CYCLICITY IN INCIDENCE VARIATIONS OF MENINGOCOCCAL INFECTIONS IN BULGARIA IS SIMILAR TO THAT OF SOLAR ACTIVITY

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SUMMARY

This is a retrospective study on meningococcal meningitis (MM) in Bulgaria that has, for the first time, reported results on non-linear temporal patterns of incidence and its variations. Methods of descriptive statistics, linear and non-linear modelling as well as periodogram regression analysis have been applied. A non-linear decreasing trend in crude incidence rates per 100 persons over the years 1940–1990 has been described ($p < 0.0001$) and cyclic variations revealed (periods T = 8.00, 18.75, 24.75 and 33.50 years, p < 0.05–0.01). Above cycles have been detected after the reciprocal trend has been removed ($y = 1.04 + 15.78/t$). A similar cyclicity (periods T = 8.25 and 27.5 years) in the variations of solar activity (sunspot number Rz) over the same time interval of 51 years has been established after the main cycle of 10.5–13 years has been removed by a two-step procedure. The results from this study have added to our previous findings on cyclic variations in mortality and lethality from meningococcal infections in Bulgaria (1, 2). Above similarity is also in accordance with earlier conclusions on relations of solar activity cycles with epidemics of cerebrospinal meningitis in New York and USA over the years 1800–1935 (3, 4).

Key words: meningococcal meningitis, incidence, cyclicity, solar activity, Bulgaria

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INTRODUCTION

Epidemiological situation of meningococcal meningitis (MM) in Europe has been reviewed (5, 6) but no studies from Bulgaria have been then reported. It is only recently that clinical epidemiology of meningococcal infections in Bulgaria has been systematically studied (7), however, not many details of temporal dynamics and patterns of variations in incidence have been described, either. Our previous studies on mortality and lethality from MM in Bulgaria have revealed cyclicity in variations over the interval 1958–1990 with periods of 12.25 and 11.75 years, respectively (1, 2). It should be noted that cyclic variations might either denote a definite intrinsic feature of incidence time-series or imply patterns modulated (provoked) by external influences, or both. In this sense, if an external effect on meningococcal meningitis in Bulgaria exists, then incidence variations should exhibit a similar cyclicity as reported for flu, mumps, malignant melanoma of the skin, etc. (4, 8–11). On the other hand, earlier studies on data from New York and USA (1800–1935) have reported conformity of solar activity cycles with epidemics of cerebrospinal meningitis (3, 4).

The aim of the present study was to more deeply analyze temporal patterns of the incidence rate of meningococcal meningitis in Bulgaria over the interval 1940–1990 and compare the patterns of incidence variations to solar activity cycles.

MATERIALS AND METHODS

Sources and description of data. The data covered the interval from 1940 to 1990 inclusive consisting of all 9,541 new cases with meningococcal meningitis in Bulgaria (the code after the International Classification of Diseases – IXth revision is Dx:036). The new cases for each calendar year were presented as annual crude incidence rate per 100 persons of the population. The data were kindly provided by Lazarova (7) as collected from the registries of the National Centre of Infectious and Parasitic Diseases (Sofia, Bulgaria). A solar activity index, the relative number of sunspots (Rz), was also analysed as the data for the above interval were obtained from the Prompt Reports of NOAA (Colorado, USA). The discretization of incidence data was on the basis of 1 year (Fig. 1).

Statistical analyses. For the purpose of the present study, descriptive statistics and linear as well as non-linear regression modelling were applied (12) whereas 12 available models were tested and the best fit was selected by the highest coefficient of correlation (r) and least variance of the regression (13). Also, a procedure of detrending was applied when necessary. For detection of cyclicity in variations, the periodogram regression analysis (PRA) with a correlation-regression function F of periodic mode was used (10, 14, 15) (Fig. 2). Within PRA, when necessary, a procedure of decycling was also applied to derive the values $F_i(t)$ of a new time series without a cycle(s) in question, after the equation:

$$F_i(t) = F(t) - \sum\left(A_i \cos\frac{2\pi t}{T_i} + B_i \sin\frac{2\pi t}{T_i}\right) \qquad [1.0]$$

where F(t) are the values of original time series, A and B are the coefficients of regression, T is the length of statistically significant cycle, t is the current moment of time (number of the year: 1, 2, 3, ..., n-1), and n is the number of values in the series. Above procedure could be repeated as many times as required ($F, F_1, F_2, ..., F_{i-1}$). Statistical significance of cycles on the periodogram (see Fig. 2) was verified by the relation of

