SOME OBJECTIVE CRITERIA FOR THE EVALUATION

OF INFLUENZA ACTIVITY BETWEEN 1991 AND 1999

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The threshold concept for baseline activity, normal activity, higher than expected seasonal level and epidemic level of influenza was used to objectively assess the seasonal influenza activity. These values are dependent on the geographic area. The defined threshold is useful to the health authorities for initiating specific policy actions aimed at each epidemic phase. The thresholds are also objective criteria about current influenza activity presented for the information of the wide public. An epidemic index (EI) was calculated for the specific influenza morbidity in the South-Eastern area of Romania and it synthesizes the seasonal evolution of influenza between 1991-1999. This type of assessment is in accordance with the recent decisions adopted by the sanitary authorities of most European countries.

INTRODUCTION

The influenza epidemics, as well as the various aspects related to the influenza virus, such as the extent of the disease in a community, the precise timing of the onset of the outbreak, the active circulating virus types and the severity of the disease, are at present more or less unpredictable[1,4]. Although the statistical studies regarding the social impact of influenza epidemics have been started over 30 years ago, the concept of epidemic threshold appeared and developed more precisely only during the recent years [3,4,5].

In this work, for the evaluation of various thresholds (including the epidemic threshold) in order to describe the influenza activity during a certain period, we used an "St.S. Nicolau" Institute of Virology database[6] containing information obtained from the Centres of Public Health of nine districts situated in the South-East of Romania, during the years 1991-1999.

MATERIALS AND METHODS

The initial data used are represented by the weekly reported morbidity rates (number of cases reported to hundred of thousands inhabitants %...) calculated by age groups for three groups of diseases: acute viral infections of the upper airways (AVIUA), diseases considered (clinically) as influenza-like illnesses and viral pneumonias. The monitored districts are: Arges (AG), Braila (BR), Buzau (BZ), Calarasi (CL), Constanta (CT), Dambovita (DB), Ialomita (IL), Prahova (PH) and Tulcea (TL). The number of cases and the calculated morbidities are stored in a database initiated and maintained at the Reference Centre for Influenza and Respiratory Viral Diseases, WHO collaborator, at the "St.S. Nicolau" Institute of Virology, Bucharest. The data used refer to the period 1991-1999 and are grouped by influenza seasons, respectively they are records referring only to the weeks 44 or 45 to 52 of the current year and to the weeks 1 to 12 or 16 of the next year, i.e. to the period of the cold season November-April. Therefore, the morbidity curves in the graphic plotting of the work, reported to time intervals, will show discontinuities to indicate the delimitation of each monitored season of the 9 years period of study (extra-season data, respectively for the months May - October, are not recorded).

The morbidity data characterizing 8 yearly seasons were analyzed for the 9 above-mentioned districts. To these were added global values calculated for two geographic areas (zone 1: BR, CT, TL; zone 2 AG, BZ, CL, DB, IL, PH) and for all the districts together (South-East of Romania). In all the caseses values for each of the three groups of diseases are shown.

We have used for calculations, analyses and graphic plotting the programs Epi-Info v6.040c/1997[7], Microsoft Excel 97 SR–1/1997, Microcal Origin v4 - Microcal Software Inc./1995.

The ratio influenza morbidity/AVIUA morbidity, considered as unit, was calculated for each week.

In the calculation of the epidemic index (EI) we have used a formula similar to that given by Chappuis[5], which uses the 1.5 coefficient for the selection of values included in the calculation and 1.4 constant in the EI formula.

In the assessment of values for the various influenza activity levels (thresholds) we have taken into account the following criteria[4]:

- *the baseline* is situated at values corresponding to interinfluenza seasons, in accordance with the virological data (virus isolations etc.);

- during the cold season, values above the baseline occur systematically, representing *a normal seasonal activity*;

- during each season appear increased maximal values, which detach from the normal values and are characterized as *higher values than those expected for the seasonal activity*;

- during the analyzed period, some much higher levels than the other maximal values of various seasons are recorded - for such cases is used the term "*epidemic*".

