Acta Paediatrica Academiae Scientiarum Hungaricae, Vol. 19 (3), pp. 225—238 (1978)

The Hungarian congenital malformation monitoring system

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Received, March 1st, 1978

The Hungarian Congenital Malformation Monitor has been operating since 1973 in order to detect the temporal and regional clusters of 12 indicator congenital malformations as early as possible. This Monitor takes part in the International Clearinghouse for Birth Defects Monitoring System. Three continuously increasing trends were detected in 1973—1976. They may be connected with the more complete notifications, although the increase of limb reduction deformities are only partly explained by this factor. Transitional (quarterly) significant clusters were observed in the case of anencephaly (1974, IV), spina bifida (1974, II; and 1975, III; 1976, III), cleft lip ± cleft palate (1974, III). The possibility of three technical biases (changes in diagnosis, notification and evaluation of the given congenital malformation) has to be excluded before accepting the fact of a real epidemic. Subsequently, a case-control epidemiological study by personal interviews and with matched controls has to be performed.

Monitoring for specific congenital anomalies is an important public health task [3, 7]. It constitutes a significant part in every congenital anomaly surveillance system, since it facilitates the early detection of temporal and regional clusters. It helps to disclose their possible association with new teratogenic (or possibly mutagenic) environmental impacts, which in turn are expected to result in the introduction of preventive measures.

The Hungarian Congenital Malformation Monitor (HCMM) has been operating since January 1, 1973. Only the so-called indicator congenital malformations (ICMs) are evaluated monthly and according to regional occurrence (Table I). ICMs can easily and unequivocally be diagnosed within the first 6 days of life. (Until 1975, congenital malformations of the ear and nose, of the external genitalia, polydactyly and multiple malformations were included in the list of ICMs. In compliance with the international programme, since 1976, instead of the former, hydrocephalus, oesophageal atresia, congenital dislocation of the hip and Down syndrome are recorded.) As in Hungary nearly all deliveries take place in hospitals, obstetricians, paediatrician-neonatologists or pathologists can usually diagnose ICMs. The reporting of congenital malformations is compulsory, thus they cannot escape attention.

TABLE I

Number of births and cases of indicator congenital malformations by year and quarter of birth, 1973—1977, Hungary

Year and quarter of birth	Number of births			Number of reported cases											
	Total	Live births	Still-births	Anen-cephaly	Spina bifida	* Hydro-cephalus	Cleft palate	12—x Cleft lip	* Oeso-phag. atresia	* Rectal atresia	Hypo-spadias	Red. def. upper	Red. def. lower	* Cong. hip disloc.	* Down syn-drome
1973 — Total	157,623	156,224	1,399	137	173	138	56	196	33	48	217	19	9	975	122
I Jan.—Mar.	38,722	38,344	378	33	51	24	14	38	13	8	50	5	2	225	29
II Apr.—Jun.	40,110	39,731	379	32	45	37	15	51	6	15	49	4	3	201	28
III Jul.—Sep.	41,282	40,963	319	34	40	44	20	57	6	15	59	6	2	271	38
IV Oct.—Dec.	37,509	37,186	323	38	37	33	7	50	8	10	59	4	2	278	27
1974 — Total	187,957	186,288	1,669	197	240	144	68	199	40	34	256	58	14	1157	157
I Jan.—Mar.	42,094	41,697	397	42	51	40	14	46	10	8	65	14	3	278	34
II Apr.—Jun.	46,288	45,903	385	41	74	34	15	49	8	8	64	14	6	262	34
III Jul.—Sep.	52,135	51,682	453	49	62	36	16	49	4	9	73	13	3	299	54
IV Oct.—Dec.	47,440	47,006	434	65	53	34	23	55	18	9	54	17	2	318	35
1975 — Total	195,740	194,165	1,575	160	239	146	59	200	39	43	322	89	43	1404	156
I Jan.—Mar.	50,087	49,684	403	44	57	41	14	64	10	12	86	20	12	364	32
II Apr.—Jun.	50,350	49,940	410	37	56	34	13	46	6	7	97	23	13	356	41
III Jul.—Sep.	50,364	49,989	375	52	71	40	15	49	13	11	52	27	10	379	51
IV Oct.—Dec.	44,939	44,559	387	27	55	31	17	41	10	13	87	19	8	305	32
1976 — Total	186,916	185,408	1,551	140	184	91	78	179	42	41	383	55	23	995	137
I Jan.—Mar.	47,418	47,022	396	36	49	17	22	51	11	9	110	14	3	283	31
II Apr.—Jun.	47,856	47,448	408	31	44	25	22	37	12	13	84	24	11	225	39
III Jul.—Sep.	48,523	48,146	377	39	32	25	16	53	9	14	61	10	2	155	39
IV Oct.—Dec.	43,119	42,789	330	34	59	24	18	38	10	5	128	7	7	332	28
1977 — Total	179,152	177,574	1,578	111	161	113	50	138	35	37	357	62	7	846	139
I Jan.—Mar.	45,480	45,076	404	31	37	40	11	29	8	10	94	15	2	257	39
II Apr.—Jun.	47,048	46,629	419	20	43	33	16	40	9	6	80	22	3	250	40
III Jul.—Sep.	45,559	45,148	411	34	35	19	9	36	8	13	98	13	0	170	33
IV Oct.—Dec.	41,065	40,721	344	26	46	21	14	33	10	8	85	12	2	169	27

