

Primary Immunodeficiency Diseases in Norway

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This study represents the first national epidemiological survey of primary immunodeficiency diseases in Norway. Uniform questionnaires were sent out in April 1998 to all hospital departments considered relevant. As of February 1999, a total of 372 patients have been registered, of whom 69 patients are deceased. With a population of 4.45 million people, the total prevalence of primary immunodeficiency diseases in Norway February 1, 1999 is 6.82 per 100,000 inhabitants. Distribution between the main immunodeficiency diagnoses is (a) antibody deficiencies 50.8%, (b) combined deficiencies included other immunodeficiency syndromes 12.4%, (c) complement deficiencies 21.0%, (d) phagocytic disorders 6.7%, (e) and immunodeficiency associated with other congenital diseases 9.1%. Compared to previous reports from other European countries, there is a smaller proportion of antibody deficiencies due to few IgA deficiencies registered and a large proportion of complement deficiencies due to many patients with hereditary angioedema.

KEY WORDS: Primary immunodeficiency; registry; Norway.

INTRODUCTION

Primary immunodeficiency diseases represent a heterogeneous group of disorders characterized by an increased susceptibility to infections and autoimmune disease, and a predisposition to malignant disease. With the progress in immunology and molecular biology including the development of diagnostic genetic tests (1) over the last two decades, a large number of primary immunodeficiency diseases (PIDs) has been recognized and characterized. The European Society for Immunodeficiencies (ESID) has established a European registry for PID (2), and many countries have their own registry (3–10). There also are PID registries outside Europe (11–14).

Some subregistries are currently planned or already started (15): BTKbase is a mutation database for X-linked agammaglobulinemia (16, 17). WASPbase is a database for Wiskott–Aldrich syndrome and X-linked thrombocytopenia-causing mutations (18, 19). IL2RGbase exists for X-linked severe combined immunodeficiency (20) and CD40Lbase for X-linked Hyper-IgM syndrome (21); databases or registries for chronic granulomatous disease (22, 23), severe chronic neutropenias (SCN International Registry) (24), and ataxia telangiectasia (2) have been established. Previous reports of national and international gathering of information have brought epidemiological information and new important knowledge about immunodeficiencies (25–27). This has inspired new countries to establish their own PID registry and to join this international collaboration.

For the first time in Norway we have performed a national survey of patients with PIDs, both children and adults. The aim was to characterize the incidence and prevalence of the different primary immunodeficiency diseases and their regional distribution, to elucidate the size of this health problem for better health planning and to achieve better knowledge of the care of these patients in Norway.

MATERIALS AND METHODS

The Norwegian Health Service

The population of Norway (4.45 million as of January 1, 1999) geographically has been relatively scattered compared to the neighboring countries. The health system therefore has been more decentralized. The country is divided into 19 counties constituting five health regions (Fig. 1), each with a university hospital. In addition, the counties have their own central hospital and a variable number of smaller local hospitals. The distribution of general practitioners and child health centers related to the number of inhabitants is similar between

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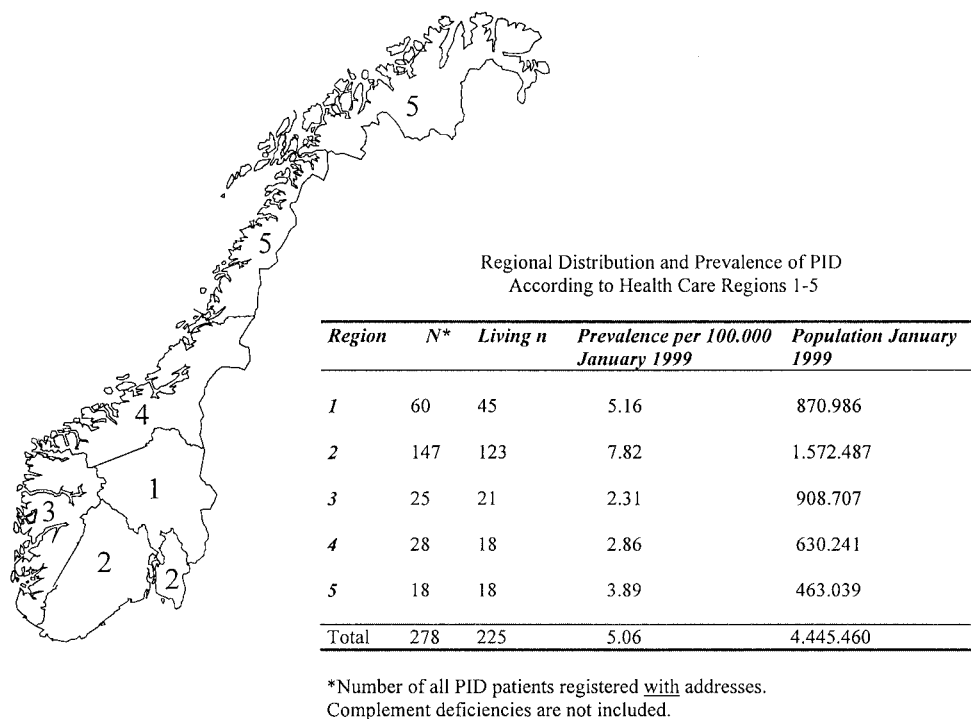