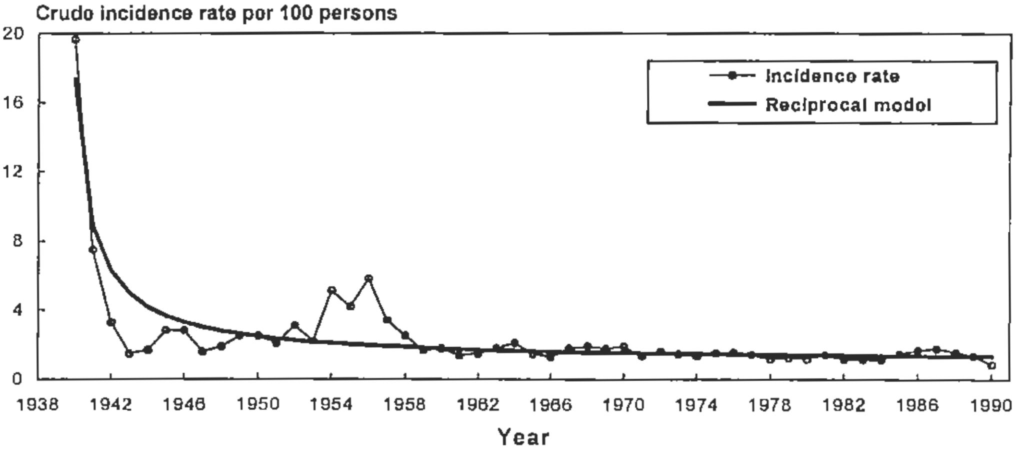

Fig. 1. Model curve of crude incidence rate per 100 persons for meningococcal infections in Bulgaria (1940–1990). Note: The best fit to a non-linear trend has been described by the reciprocal equation y = 1.04 + 15.78/t (r = 0.895, z = 32.35, n = 51, p < 0.0001) where t is the number of the calendar year of registration (t = 1, 2, 3, ...51).

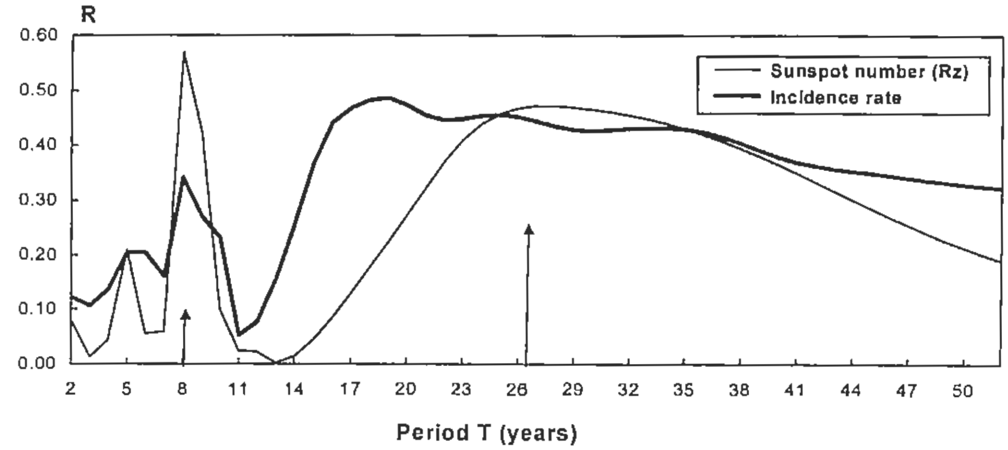

Fig. 2. Periodogram regression analysis of variations in incidence rates for meningococcal infections in Bulgaria and solar activity (1940–1990). Legend: The spectra of coefficients R present infrannual cycles in the variations of crude incidence rates per 100 persons for meningococcal infections in Bulgaria (periods T = 8.00, 18.75, 24.75 and 33.50 years, thick curve) and sunspot number Rz (periods T = 8.25 and 27.50 years, thin curve). The periodograms have been constructed after the meningococcal series has been detrended (the non-linear trend y = 1.04+15.78/t has been removed) and sunspot series decycled in two steps (the cycles of 10.5 and 13 years have been removed consecutively). The arrows indicate zones with significant peaks on periodograms (p < 0.05–0.01).