* Monitoring of these categories began Jan. 1, 1976. Previous years' data were obtained from the Hungarian Congenital Malformation Registry.

International collaboration is of basic importance in the monitoring of birth defects. This is why the WHO initiated a cooperation in 1972. First 8, at present 11 countries send quarterly reports on the figures of ICMs to the international centre. The collaborating countries do not use identical criteria (Table II). Moreover, some problems have arisen in certain programmes (e.g. the low number of births in the material of Israel, the lack of base-line data in France, the Swedish monitoring system is just being reorganized). In spite of the difficulties, the international monitor system ensures early information for specialists about a cluster occurring in any participating country. Thus, it can be established whether the trend is a general or a local one. The National Foundation, established from international funds, undertook to give professional and financial support to clarify the aetiology of real clusters and to issue documents on new potential teratogenic noxae. Since 1972, the National Foundation and the WHO have convened the heads of the national monitors every year, thus the national monitoring systems work in a closer co-operation and can use standardized methods.

At present, the activities of the HCMM are as follows.

(i) Monitoring of ICMs according to the principles and methods defined in the international collaborative study. The present paper reports on this activity.

(ii) The country-wide follow-up of multiple malformations conducted since 1973 in co-operation with 6 regional centres.

(iii) Monitoring for chromosomal mutations recorded in the Hungarian Chromosomal Aberrations Register [8], in the framework of the Repository of Chromosomal Variants and Anomalies in Man (The Johns Hopkins University).

Operation of the Hungarian Congenital Malformation Monitor

Reporting of congenital malformations diagnosed in the first year of life in liveborns or in stillborns has been compulsory since 1962. From January 1, 1970, onwards, the Hungarian Congenital Malformations Register (HCMR) operating at the Laboratory of Human Genetics, National Institute of Hygiene, has taken over the processing and evaluation of data. Because of increasing demands, the Hungarian Congenital Anomaly Surveillance was established and entrusted with other tasks, such as monitoring. Since January 1, 1973, the number of ICMs are entered into two tables. The first comprises the figures of ICMs according to 25 Hungarian administrative units, the second according to distribution during the 12 months of the year. Ninety days after the end of a given quarter, the cumulated data are sent to the centre of International Clearinghouse for Birth Defects Monitoring System (Table III). (Regional evaluation is done by the National Centre [9].) The Quarterly Report published by the National Foundation summarizing the recorded