Fig. 1. Map of Norway showing the health care regions 1-5 and the prevalence of PID according to the regions.

the counties (28). The specialized health service and consultants are concentrated in densely populated areas. Health regions No. 1 and No. 2 cover the most densely populated areas in Norway. Rikshospitalet, the National University hospital, has served health region No. 2. There has not been a Norwegian consensus concerning the organization of treatment of PID patients. Most of the PID children are treated at the regional pediatric departments, while the adult PID patients traditionally have been treated at the medical departments or at the departments of infectious or hematological diseases. However, many PID patients from all five regions have been referred to Rikshospitalet.

The Collection of Information

Permission was obtained from the Norwegian Data Protection Agency to establish a preliminary research registry of PID patients and the Norwegian Board of Health allowed the physicians to report patients to the registry. The physicians were asked to classify their PID patients in one of the following categories: antibody deficiency, T-cell or combined B- and T-cell deficiency, phagocyte deficiency, complement deficiency, and other immunodeficiencies. When necessary, additional information such as laboratory results were obtained at a later stage of the study. The questionnaire also permitted

reporting those patients where PID was suspected but not established as a diagnosis. In April 1998, the questionnaires were mailed to 140 different departments in 60 hospitals. All nonpsychiatric hospitals in Norway were contacted. Also, the patient organization, the Norwegian Immune Deficiency Association, distributed the questionnaire to their members. One reminder, with relevant ICD-9 numbers, was sent to nonresponders. In addition, several departments were contacted by telephone to clarify information already given and to repeat the request for replies. The authors also arranged lectures, seminars, and presentations for health personnel about PID and this particular study during the study period. All PID patients' medical records accessible at Rikshospitalet were reviewed and the diagnosis confirmed or reclassified.

The Registry Database

The collected data were registered in a non-network-connected database. In order to meet legal requirements (29), all patient administrative and personal data were coded when registered. PID diagnoses were based on a phenotypic characterization as defined by a World Health Organization (WHO) scientific group (30). In recently diagnosed pediatric PID patients, DNA mutation analysis was usually performed when indicated in addi-

tion to quantitation of CD40L (21) or Bruton tyrosine kinase (*BTK*) (17). Congenital agammaglobulinemia in females was defined as common variable immunodeficiency (CVID) (1). All patients with DiGeorge anomaly had a verified deletion of chromosome 22. Patients with DiGeorge anomaly and normal number and function of T cells were not included in the registry. Auto- and alloimmune neutropenias as well as transient hypogammaglobulinemia of infancy were excluded.

Statistics

Children were defined as individuals below 16 years of age (as of January 1, 1999). Demographic statistics were obtained from Statistics Norway (31). The point prevalences were calculated using population data from January 1999. The regional prevalence is based on the patients' home addresses. C1-inhibitor deficiencies and other complement deficiencies were reported to us with no more personal information than gender and year of birth, and these patients therefore are excluded from calculations of geographic prevalence. Incidences of severe combined immunodeficiency, ataxia telangiectasia, Wiskott–Aldrich syndrome, and X-linked agammaglobulinemia related to live births were calculated using population data from 1961 to 1998.

