Congenital Toxoplasmosis in Switzerland: Epidemiological Data and Medical and Public Health Strategies

P. Jacquier

Introduction
What is the present epidemiological situation on congenital toxoplasmosis in Switzerland? Does Switzerland need a systematic serological screening for pregnant women like its neighbours Austria (since 1975) and France (since 1978)?

The introduction of a systematic serological screening to prevent congenital toxoplasmosis relies upon a multi-disciplinary reflection and a defined strategy bearing different steps. Switzerland started such a reflection on the prevention of congenital toxoplasmosis in 1990. We report here a condensed description of the different steps which were initiated in Switzerland since 1989 (figure 1).

1st step: Seroepidemiological study at a local level.

In 1988 - 1989, not enough data were available in Switzerland regarding the seroepidemiology of *Toxoplasma gondii* infection as well as for the general population as for the pregnant women, more globally for the women at childbearing age. Therefore, the Swiss Federal Office of Public Health (Swiss FOPH) decided to support a seroepidemiological study at a small geographical scale concerning the general population (from birth up to 70 years old) in order to update epidemiological data (4). This starting step was absolutely necessary before the elaboration of a specific study oriented towards congenital infection in order to optimize the sampling strategy at a national level planned in a second step.

We started a random seroepidemiological sampling of a general population in a geographically limited area. The study was conducted in the area of Zürich from 1989 to 1990 and included 4300 persons aged between 1 month and 70 years old, equally divided into sex-groups. The samples from persons under 18 years (n=500) were obtained at the Children’s Hospital in Zürich (the children were hospitalized at the Surgery’s Department for emergency without any infectious problem); the sera of persons between 18 and up to 70 years old were obtained at the Blood Doner Center (n=3500) and the last group concerned 300 maternal sera collected at delivery (from a mother-child serum collection which belongs to the University Children’s Hospital of Zürich). The samples were systematically collected by age- (5 years) and sex–groups (sex ratio 1:1), until we reached the desired amount.

The crude seroprevalence of specific anti-*T. gondii* IgG was 52.4% (confidence interval at 95% [p < 0.05]: 50.9–53.9) with the highest obtained value of 80% among people aged over 65 years old (figure 2). There was no significant difference between males and females. The seroprevalence of the group of women in childbearing age (between 20 and 40 years old) was 40%. The comparison of this value with the results obtained from the 300 maternal sera revealed no significant difference between the two groups.
On the basis of those results and assuming that the information obtained at the level of the general population in the region of Zürich is representative of Switzerland, we were then enabled to calculate the required sample's size, which was statistically representative, in order to initiate the 2nd step of our strategy, that means a national study on seroprevalence of the infection with *T. gondii* among women at time of delivery.

2nd step:
Sero-epidemiological study at a national level.

In 1990 - 1992, a national study was performed to assess the seroprevalence of anti-*T. gondii* IgG in pregnant women at the time of delivery (5). The study was organized in 23 out of 26 Swiss cantons. 9059 women corresponding to 11.89% of the annual total of births in those cantons were concerned. The global seroprevalence of specific IgG was 46.1% (confidence interval at 95% [p<0.05]: 45.0-47.1). Regarding the age distribution, there was a significant increase of the anti-*T. gondii* IgG seroprevalence (fig. 3). There was no significant difference in seroprevalence between different cantons after adjustment according to age. Thus at the national level the seroprevalence was 46.0% for Swiss women and 45.8% for women of other nationalities (14).

3rd step:
The use of the data collected through the 2nd step, for medical and economical purposes.

The use of these data consisted of two parts: the official statistical use of biological data in order to get a practical answer considering the risk of seroconversion for seronegative pregnant women and then to simulate an epidemiological situation. The second part was to be able to run a cost-benefit analysis with Swiss data.
At that time, the Swiss FOPH created a multidisciplinary working group whose objects were to review the subject of congenital toxoplasmosis, to strengthen, as far as possible, the level of knowledge concerning congenital toxoplasmosis in Switzerland (particularly the epidemiological and economical aspects) and to propose a programme for prevention acceptable by all concerned medical disciplines (8, 9).

1st part: the statistical use of seroepidemiological data.

The use of a model of linear regression according to age showed that in Switzerland the theoretical risk of seroconversion among seronegative women during their 9 months of pregnancy was of 1.21%. Basing on this result, some data were calculated in order to simulate an epidemiological situation with absence of specific serological screening during pregnancy at a national level and, consequently, absence of appropriate treatment. It was estimated that 548 cases of seroconversion would occur annually during pregnancy. This would lead to 183 congenital transmissions of toxoplasmosis, among which 75% would be asymptomatic at birth. The number of expected pathologies would be 40 cases of chorioretinitis with impaired vision, 18 cases of cerebral lesions, and 2.7 cases of perinatal death (5).

