation when viruses can affect more target cells. This increases the severity of the disease, leads to a cough, and accelerates the transmission of the virus to other individuals. The following model is devoted to the description of this phenomenon.

The principles of the construction and study of models of spread of infectious diseases were described in detail in [2]. The model flowchart for the case of a single virus is presented in Fig. 8. It is supposed that the population can be divided into

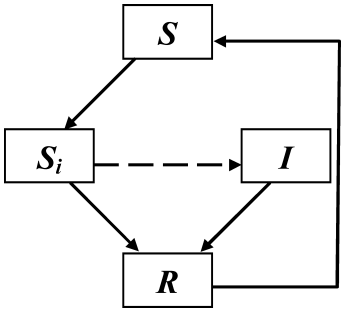


Figure 8. Flowchart of the mathematical model for respiratory infection spread. Sensitive S, infected S_i, infectious ill I, and immune R groups. Dotted lines denote the transitions whose speed depends on the air temperature.

four groups: sensitive S, infected S_i, infectious ill I, and immune R.

$$\frac{\mathrm{d}S}{\mathrm{d}t} = -\alpha SI + \eta R \tag{4.1}$$

$$\frac{\mathrm{d}S_i}{\mathrm{d}t} = \alpha SI - (k+\mu_1)S_i \tag{4.2}$$

$$\frac{I}{\mathrm{d}t} = kS_i - \mu_2 I \tag{4.3}$$

$$\frac{\mathrm{d}R}{\mathrm{d}t} = \mu_1 S_i + \mu_2 I - \eta R. \tag{4.4}$$

The parameter k depends on the air temperature. This model allows one to describe the winter epidemic rise of ARD and its dependence of air temperature.

The data analysis results allow us to make the following conclusions:

(1) The morbidity of ARD in interepidemic periods depends on air temperature: the morbidity grows as the temperature decreases. This dependence is linear.
(2) The morbidity in the beginning of an epidemic and its peak rate do not depend on air temperature.
(3) Under a low air temperature the epidemic process tends to continue.

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