Haemophilia Registry of the Medical Committee of the Swiss Haemophilia Society
Update and annual survey 2009

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Summary
The Swiss Haemophilia Registry of the Medical Committee of the Swiss Haemophilia Society started in 1996 but was set as an internet-based, double password-protected facility in the year 2000. With the inclusion of patients’ data from two new centres in 2009, we assume a coverage rate of about 90% of all patients with inherited bleeding disorders in our country. Data concerning the phenotype and genotype of the disorder, its severity, its therapy, the prevalence of inhibitors are readily available to the registered users, allowing quality control of haemophilia therapy at a national level, but also rapid care of the patient visiting the emergency room of another treatment centre. Basing on the available data, about two thirds of the WFH global survey can be answered; the mortality statistics shows that bleeding remains a cause of death in haemophiliacs, also in the 21st century. The Registry allows for comparisons with international datasets, especially with respect to treatment (prophylaxis vs. on-demand therapy), factor consumption and costs.

Patients
A total number of 904 patients (compared to 856 in year 2008) were included in the Registry, corresponding to a plus of 5.6%. This large increase reflected the fact that 2 new Haemophilia treatment Centers were acknowledged in 2009 by the Medical Committee; the real incidence and prevalence of haemophilia in Switzerland remained very stable over the last 5 years. Forty patients (compared to 51 in 2008) could not be assigned to a specific center and, because of lack of updating, excluded for the evaluation.

Haemophilia and other rare coagulation disorders
Generally speaking, the distribution of the registered coagulopathies has not changed over the last years (Fig. 1):
- haemophilia A 560 (65%),
- haemophilia B 112 (13%),
- von Willebrand disease 126 (15%),
- other coagulopathies 66 (7%), including deficiencies concerning:
  - afibrinogenaemia (n = 10),
  - factor VII (n = 26),
  - factor X (n = 4),
  - factor XI (n = 8),
  - factor XIII (n = 14),
  - factor V/VIII (n = 4).

The base for the IT concept of the Swiss Hemophilia Registry was set in the year 2000. In 2004 the Registry has been transformed to the actual internet based form with double password security. The latest records from October 31st 2009 are presented here.

Epidemiologie

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Haemophilia severity was classified according to the ISTH standards (1): severe A/B <1%, moderate 1–5%, and mild 6–40%. The corresponding results (Fig. 2):
- severe type A patients 199 (37%),
- moderate type A 105 (19%),
- mild type A 236 (44%),
- severe type B patients 35 (34%),
- moderate type B 35 (34%), and
- mild type B 32 (32%).

Data were missing in 30 patients.

In 2009 there were four newborns with newly diagnosed haemophilia A. Age distribution of the patients with haemophilia A/B slightly shifted to the right over the years with a current average age of 40 years, compared to 37 years in 2006.

The inhibitor status was positive in 17 patients with haemophilia A and 1 patient with haemophilia B. High responding inhibitors were present in 10 patients (9 with haemophilia A, 1 B) and low responding inhibitors in 8 patients, all with haemophilia A. However the numbers were not fully representative, as data on inhibitor status were missing in 125 patients.

Data concerning treatment types are shown in Figure 3: In Switzerland, on-demand treatment still exceeds prophylaxis for haemophilia A and B. In
- haemophilia A 349 (62%) patients performed on-demand treatment vs. 106 (19%) prophylaxis,
- haemophilia B: 78 (70%) on-demand vs. 15 (14%) prophylaxis.

However, in the course of time a progressive shift was observed towards prophylactic treatment, also in adults (data not shown).

Recently, a new treatment group (sporadic therapy) (2), representing 8% of haemophilia A and 7% of haemophilia B patients, was introduced to describe mainly mild haemophiliacs requiring such a minimal treatment that it cannot be called “on-demand”. It’s highly probable that not all concerned patients have already been correctly transferred from the “on-demand” to the “sporadic” group. Treatment status of about 10% of all patients remained unknown.

Figure 4 shows the proportion of patients under prophylactic treatment according to age. During the first decade, 89% of children with haemophilia A and 75% with haemophilia B were under regular prophylaxis; in the second decade of life, 84% of adolescents with factor VIII deficiency and 33% of those with factor IX deficiency were still under prophylaxis. Numbers declined then rapidly, with a trend towards a new increase in prophylactic therapy over the age of 60–70 years.