TABLE II

Participating in the International Clearinghouse for Birth Defects Monitoring System

Monitoring system	Number of births (Apr.—Jun., 1977)			Maximum age at diagnosis	Criteria defining stillbirths	Data used for baselines	Program director
	Total	Livebirths	Still-births				
Canada: 4 Provinces (Alberta, British Columbia, New Brunswick, Manitoba)	25,444	25,240	204	7 days (168 hours) and reported within 45 days	20 weeks and/or 500 grams	4 quarters of 1976 plus 1st quarter 1977	Dr. Philip Banister, Director, Bureau of Surveillance Services Room 12A, L.C.D.C., Tunney's Pasture, Ottawa, Ontario K1A OL2, Canada Telephone: (613) 992-7995
Province of Ontario	32,309	32,020	289				
Czechoslovakia:	49,709	49,421	288	Hospital discharge (usually 5 days)	28 weeks and/or 1,000 grams	1961—70	Dr. Jiri Kučera, CSc. Institute for Health Statistics nabr. K. Marxe 157 147 10 Praha 4 — Podoli, ČSSR
England and Wales	137,000	*	*	Usually 36 hours	28 weeks	1972	Dr. J. A. C. Weatherall O.P.C.S. St. Catherines House, 10 Kingsway London WC2B 6JP, England Telephone: 01-242-0262
Finland	17,306	17,216	90	1 year (90% within 14 days)	180 days	1970—75 (1975 for codes 749.0, 750.2, 571.2, 752.2, 755.2, 755.3)	Mrs. Anneli Ruusinen National Board of Health Siltasaarenkatu 18 00530 Helsinki 53 Finland Telephone: 90-718511
France: Rhône-Alpes region	19,160	18,975	185	7 days	28 weeks	Not compiled	Dr. Madeleine Dessemond Department of Medical Genetics Hôpital de l'Hôtel Dieu 1, rue de l'Hôpital 69288-Lyon Cedex 1, France

Hungary	46,956	46,564	392	1 week and reported within 90 days	28 weeks	1973—76	Andrew Czeizel, M.D. National Institute of Hygiene IX. Gyáli út 2—6. 1966 Budapest, Hungary Telephone: 142-250
Israel: Kaplan Hospital Rehovot	1,186	1,174	12	Hospital discharge (usually 4 days)	28 weeks	1966—68	Prof. Marcus A. Klingberg, M.D. Head, Department of Epidemiology Israel Inst. for Biological Research P.O.B. 19, Ness-Ziona, Israel Telephone: (03) 958861
Norway	13,789	13,625	164	9 days	16 weeks	1967—71	Prof. Tor Bjerkedal Institute of Hygiene Gydas vei 8 Oslo 3, Norway Telephone: (02) 466850
South America: 20 Hospitals in 7 countries (Argentina, Brazil, Chile, Ecuador, Peru, Uruguay, Venezuela)	*	14,893	*	72 hours	Not included	Not compiled	Dr. Eduardo Castilla Laboratorio de Genetica Inst. de Biologia/Univ. de Brasilia Brasilia 70.000, DF, Brazil Telephone: 72.00.00, Ext. 2161
Sweden	*	*	*	Usually 7 days	28 weeks	1965—72	Prof. Bengt Källen Dept. of Embryology University of Lund S-223 62 Lund, Sweden Telephone: 046-11 25 50
United States:							
Metropolitan Atlanta	6,172	6,104	68	Hospital discharge (80% by the 7th day)	20 weeks and/or 500 grams	1968—75	J. William Flynt, Jr., M.D. Center for Disease Control Building 1, Room 5112 Atlanta, Georgia 30333, U.S.A. Telephone: (404) 633-3311 Ext. 3961
1200 Hospitals nationwide	195,701	193,913	1,788	Hospital discharge (usually 7 days)	20 weeks	1970—73	

* Not available.