2nd part: the use of seroepidemiological data to run a cost-benefit analysis.

A cost–benefit analysis, using the recent seroepidemiological data, was performed in 1992–1993 (10). A comprehensive cost–benefit analysis of possible screening strategies for congenital toxoplasmosis is absolutely necessary and, let's say, essential, because it served as the basis for the decision whether or not screening was efficient and socially desirable. The total costs of the disease in Switzerland were calculated for the year 1990. Direct costs (all diagnostic and therapeutic interventions, including care of handicapped children) and indirect costs (partial and total work losses in the future) were taken into account. The direct costs amounted to approximatively Sfr. 20mio per year; the indirect costs amounted to Sfr. 4mio per year. The total costs of the disease, without any screening, were Sfr. 24mio (i.e. nearly Sfr. 3.4 per inhabitant). The costs incurred with three possible screening programs (1st prg.: 2 samples, one at the beginning of pregnancy and the second at delivery; 2nd prg.: 3 sampling dates...
corresponding to each trimester like in Austria; 3rd prg.: screening with a monthly sampling system, like in France) were estimated, together with the concomitant cost savings. By definition, the cost-benefit coefficient corresponds to the ratio between the cost of the disease without screening divided by the cost of the disease including screening. The coefficient is respectively 0.95, 1.0 or 0.86 according to the strategies 1, 2 or 3. As long as this coefficient is below 1, the screening system doesn't reach the break-even point. In conclusion to this study, only the 2nd strategy (one sample per trimester) reaches the rentability's aim. However, the theme of “cost-benefit analysis” remains a very controversial one. For further comments on this subject, please refer to the article of SAGMEISTER et al. (10).

4th step: Information for medical practitioners and specialized physicians.

It is of utmost importance to collect enough data before the decision to proceed to a national systematic screening is taken. However, it is also important to take into account the individual diagnosis. It is thus a priority for every Public Health organization to make sure that enough information is communicated to general practitioners or to specialized physicians. In Switzerland, the FOPH handled the coordination of a publication on different aspects of congenital toxoplasmosis. A special issue of the Swiss Medical Journal was published in 1995 included many components of this problem (11). Some articles on epidemiological studies were already cited and other articles are now mentioned in order to underline their impact at a national level and, consequently, to help physicians in need of information to receive a support for their medical strategy.

The “Swiss Working Group on Congenital Toxoplasmosis”, under the supervision of FOPH, reached a consensus in the text and also in the daily practice concerning medical strategy for pregnant women (surveillance, diagnostic and therapeutic regimes) (2) and for children (12); one article was dedicated to the practical use of diagnostic tools (6).

5th step: The information network.

1. Seminars and workshops have to be regularly organized for persons working in laboratories.

2. The “Extern Quality Control” is a major component which becomes now mandatory for every laboratory performing serological tests; it has also to be one of the major information vectors for laboratory staff.
3. To make a leaflet on primary prevention available to medical doctors and pregnant women in order to avoid, as much as possible, Toxoplasma infection (a project on this subject is actually finalized for Switzerland).

4. To update all systems obliging to declare every case of clinical infection in relation with the "Swiss Paediatric Surveillance Unit". All cases related to T. gondii have to be reported to a national register. In Switzerland there are two systems of registration: one for clinical neo-natal infections and one for laboratories. For the registered laboratories, officially recognized by the Swiss FOPH, all cases of acute infection have to be reported monthly at a cantonal and a national level. A new definition of the laboratory's parameters, necessary for these declarations, has to be finalized in order to optimize the use of the data, especially in the differentiation between serious and recent infection.

5. Another priority is to collaborate with other European working groups. The “Swiss Working Group on Congenital Toxoplasmosis” has to work in connection with other working groups all over Europe. For this purpose, we participate to different activities of the “European Network on Congenital Toxoplasmosis” since its creation. Are there actual differences of the epidemiological situation between Austria, France and Switzerland? To cite one example, you can see on the figure 2 the parallel representation of some seroepidemiological data from France (Strasbourg) (13) and from Switzerland (4); obviously, there is no statistical difference between the two groups of data.

6th step: 
Toxoplasmosis and the other infections with potential risks for congenital diseases.

We have to keep in mind that, besides toxoplasmosis, there are other infectious diseases which can occur to a pregnant woman and which present a potential risk for congenital diseases. For that reason, the Swiss FOPH has encouraged some studies on CMV, rubella (15) and hepatitis infections (1).

On the other hand, it is not longer possible to accept the kind of situation where some people are talking for many years on congenital toxoplasmosis, some others on rubella, CMV or congenital hepatitis and where it exists no interaction or collaboration with different working groups either at a national or at an European level! In Switzerland, we are actually trying to change this situation in collaboration with the swiss FOPH.

Conclusions

Although the 5th and 6th steps are still in progress, the entire steps already achieved allow us some comments.