RESULTS

The thresholds for each districts of the zones or for whole South-East territory were established by usual recording, taking into account the above mentioned criteria and conserving the main features of the morbidity data evaluation. Thus, for the whole monitored territory four thresholds were established at morbidity values of 3 for the baseline, 3-8 for the normal seasonal level, >8-25 for the higher level than the normal one and >25 for the epidemic area (Fig. 1).
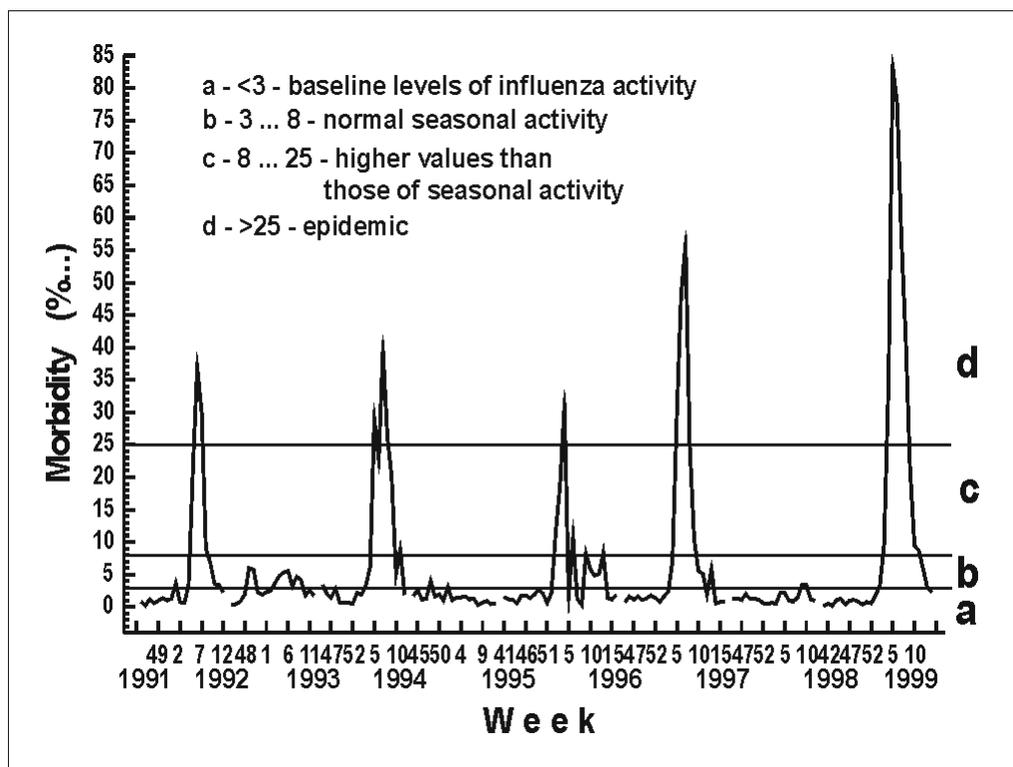

Fig. 1. - Influenza morbidity values in the South-East of Romania during the period 1991-1999. The discontinuous curves represent the values recorded only during the seasonal periods. By the horizontal lines are represented the influenza activity thresholds (a, b, c, d) with their significances.

We obtained for each district by means of this procedure values from 1 to 3 for the baseline, from 1 to 20 for the normal seasonal level, from 2 to 100 for the higher level than the normal one and from >4 to >100 for the epidemic area. The analysis of the mentioned values for each district allowed us to group them into two categories. The districts BR, CT and TL with the highest values, respectively <2.6 for the baseline, 2.6–16.7 for the normal seasonal level, >16.7–65, for

the higher level than normal one and >65 for the epidemic phase make up the zone 1. In the districts AG, BZ, CL, DB, IL and PH, which form the zone 2, the values recorded are <1.5 for the baseline, 1.5 to 4 for the normal seasonal level, from >4 to 11.3 for the higher level than the normal one and >11.3 for the epidemic phase (Table 1).

Concomitantly with the recording of influenza cases we have studied also the course of acute infections of the upper airways and the morbidity from viral pneumonias. The last category of diseases represents the expression of a severe impact of the influenza infections on the population of a territory, caused both by the aggressiveness of the pathogen and by the ecological conditions dependent on the moment or period studied.