TABLE III

Data for births occurring in 1975

Data used for calculation of baseline rates: *Hungarian Congenital Malformation Monitor 1973—1974*

Category	Base-line Rate/ 10.000	Quarter of birth: January 1 - March 31			April 1 - June 30			July 1 - September 30			October 1 - December 31		
		Expected Number	Observed Number	Rate	Expected Number	Observed Number	Rate	Expected Number	Observed Number	Rate	Expected Number	Observed Number	Rate
Total births			50087			50350			50364			44939	
Liveborn			49684			49940			49989			44552	
Stillborn			403			410			375			387	
Selected malformations:													
740 Anencephaly	9.8	49	44	0.90	49	37	0.76	49	52	1.06	44	27	0.61
741 Spina bifida	13.1	66	57	0.86	66	56	0.85	66	71	1.08	59	55	0.93
742 Hydrocephalus	7.6	39	41	1.05	38	34	0.89	38	40	1.05	34	31	0.91
749.0 Cleft palate	3.8	19	14	0.74	19	13	0.68	19	15	0.79	17	17	1.00
749.1, .2 Total cleft lip	11.8	59	64	1.08	59	46	0.78	59	49	0.83	53	41	0.77
750.2 Oesophageal atresia and stenosis	2.2	11	10	0.91	11	6	0.55	11	13	1.18	10	10	1.00
751.2 Rectal and anal atresia	2.8	14	12	0.86	14	7	0.50	14	11	0.79	12	13	1.08
752.2 Hypospadias	12.1	61	86	1.41	61	97	1.59	61	52	0.85	54	87	1.61
755.2 Reduction deformity upper limb	0.9	4	20	5.00	4	23	5.75	4	27	6.75	4	19	4.75
755.3 Reduction deformity lower limb	0.6	3	12	4.00	3	13	4.33	3	10	3.33	2	8	4.00
755.6 Congenital dislocation of hip	59.1	296	364	1.23	297	356	1.19	297	379	1.27	265	305	1.15
759.3 Down syndrome	7.3	36	32	0.86	36	41	1.14	36	51	1.41	33	32	0.97

cases is sent four times yearly to the heads of the national centres.

In the course of monitoring, the following items require special attention.

1. The principle of monitoring babies with two or more congenital malformations. Thus, it may be questionable whether newborns with anencephaly, cleft lip and dislocation of the hip should be monitored at all, since multiple malformations are not ICMs. Or anencephaly, in itself being the principal ICM should be monitored, or else all the three malformations have to be taken into consideration independently as they all represent ICMs. We follow the practice of keeping two parallel monitoring records, one for isolated ICMs and one for those occurring as part of unspecified multiple malformations. The latter facilitates the recognition of clusters of congenital malformation syndromes and associations. The sum-total of the two values is reported to the International Centre (Table IV).

2. The interval between birth and monitoring should be short in order to detect the clusters as early as possible. In compliance with the international agreement, only notifications received within 90 days after birth are taken into account. In consequence, notifications after the deadline have to be disregarded in monitoring. Table III illustrates the number of monitored ICMs as compared to the registered number of congenital malformations in the HCMR up to the last day of the year following birth. Surprisingly, anencephaly and lower limb reduction malformations are represented in higher numbers in the HCMM of 1975. The difference can be ascribed to the monitoring of ambiguously notified ICMs, and to the fact that ICMs constituting a part of unspecified multiple malformations had been taken into account in the HCMM but not in the HCMR. It is the case of later identified syndromes which are coded into the specified malformation syndrome entities. With the exception of hydrocephalus, values below 80% represent ICMs with internal localization.