1. It was the responsibility of the “Swiss Working Group on Congenital Toxoplasmosis” to gather the maximum of actual data on different subjects: seroepidemiology, strategy for diagnosis, strategy for therapy as well as for the mother as for the child. We can actually say that the principal objects are achieved:

   • every Swiss practitioner has the possibility to get sufficient information and access to adequate diagnostic and therapeutic medical tools in order to care for the best for every pregnant woman he has as a patient. That’s the individual health system.

   • every Swiss laboratory has the possibility to get sufficient information and access to specialized laboratories, although the procedure for the recognition of the title “Reference Laboratory” is not yet finished.

2. The decision for or against a national systematic screening of congenital toxoplasmosis for pregnant women in Switzerland is within the sole competence of the Swiss FOPH after taking in consideration every medical and economical aspect of the problem.
In addition, the only logical strategy which could be promoted by the Swiss FOPH at a national level should integrate absolutely the strategy for the prevention (primary and secondary) of congenital toxoplasmosis into the prevention of other congenital infections. Thus it can decided in an objective way on the priorities of Public Health in Switzerland.

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Summary In developing countries, the issue concerning the distinction between medical strategy for individuals and Public Health strategies at a national level is often under debate and sometimes is a very controversial one.

*Toxoplasma gondii* infection during pregnancy, with the risk of congenital toxoplasmosis (CT), represents a classical issue often debated. Geographically situated between France (where a combination of primary and secondary prevention of CT is compulsory since 1978) and Austria (where a strategy for prevention exists since 1975), Switzerland has not yet regulated primary or secondary prevention of CT.

In 1990 the Swiss Federal Office of Public Health (Swiss FOPH) has decided to support some studies focussing on different aspects of the public health components of CT in Switzerland. The modes of action implemented since then can be described as follows:

1st step: Seroepidemiological study for the whole population at the local level. 2nd step: Seroepidemiological study for the pregnant women at the national level. 3rd step: Data use (Data collected through the 2nd step) for medical and economical purposes (especially benefit–cost analysis). 4th step: information for medical practitioners and specialized physicians. 5th step: Creation of an information network (including seminars, extern Quality Control for laboratories, national registration of clinical and biological cases, collaboration with the “European Network on Congenital Toxoplasmosis”). 6th step: Attempt to sum up, at the national level, the relative risk of CT compared to other infections which can play a role in congenital diseases (CMV, rubella, hepatitis . . .).

The 5th and 6th steps are still in progress. Nevertheless, the available medical tools allow us to solve the individual primary and secondary prevention in Switzerland. At the level of the pregnant women, its the responsibility of each practitioner to deal with the primary and secondary prevention of CT. At the public health level, the decision for a secondary prevention of CT is within the sole competence of the Swiss FOPH after taking in consideration every medical and economical aspect of the problem. This strategy has to be integrated with that concerning other congenital infections.

Key words *Toxoplasma gondii*, Congenital Toxoplasmosis, Epidemiology, Public Health, Strategy, Switzerland, Europe.

Zusammenfassung In Entwicklungsländern wird das Problem bezüglich der Unterscheidung zwischen der medizinischen Strategie für eine Einzelperson und den Strategien des öffentlichen Gesundheitswesens auf nationaler Ebene häufig kontrovers diskutiert.

*Toxoplasma gondii*-Infektionen während der Schwangerschaft mit dem Risiko einer congenitalen Toxoplasmose (KT) ist ein klassisches Thema, über das vielfach debattiert wird. Obwohl geographisch zwischen Frankreich (wo eine Kombination von Primär- und Sekundär-prävention der KT seit 1978 gesetzlich vorgeschrieben ist) und Österreich (wo eine Strategie
zur Prävention seit 1975 existiert) gelegen, hat die Schweiz die Primär- und Sekundärprävention noch nicht reglementiert.

Seit 1990 hat das Schweizerische Bundesamt für Gesundheitswesen (BAG) beschlossen, einige Studien zu unterstützen, die verschiedene Aspekte des öffentlichen Gesundheitswesens im Zusammenhang mit der KT untersuchen.

Die entsprechenden Tätigkeiten der vergangenen 5 Jahre können wie folgt beschrieben werden:

1. Stufe: Seroepidemiologische Studie für die gesamte Bevölkerung auf lokaler Ebene.  


Schlüsselwörter  
Toxoplasma gondii, kongenitale Toxoplasmose, Epidemiologie, Gesundheitswesen, Strategie, Schweiz, Europa.

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Korrespondenzadresse:
Patrick Jacquier
ParaDiag
Laboratory of Medical Parasitology
Tel. +41 31 328 20 20 • Fax +41 31 328 20 21 • E-mail: ParaDiag.PJ@thenet.ch
Weihergasse 8
CH-3005 Bern • Switzerland
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