Table 1

Morbidity values (%…) for the thresholds describing influenza activity levels in the monitored territory (records 1991-1999)

Territory (No. of persons*)	Interepid. activity	Normal activity	Higher than expected	Epidemic
AG (678150)	<1	1-2	>2-4	>4
BR (391578)	<3	3-15	>15-50	>50
BZ (513119)	<2	2-5	>5-12	>12
CL (333561)	<2	2-5	>5-25	>25
CT (742234)	<3	3-15	>15-45	>45
DB (555849)	<2	2-5	>5-10	>10
IL (306361)	<1	1-5	>5-12	>12
PH (867044)	<1	1-2	>2-5	>5
TL (266146)	<2	2-20	>20-100	>100
Zone 1**	<2.6	2.6-16.7	>16.7-65	>65
Zone 2 **	<1.5	1.5-4	>4-11.3	>11.3
South-East (4654051)	<3	3-8	>8-25	>25

* - Records of 1997 (Anuar de statistica sanitara, Ministerul Sanatatii, România, 1997, p.9); **Zone 1 (BR,CT,TL), Zone 2 (AG,BZ,CL,DB,IL,PH) - averaged values

The weekly percent reporting of the influenza morbidity to the AVIUA morbidity permits to establish the degree of influenza participation in the totality of respiratory diseases recorded

during their peak period. Thus, during the seasons 1992/93, 1994/95 and 1997/98 the participation of influenza in the increase of the AVIUA was much lower than during the seasons 1991/92, 1993/94, 1995/96, 1996/97 and 1998/99, when the influenza morbidity was higher than during the anterior period, but the participation of influenza in the totality of AVIUA did not exceed the previous level, a finding which show that in this laps of time, an active circulation of other viruses than influenza had a significant weight.

In addition to the quantitative evaluations which are reported to each week of the surveillance period, we considered also, in agreement with the data of the literature[5], a global quantitative parameter for the whole season: the epidemic index of influenza (EI).

In order to apply the most adequate formula to the calculation of the EI, including a constant[5], specific to the values characteristic of a certain territory, we calculated EI with values of the constant of 1.5; 2.5; 3.5 and 5 for the morbidity data referring to the South-East of Romania. Among these we selected the 3.5 value as that which reflects the best the morbidity profile of the period 1991-1999. Hence, the calculation formula for the epidemic index was:

$$EI = [\sum Ca - (3.5 * n)]/n$$

in which *Ca* represents the morbidity values ≥ 3.5 and *n* the number of weeks with *Ca* ≥ 3.5. The values obtained are shown in Fig. 2. These data are consistent with the results illustrated by the graphic representation of the influenza morbidity in dependence on their weekly course (Fig. 1); seasons with an increased epidemic activity alternating with seasons characterized by a low epidemic activity are observed.

The EI values for each season may be appreciated, in agreement with other authors[8], as expressing the intensity of an epidemic activity. Thus, EI values below 2 show a weak epidemic activity, the 2-12 range for EI expresses a moderate activity and EI > 12 reflect a relatively severe course of influenza during the period for which this index is calculated. It results from Fig. 2 that the seasons 1992/93, 1994/95 and 1997/98 were characterized by a low activity, whereas for

the years 1991/92, 1993/94, 1995/96, 1996/97 and

especially 1998/99 the epidemic index expresses relatively severe courses of influenza in the South-Eastern area of Romania.