3. Monitor values for the individual ICMs differ because some ICMs occurred in very low numbers, and also because much depends on the validity and reliability of the diagnosis. For instance, the diagnosis of congenital dislocation of the hip is based on Ortolani positivity, therefore babies with unstable hip joint too may be reported. It would seem justified to exclude congenital dislocation of the hip from the ICMs, and to include exomphalos. Hydrocephalus is often diagnosed erroneously in macerated stillborn babies. The diagnosis at birth of Down syndrome requires great clinical experience.

The monthly, quarterly and yearly trends of non-indicator congenital malformations registered in the HCMR are also checked. This may contribute to selecting the most suitable ICMs, and to detect possible clusters in non-ICMs. Attempts have been made to adopt the HCMR to computerized data processing and to demonstrate any clusters occurring in all congenital malformations.

TABLE IV

Quarterly number of indicator CMs

Quarter of birth	Number of births			Denomination of indices	Indicator congenital		
	Total	Live	Still		Anencephaly	Spina bifida	Hydrocephalus
Total	195,740	194,165	1575	HCMM	160	239	164
				HCMR	(156)	(243)	(200)
				%	102.6	98.4	73.0
Jan.—Mar.	50,087	49,684	403	HCMM	44	57	41
				HCMR	(44)	(56)	(56)
				%	100.0	101.8	73.2
Apr.—Jun.	50,350	49,940	410	HCMM	37	56	34
				HCMR	(42)	(54)	(47)
				%	88.1	103.7	72.3
Jul.—Sep.	50,364	49,989	375	HCMM	52	71	40
				HCMR	(42)	(61)	(46)
				%	123.8	116.4	87.0
Oct.—Dec.	44,939	44,552	387	HCMM	27	55	31
				HCMR	(28)	(72)	(51)
				%	96.4	76.4	60.8

EVALUATION OF CLUSTERS

Changes in the absolute number of ICMs are evaluated by three methods in the HCMM.

1. Based on the baseline data that is the occurrence of ICMs in the 3 previous calendar years, the expected absolute number (E) of a given ICM per 10,000 births is calculated for the given quarter. This is compared to the observed quarterly number (O) of the specific ICM by means of the O/E ratio (Table III). The quotient obtained may be considerably above 1, around 1, or considerably below 1. The problem is what to regard as considerable? At the first approach, plus and minus 0.50 and greater deviations are taken as a "warning sign". (It goes without saying that in the evaluation of deviations the number of a given ICM is also important.)

2. The preliminary evaluation described above is supplemented by the following biomathematical analyses if a "warning sign" is observed.

(i) Standard deviation can be calculated from the baseline data. If the observed quarterly value is above the expected plus 2 SD, it is taken as a "danger sign"; if above the expected value plus 3 SD it is taken as an "alarm sign".

(ii) By the help of the χ^2 test, the p value of the difference between expected and observed ICMs can be calculated.

(iii) The Cusum (cumulative sum) method [6, 10].

3. The duration of a cluster is also of importance. Changes in case numbers are analysed monthly in HCMM. In international cooperation, a significant increase for a given quarter requires conceptual commen-

in the HCMM and in the HCMR, 1975

malformations								
Cleft palate	Cleft lip ± palate	Oesophag. atresia	Rectal atresia	Hypospadias	Red. Def. Upper	Red. Def. Lower	Cong. Hip. Disloc.	Down syndrome
59	200	39	43	322	89	43	1404	156
(78)	(231)	(52)	(64)	(352)	(90)	(39)	(1529)	(168)
75.6	86.6	75.0	67.2	91.5	98.9	110.3	91.8	92.9
14	64	10	12	86	20	12	364	32
(20)	(65)	(11)	(12)	(93)	(30)	(10)	(386)	(35)
70.0	98.5	90.9	80.0	92.5	66.7	120.0	94.3	91.4
13	46	6	7	97	23	13	356	41
(18)	(55)	(9)	(10)	(98)	(18)	(11)	(379)	(46)
72.2	83.6	66.6	70.0	99.0	127.8	118.2	93.9	89.1
15	49	13	11	52	27	10	379	51
(17)	(57)	(16)	(20)	(74)	(25)	(9)	(366)	(45)
88.2	86.0	81.3	55.0	70.3	108.0	111.1	103.6	113.3
17	41	10	13	87	19	8	305	32
(23)	(54)	(16)	(19)	(87)	(22)	(9)	(398)	(42)
73.9	75.9	62.5	68.4	100.0	86.4	88.9	76.6	76.2