Mortality

Death registration represents a small file in the Registry. In the period 1996–2009, a total number of 62 patients have been reported to be dead. During the year 2009 four patients died: two from cancer and one each from bleeding and end-stage liver disease. The last HIV-related death was in 2003.

Factor concentrate

The module includes the components:
1. name and type of the concentrate,
2. delivery of the concentrate: amount in U or mg, date of delivery and treatment indication (4 options: home treatment – acute bleeding – surgery – stockpile for holidays),
3. total amount of concentrate consumption per year,
4. history of the actual concentrate and former ones

The main data input to this module comes from an automatic file transfer from the pharmaceutical companies which deliver...
the concentrates for home treatment to the Registry. The total amounts of delivered concentrates are reported quarterly to the administrator responsible for the data input.

Data can also be put in manually by any user. Despite the convenient and easy handling of the module, data are probably not completely collected yet.

In 2004 the software was enhanced by a statistics program allowing evaluation of the concentrates in various combinations of selection, quantity and period of time. The factor concentrates used are presented in Fig. 6.

In Switzerland as in other countries (3), recombinant products clearly lead the market in haemophilia A with about 75% of patients receiving recombinant vs. 25% plasma-derived factor VIII. In haemophilia B, plasma-derived factor IX concentrates remain clearly on top: 92% vs. 8% rFIX.

It is somewhat disappointing to note that the type of concentrate remains unknown in 30–40% of patients.

Fig. 7 shows the total amounts of concentrates used between November 1st 2008 and October 31th 2009.

Quality control

Currently, there are 49 authorized users in the registry, all accredited members of the Medical Committee of the Swiss Hemophilia Society. The history of their logins as well as the quality and the regularity of their inputs in the Registry are controlled once per year. Compliance to the rules set by the Medical Committee and the compliance is one of the key criterion for the accreditation and re-accreditation/validation of the corresponding hemophilia reference or treatment Center. Currently there are

- 2 reference and 9 treatment centers for children and
- 5 reference and 7 treatment centers for adults in Switzerland.

Apart from three small centers, all others actually meet the compliance criteria, yearly editing the medical data of over 85% of their patients and reporting on the follow-up of at least 3 (for treatment centers) or 20 (for reference centers) severe haemophiliacs during the last 12 months.

Since 2009, the Registry exerts a continuous control of the last check-up dates; this is a very valuable tool to prospectively assess quality of medical care in hemophilia and help to ensure at least one annual check-up in an accredited center for patients with severe disease. Currently, compliance rate to this rule is 72%, far from ideal but significantly better than last year as it reached only about 50%.

Conclusion

Status and future of the Registry are very encouraging. After 15 years it really starts to be self-acting. For haemophilia specialists it

### Table 1

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<th>haemophilia A</th>
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<td>total</td>
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<td>activated prothrombin</td>
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Fig. 4 Percentage of patients under prophylaxis, according to age

Fig. 5 Cumulative death statistics, over the 14 years of the Registry (year 1 = 1996)
has become a motivating tool to put in data, as it provides useful epidemiological, clinical but also economical data (e.g. global and per capita use of factor concentrates). In the near future the registry will be used for prospective quality control of haemophilia centers and care in Switzerland. The data of the Swiss Registry will enable international comparisons in the fields of clinical and epidemiological research in hemophilia. We are still in the process of expanding the spectrum of registered diagnoses, more specifically opening registration to severe inherited platelet disorders (a.o. Bernard-Soulier syndrome and Glanzmann’s thrombasthenia) as well as other rare coagulopathies. In haemophilia A and B, patients’ data are being completed, after obtaining every individual informed consent, with the results of the mutation analysis.

Patients indirectly take advantage from the Registry, as they get accurate and up-to-date information on accredited haemophilia centers in Switzerland.

Swiss medical authorities as well as suppliers show increasing interest in the figures of the Registry for their planning of emergency supplies of factor concentrates and prediction of overall usage in Switzerland. The Registry will require continuous efforts of the Medical Committee and support from the Swiss Hemophilia Society Board to maintain highest quality requirements.

Conflict of interest
The author declares that there is no conflict of interest.

References