The period 1998/99 differs from the other analyzed periods. During this season the influenza morbidity level (Fig. 1), the participation rate of influenza among the respiratory diseases of the upper respiratory airways and the epidemic index value exceed significantly any of the maximum values of the anterior periods. On the other hand, the morbidities from AVIUA and pneumonias have not a particular course during the whole period 1991-1999.
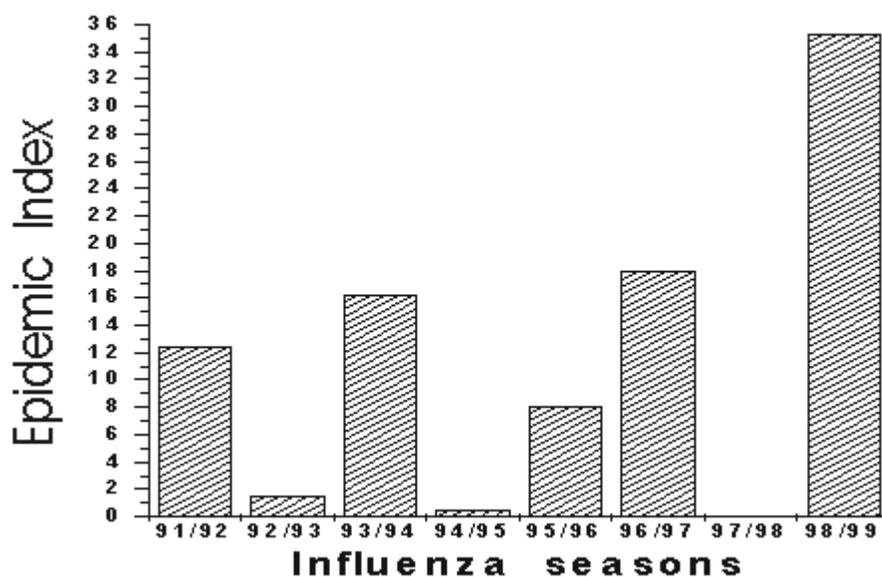
Fig. 2. - Epidemic index (EI) values for the influenza seasons 1991-1999 calculated for the South–East of Romania.

DISCUSSION

The threshold values are specific to the monitored area and they were established in our study in accordance with the assessment techniques used on the international scale. For example, the PHLS Communicable Disease Surveillance Centre of the United Kingdom, beginning with the cold season 1996/97[3] adopted this type of reporting, which is currently used in the report for 1997/98[9]. Such influenza activity thresholds and limits are able to characterize and delineate more precisely the phases of the epidemiological process in the case of influenza infections, showing all the characteristics of the morbidity course. In the epidemiological data processing performed in our study we reported the number of cases recorded in a district to its whole population (morbidity).

The notions and values for influenza activity thresholds once accepted and correlated with specific virological data, the anti-influenza actions provided for in the yearly useful plans of competent health authorities may be started in a differentiated way, according to the epidemic phase[10].

The influenza activity threshold values involve also a number of limitations and therefore more detailed informations on the course of this type of disease are further required from the field. Among the limitations may be mentioned the considerable variation of thresholds from year to year in dependence on the age, or much different values within a region between various geographic areas.

In this respect we mention the grouping into two zones of the nine districts monitored by us, which broadly respects certain specificity related to the geographic position. The zone with the highest morbidity values, both as the maximum value (154.8) and as the mean (129.0) for the

period 1991-1999, zone 1, is represented by the districts borders either to the seashore (CT) or to the banks of a river (BR and TL). Comparatively, in zone 2 the morbidity values are lower, respectively 47.6 for the maximum value and 3.2 for the mean. This zone is represented by the districts AG, BZ, CL, DB, IL and PH, which have a combined relief – mountainous, submontan and plain. The above established threshold values (baseline, seasonal activity etc) are clearly different from the zone 1 (Table 1). These data strengthen the conclusion[1,3,4,6] of the necessity to establish epidemic thresholds specific to each geographic area.

The examination of influenza morbidities during the period 1991-1999 by districts separately, correlated with the epidemic threshold show that all the districts in zone 2 have attained the epidemic level only in 1998/99; in three of these districts (DB, CL, BZ) the epidemic level was attained during two or three of the studied seasons. In the districts of zone 1 the course is relatively unitary, determining the periodical course of the influenza morbidity in the South-East of Romania.

Other limitations of the established thresholds refer to the fact that linear limits have been set up for phenomena which, by their nature, are non-linear and are strongly dependent on the cold season, hence the analysis should be complex, taking into account also other associated diseases.

From the analyzed data ensues the possibility of correlating the values and trends of the course of viral pneumonias with those of the morbidities from acute infections of the upper airways and influenza, which may characterize more significantly a so–called epidemic period.

As it was shown at the section "Results" we calculated also the epidemic index (EI) for the period 1991-99, which represents an alternative of objective assessment of the influenza activity.

It is incontestable that, for the characterization of an influenza epidemic, the isolation and typing of the virus strains responsible for its occurrence are absolutely necessary. The antigenic differences between previously circulating flu strains and the present isolated ones are important predictors for the character of the respective epidemic. This strengthens the condition that the extent of an epidemic depends also on other factors, in addition to the above mentioned geographic factor and to the isolated virus types, namely on meteorological, demo-graphic (birth rate, population density, urban agglomeration) or other conditions.