tary. A cluster observed for two consecutive quarters can be regarded as an "alarm situation" calling for international consultation. If perusal of relevant literature and consultation can exclude the possibility of technical biases, case-control epidemiological study has to be organized, trying to reveal the aetiological factor(s).

Some important rising trends in Hungary between 1973 and 1976

Evaluating the changing trends in ICMs, attention is mainly focussed on increased occurrence. (Nevertheless, decreased occurrence too deserves attention because of the underlying causes e.g. neglect of reporting, decrease in occurrence due to unknown causes or to the effect of introduced preventive measures.)

An increase in ICMs can be divided into two types.

1. *Continuously* increasing trend. Between 1973 and 1976, three ICMs showed such trend: congenital dislocation of the hip, congenital limb reduction malformation (CLRM) and hypospadias (Fig. 1).

Since point prevalence at birth of congenital dislocation of the hip is 2.8% in Hungary [2], it can be taken for granted that the increase was the result of the more frequent diagnoses owing to the extension of orthopaedic screening of newborns. CLRM increased to a small extent in 1974, considerably in 1975 and 1976. It seems to be a real cluster. The unbroken rising trend of hypospadias necessitates a detailed evaluation which is in progress.

2. *Transitional* clusters observed for shorter periods (Fig. 2). Such were

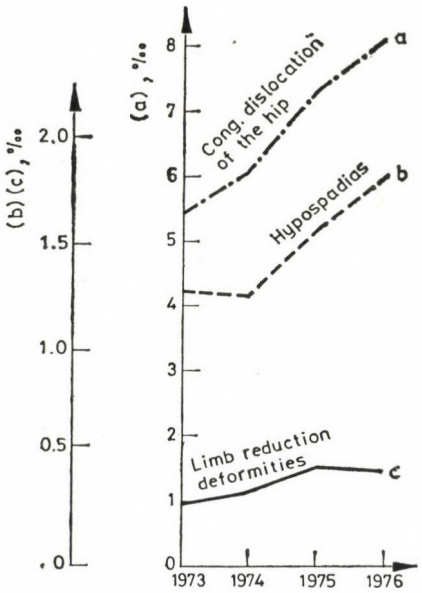

FIG. 1. A continuous increasing annual trend of three congenital malformations in the material of the Hungarian Congenital Malformation Monitor

anencephaly in the 4th quarter, 1974; spina bifida in the 2nd quarter of 1974, in the 3rd quarter of 1975 and in the 4th quarter of 1976; further cleft lip ± palate in the 3rd quarter, 1973. Biomathematical analysis proved that these increases have reached the level of a danger sign, with the exception of anencephaly in the 4th quarter, 1974, as it showed the alarm sign. Occurrence in the consecutive quarters, howewer, was not above the expected figure in these ICMs, thus no "alarm situation" developed and no epidemiological survey had to be conducted.

In accordance with the increasing yearly trends in hypospadias and CLRM, the quarterly values corresponded to a danger sign. Hypospadias reached the level of an alarm sign in the 1st and 4th quarters of 1976. In 1975, the frequency of CLRM indicated an "alarm situation". Investigations of the underlying causes will be published elsewhere [4].

Beside operating the HCMM, the frequency of all congenital malformations represented in the HCMR is regularly evaluated. Fig. 3 shows notably higher occurrence of cleft lip ± palate in 1972, of congenital pyloric stenosis in 1971, of congenital hypothyroidism in 1974. At present, no explanation can be offered for these observations.