the coefficient of correlation (R) to its standard error (S_R). Two different criteria were applied: for the normal upper 95% limit – $R/S_R > 1.96\sigma$ and, for the upper 95% limit in a series of random number – $R/S_R^* > (453.2/n^2+3.56)\sigma$. A version of the normal sigma-method was described earlier by Dimitrov (15). Routine statistical and graphical software was used and, for the particular aims of this study, was another statistical package (6-D Statistics ver. 5.0/98 by B. P. Komitov).

RESULTS

Descriptive statistics has not shown a normal distribution of crude incidence rates of MM over the study period (n = 51). The histogram has shown very high values of kurtosis and skewness (k = 28.64, s = 5.10). The best fit to the decreasing rates has been found to be that of a non-linear model (reciprocal equation y = 1.04+15.78/t). The trend, although non-linear, has allowed an explanation of 80.1% of variations in time series of incidence rates for meningococcal meningitis in Bulgaria only.

The variations from the trend (about the rest 20% of temporal dynamics) were analysed by PRA. Two cycles of 7.5 and 14.5 years have been detected but with significance below the upper 95% level for a series of random numbers (not shown). The non-linear trend was removed to allow a relative increase of the power of the significant cycles and their correct determination. Thus, a middle-frequency infrannual cycle of 8.00 years was found (p < 0.05) as well as three low-frequency infrannual cycles of 18.75, 24.75 and 33.50 years were revealed (p < 0.01) (see Fig. 2). Although with a multicomponent cyclic patterns, variations might be divided into two main groups: circaundecennian (period T = 8 years) and circatridecennian (period T ≈ 26 years) cyclicity. Similar cyclicity has been found in variations of solar activity (sunspot number Rz) over the same time interval 1940–1990 – periods T = 8.25 and 27.5 years. The latter patterns of cyclic variations have been detected after the original F series of Rz has been decycled for the main 11-year cycle in a two-step procedure. At the first step, a 10.5-year cycle has been removed and F_1 series constructed and, at the second step – a 13-year cycle has been removed and F_2 series derived and further analysed (see Fig. 2). Obviously, there is a strong similarity between the cyclic variations of solar activity and the cyclic variations in incidence rates of meningococcal meningitis in Bulgaria over the years 1940–1990.

DISCUSSION

Earlier studies have suggested the existence of cycles in meningococcal infections in Bulgaria (16), however, no statistical significance or possible causes have been then provided. The present study has, for the first time, reported results on non-linear dynamics and variations in incidence of meningococcal infections iu Bulgaria and similarity to cyclic variations of solar activity. Main patterns could be summarised as follows: (i) a stable non-linear decrease of annual crude incidence rates over the years 1940–1990 as best fitted to a reciprocal equation ($p < 0.0001$); (ii) multicomponent cyclicity in temporal variations of annual crude incidence rates with two main types of oscillations: circaundecennian and circatridecennian; and (iii) similarity of cyclic patterns in incidence variations for MM to cyclic variations of the sunspot number Rz over the same time interval (1940–1990). These results have added to our previous findings on cyclic variations in mortality and lethality from MM in Bulgaria (1, 2). Above similarity is also in accordance with conclusions on relations of solar activity cycles with epidemics of cerebrospinal meningitis in New York and USA over the years 1800–1935 (3, 4).

It should be noted also that in Bulgaria, although in a rare disease, the time series of new cases has shown the same temporal patterns as incidence rates which means the non-linear trend and cyclic variations of MM are real and have not depended upon the size of the total population. The decrease of incidence over years is probably due to the wide use of sulfonamides and antibiotics from 1939 onwards (7). However, this fact alone could neither explain the peaks in 1954–1957, 1970 and 1987 or the variability of annual rates in Bulgaria. Such variations might be better discussed within the complex influence of the environment on both immune resistance and bacterial pathogenicity as depicted by the so-called "linear time effect" (15). Above interactions could be studied further by additional statistical approaches such as "Phase-Correlation Analysis" or "Cross-Correlation Analysis" (8, 10, 15) in the view of environmental factors exhibiting alike cyclicity (heliogeophysical activity, climatic factors, pollution cycles, etc.). Such relationships might not only allow for better forecasting models (8, 13) but also provide more plausible explanations for causes of the emerging infections and give opportunities for optimal design of preventive strategies (2, 6, 17).