The epidemic threshold, the epidemic index, as well as any quantitative parameter characterizing the influenza epidemic are useful for the retting up of a mathematics model regarding the multanual curve and intensity of influenza epidemic.

As regards the possibility of prediction offered by the establishment of the epidemic threshold and of the epidemic index, were confirmed, on the basis of the observation achieved during many years of the period 1991–1999 (Fig. 1 and Fig. 2), that the periods with a low epidemic level (1992/93, 1994/95, 1997/98) are followed by a period with a considerably increased epidemic activity (1993/94, 1995/96, 1998/99). On the other hand, a season with a high epidemic level may be followed by a weakly epidemic season (1991/92 with 1992/93; 1993/94 with 1994/95; 1996/97 with 1997/98) or by an intensely epidemic season (1995/96 with 1996/97).

The short term prediction, in the course of an epidemic, is based on the analysis of the time interval characteristic for the fast course of the influenza morbidity, respectively the weeks 1-3. If during this period the morbidity values are higher than those expected for the seasonal activity,

attaining or tending to attain the established value of the epidemic threshold (Fig. 1), a severe epidemic will occur with a great probability during the immediately next weeks.

Our research is in accordance with the present WHO recommendations regarding the influenza activity monitoring, recommendations adopted by most European countries[10].

The establishment of absolute values or coefficients able to accredit the notion of epidemic, as well as of graduations characterizing the severity of the epidemic involves possibly the drawing up of protocol aimed at the gain of scores. The latter will permit the objectivization of the elements used as appreciation criteria of the influenza epidemic threshold. This objective approach could represent a possibility of obtaining quantitative analysis and processing methods of the epidemiological influenza surveillance data, which may be used in various communities and geographic areas.

CONCLUSIONS

The use of values for the influenza activity thresholds in various areas of the South-East of Romania represents a prerequisite for the objective assessment of this activity and for signaling the soonest possible the appearance of an influenza epidemic. The thresholds are also useful for an objective information of the general public, yearly faced with this disease. On the international scale, a trend towards the acceptation of this assessment type, technique, adopted by several European countries, is observed.

REFERENCES

1. Dedman D.et al. Influenza surveillance, England and Wales: October 1992 – June 1993. *Commun Dis. Rep. Rev.,* **1993**, *3*, R184-1846.

2. Hutchinson E.J. et al. Influenza surveillance in England and Wales: October 1995 to June 1996. *Commun Dis. Rep. Rev.,* **1996**, *6*, R163-169.

3. Dedman D.J. et al. Influenza surveillance in England and Wales: October 1996 to June 1997. *Commun Dis. Rep. Rev.,* **1997**, *7,* R212-209.

4. Dedman D.J., Watson J.M. The use of thresholds to describe levels of influenza activity. *PHLS Microbiology Digest,* **1997**, *14,* 206-208.

5. Chappuis S. et. al. Surveillance of influenza in Switzerland between 1987 and 1995. *Schweiz. Med. Wochenschr.,* **1996**, *126*, 1135-1142.

6. Zaharia C.N., Petrescu Al. Doua baze de date folosite pentru supravegherea epidemiologica in infectii respiratorii virale (Two databases used for the epidemiological surveillance in viral respiratory infections). In: *Proceedings of the Twentieth National Conference of Medical Data, 22-24 oct. 1997, Satu Mare – Romania,* **1997**, 38-40.

7. Dean A.D. et al. Epi Info, Version 6.04c: a word processing, database, and statistics program for epidemiology on microcomputers. *USD, Inc., Stone Mountain, Georgia*, 1997.

8. Wunderli W., Chappuis S. Influenza surveillance, Sentinella study, Winter season 1996/97. *Annual Report from the National Influenza Center and Central Laboratory of Virology*, University Hospital of Geneva, 1997.

9. Dedman D.J. et al. Influenza surveillance in England and Wales: October 1997 to June 1998. *Communicable Disease and Public Health*, **1998**, *1***,** 244-251.

10. Influenza Sub-Committee of the PHLS Virology Committee. The PHLS response to a pandemic of influenza: an action plan. *PHLS Microbiol Dig.*, **1993**, *10***,** 148-154.