The analysis of a periodic occurrence of congenital malformations can be useful from several other aspects, e.g. the occurrence of all and the specific types of congenital malformations have been evaluated for months

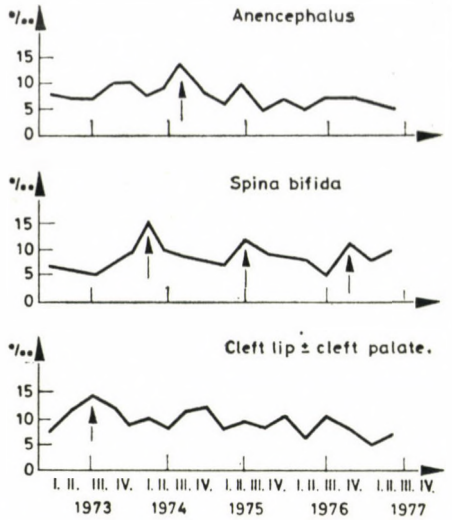

FIG. 2. Transitional clusters in the quarterly occurrence of three congenital malformations in the material of the Hungarian Congenital Malformation Monitor

following a great influenza epidemic (Fig. 4). No correlation was noted and this speaks against the teratogenic effect of *Myxovirus influenzae-A*.

ANALYSIS OF CLUSTERS

When biomathematical analysis has proved that more than a chance cluster had occurred, the possibility of three technical biasing factors has to be excluded before accepting the fact of a real epidemic.

1. Changes in the diagnosis of the given congenital malformation.

(i) New examination procedures (e.g. PKU or orthopaedic screeing can considerably increase the fre-

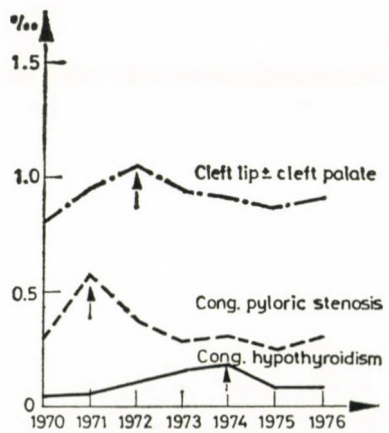

FIG. 3. Higher annual occurrence of three congenital anomalies in the material of the Hungarian Congenital Malformation Register

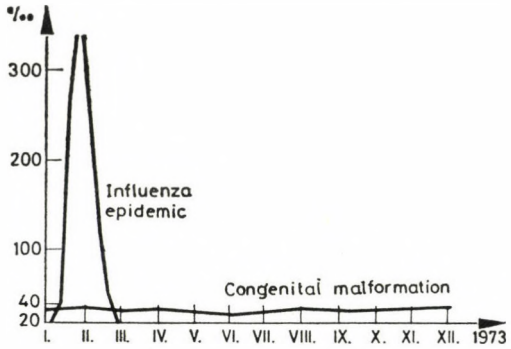

FIG. 4. There wars no correlation between the occurrence of congenital malformations and the influenza epidemic in 1973

quency of diagnosed cases. In internal malformations there will be a parallel increase with the increase in the frequency of necropsies.

(ii) Changes in diagnostic attitudes. Reporting of minor variations or of borderline cases will primarily elevate the number of mild malformations.

(iii) More accurate definition or classification of a given congenital malformation can increase its participation usually at the expense of another malformation.

All the three biasing factors could be excluded in the case of CLRM [4].

2. More complete notifying.

(i) Data of the HCMR show that in 1975 the occurrence of all reported congenital malformations increased by 18.4% as compared to the period 1971—1974. In contrast, the increase in the occurrence of CLRM amounted to 48.3%, more than two-fold of all congenital malformations.

(ii) A comparison of international data. The point-prevalence at birth of CLRMs varies for example between broad limits (0.25—0.82 per 1000 total births). This is mainly due to differences in notification [5]. Significant increases were, however, observed in other countries too, so e.g. in Canada [1].