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REFERENCES

1. **Dimitrov, B. D., Komitov, B. P.**: Cyclic variations of mortality from meningococcal infections in Bulgaria. In: Modern Tendencies in the Development of Fundamental and Applied Sciences. USB, Stara Zagora, 1994, 199–203. (In Bulgarian.)
2. **Lazarova, G. T., Dimitrov, B. D.**: Cyclic patterns of lethality from meningococcal infection in Bulgaria over the years 1919–1990. Arch. Union Med. Balk. 31 (1–5), 1996, 65–68.
3. **Budai, E.**: Taches solaires et méningite cérébrospinale. Rev. Pathol. Comp. Hyg. Gen. 446, 1931, 25–29.
4. **Tchijevsky, A. L.**: The Earth in the Universe. 2[nd] edition. Myisl, Moscow, 1976. (In Russian.)
5. **Velimirovic, B.**: The situation of meningococcal meningitis in Europe. Med. Trop. 43, 1983, 15–20.
6. **Greenwood, B. M.**: Meningococcal infection. In: Weatherall, D. J., Ledingham, J. G. G., Warrell, D. A. (eds) Oxford Textbook of Medicine, Vol. 1. ELBS/Oxford Univ. Press, Oxford, 1988, 5.199–5.208.
7. **Lazarova, G. T.**: Clinico-microbiological and epidemiological investigations of meningococcal infections. PhD Thesis 1994. Medical Faculty, Thracian University, Stara Zagora, Bulgaria. (In Bulgarian with English abstract.)
8. **Rauchov, G.**: Quantitative investigation of the heliogeophysical effects on the dynamics of the epidemic process in some infectious diseases. Probl. Infect. Parasit. Dis. (Sofia) 15, 1988, 5–11.
9. **Dimitrov, B. D.**: Comparative statistical study of relations between solar activity indexes and skin cancer incidence: temporal and spatial aspects. Cahiers Anthropol. Biométrie Hum. (Paris) 10 (3–4), 1992, 173–183.
10. **Dimitrov, B. D.**: Influence of heliogeophysical activity and ultraviolet radiation on the epidemiology of malignant melanoma of the skin in the North-West Region of England. MSc Dissertation 1993, Faculty of Science, University of Manchester, England.
11. **Dimitrov, B. D., Dinev, D. K.**: Solar activity and parotitis incidence in Bulgaria for the period 1922–1986. Ann. High. Med. Inst. St. Zagora (Bulgaria) 5, 1996, 25–26. (In Bulgarian with English abstract.)
12. **Knapp, R. G., Clinton Miller III M.**: Clinical Epidemiology and Biostatistics. Williams & Wilkins, Baltimore 1992.
13. **Dimitrov, B. D.**: Similar high-frequency cycles in the annual levels of solar ultraviolet radiation, stratospheric ozone concentration and incidence of malignant melanoma of the skin. Dept. Environ. Sci. Policy J. 1, 1998, 14–20.
14. **Komitov, B. P.**: Seasonal and century effects related to the influence of the solar cycles on the rains in Plovdiv (Bulgaria). Soln. Dannye, 9, 1986, 92–96. (In Russian with English abstract.)
15. **Dimitrov, B. D.**: Heliophysical activity and incidence variations of skin malignant melanoma in Czechoslovakia: a regional study. Int. J. Biometeorol. 37, 1993, 68–71.
16. **Verhev, P.**: Special Epidemiology. Med. Fizk., Sofia 1957, 310–321. (In Bulgarian.)
17. **Stoupel, E.**: Solar-terrestrial predictions: aspects for preventive medicine. In: Proceedings. International Symposium on Solar-Terrestrial Predictions. Vol. 4, NOAA Space Environment Services Center, Boulder, Colorado, 1980, C29–C40.

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