An estimated 30% increase in CLRM cases but by no means the whole, could be attributed to improved completeness of notification.

3. Changes in the evaluation and recording of notified cases. It was excluded in CLRMs.

An estimate of 0.3—0.4 point prevalence per 1000 total birth of CLRM seems to be the real figure in Hungary. The 1971—1974 findings correspond to this value. However, in 1975 and 1976 the occurrence was somewhat less but significantly increased.

POLICY IN REAL CLUSTERS

If a significant cluster is observed exceeding the limits allowed by chance for over six months, i.e. facing an "alarm situation", actions should be introduced to detect possible aetiological factors. It is generally recom-

mended to carry out a retrospective case-control epidemiological study with personal interviews and matched controls. The stages of an epidemiological study are as follows.

(i) *Careful preparation.* It involves the perusal of the literature and preliminary consultations with experts. It is of major importance that different nosologic (aetiologic) types of the given malformations be treated separately.

(ii) *Selection of controls.* The mode of selecting matched controls depends on the character of the given malformation. The date of birth (at least the same week), the place of birth (at least the same district or city) and sex are essential criteria. In principle, matched control cases have to be identical in every but one parameter: the occurrence of the congenital malformation under study. Overdone matching may, however, hinder the tracing of adequate controls and useful information may be lost. For instance, if identity of the social status of the parents is set as a criterion, it will be impossible to examine the effect and importance of this very factor on malformation prevalence.

(iii) *The epidemiological study.* It is a drawback of retrospective case-control surveys that the parents of the index patients and especially the mothers speculate too much about the alleged or real causes why the child was affected by the malformation. As a consequence, the mother can give more accurate answers but also subjectively exaggerated ones. In contrast, the mothers of the matched controls meditate less upon their previous pregnancies, thus give less detailed answers. The distorting effect of this factor can be illustrated by the frequency at which the taking of common harmless drugs is listed. To eliminate this disturbing effect, the following can be recommended.

(a) Personal interview with the parents of the index patients and the controls. Preferably, one and the same person should interview both groups, using identical methods.

(b) Checking and supplementation of interview information by the "prospective" data recorded in the course of prenatal care.

(c) Special emphasis on the critical period when the given malformation develops. Concentrating the questions to this period may considerably improve the value of information.

If an aetiological correlation has been revealed, a prospective survey has to be organized, and it is preferable to extend the survey to other countries.

The monitoring of congenital malformations done in international collaboration is one of the most important means in detecting new and old aetiological factors. It contributes to the limitation of their effects and in turn to the decreased occurrence of certain congenital malformations.

References

1. Banister, P.: Congenital malformations; preliminary report of an investigation of reduction deformities of the limbs, triggered by a pilot surveillance system. Canad. med. Ass. J. **103,** 466 (1970).

2. Czeizel, A., Szentpétery, J., Kellermann, M.: Recent study on the incidence of congenital dislocation of the hip in Hungary. Brit. J. prev. soc. Med. **28,** 265 (1974).
3. Czeizel, A.: Surveillance of congenital anomalies in Hungary. Acta paediat. Acad. Sci. hung. **17,** 123 (1976).
4. Czeizel, A. et al.: 1978. in preparation
5. Flynt, I. W.: Techniques for assessing teratogenic effects: epidemiology. Environ. Hlth Perspect. **18,** 117 (1976).
6. Hill, G. B.: The computer surveillance of congenital malformations. Brit. med. Bull. **24,** 215 (1968).
7. Miller, J. R.: Birth defects monitoring systems: an overview. Cong. Anom. **17,** 1 (1977).
8. Osztovics, M.: 1978 (in preparation)
9. Pazonyi, I.: 1978 (in preparation)
10. Weatherall, J. A. C., Haskey, J. C.: Surveillance of malformations. Brit. med. Bull. **32,** 39 (1976).

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