RESULTS

In the period from April 1998 to January 1999 a total of 227 completed questionnaires were received from 35 hospitals. Fifty-one were sent from other university hospitals, except Rikshospitalet, and 109 from other hospitals. One hundred came from hospitals in regions No. 1 and No. 2 and 60 from hospitals in regions Nos. 3–5, when all 67 C1 inhibitor deficiencies are excluded. An approximately equal number of pediatric and medical departments responded, and only a few patients were included from other departments. Departments in some hospitals coordinated their response. Therefore the exact number of responding departments is not available. Twenty departments reported by letter that they had no PID patients at all. Twenty-five hospitals did not respond. These were mainly smaller local hospitals covering less than 10% of the total population. Most of them were contacted by phone and confirmed that they had no patients with PID. Of the registered PID patients, 163 were found through the questionnaire. In addition, 240 PID patients—90 children and 150 adults—were previously known from Rikshospitalet, including 31 patients who also were reported via the questionnaire. Thus, a total of 372 PID patients were found, including 117

Table I. Distribution and Prevalence of the Five Main PID Diagnoses

Primary immunodeficiency	N	%	Living n	Prevalence per 100,000 in Norway
Antibody deficiencies	189	50.8	155	3.49
Combined deficiencies, immunodeficiency syndromes	46	12.4	20	0.45
Complement deficiencies	78	21.0	78	1.75
Phagocytic disorders	25	6.7	22	0.50
Immunodeficiencies associated with other congenital disorders	34	9.1	28	0.63
Total PID	372	100	303	6.82

children and 255 adults, 162 females and 210 males, respectively. Of these patients, 303 are alive, and the January 1999 prevalence of PIDs therefore is 6.82 per 100,000 inhabitants in Norway (Table I).

Most PIDs in children were diagnosed after 1980, while PIDs in adults were diagnosed after 1970. Before that time there are only a few patients diagnosed with PID retrospectively. The approximate number of PID diagnosed each year has increased from 10 per year in the 1980s to 15 per year during the early 1990s and 30 per year since 1995. Sixty-two patients had relatives in the registry (C1-inhibitor deficiency excluded). They came from 29 families, with 2–3 patients in each family.

We have registered 69 deceased PID patients, including 12 who received the PID diagnosis postmortem after a new diagnosed patient occurred in the family. Six died before 1981, 20 died during 1981–1990, 20 died during 1991–1995, and 23 died within the 3-year period of 1996–1998. Twenty-seven died during childhood (7 girls and 20 boys), including 18 who died within their first year of life. Of the dead boys, 11 had verified X-linked PID (Tables II and III), and three had an X-linked, probable PID. Among adults 16 women and 26 men are deceased.

The patient's home address was known in 278 cases and the geographic distribution and prevalence in each health region were defined according to this information (Fig. 1). Significantly more patients lived in the southern and eastern parts of the country compared to the western and the northern parts. The health region No. 2 served by Rikshospitalet had more than a doubled prevalence of PID compared to three of the other regions. In spite of the large variation between the regions, the prevalence in each county was calculated, and since with only one exception no large discrepancy from the region's total prevalence was found, the distribution within each region is not further discussed.

Table II. Characteristics of Predominantly Antibody Deficiencies

Antibody deficiencies	N	Male	Female	Children	Adults	Living	Decreased
X-linked agammaglobulinemia	15	15	0	6	9	11	4
Common variable immunodeficiency ^a	117	65	52	3	114	94	23
Hyper-IgM syndrome ^b	11	9	2	8	3	6	5
IgA deficiency	36	19	17	13	23	34	2
IgG subclass deficiency	10	9	1	8	2	10	0
Total	189	117	72	38	151	155	34

^aFemales with congenital agammaglobulinemia are included here.

^bNot distinguished between X-linked and non-X-linked hyper-IgM syndrome.

Antibody Deficiencies

Antibody deficiencies (Table II) predominate in the registry with 189 patients (50.8%), including 151 adult patients (64 women and 87 men) and 38 children (8 girls and 30 boys). As of January 1999, 155 were alive, giving a prevalence of 3.49 per 100,000 individuals in Norway. Of the deceased adult and childhood PID patients, 31 and 3, respectively, had antibody deficiency. Common variable immunodeficiency (CVID) ($n = 117$) was most frequent among the adult patients. All with IgG subclass deficiencies ($n = 10$) and selective IgA deficiency (IgAD) ($n = 36$) had been referred to the hospitals because of various clinical symptoms such as recurrent infections, autoimmune disease, and celiac disease. Other reported deficiencies were hyper-IgM syndrome (HIM) ($n = 11$; 9 male and 2 female) (27), and X-linked agammaglobulinemia (XLA) ($n = 15$; including four pairs of brothers). The incidences of XLA per million live births related to different periods of time are calculated in Table VII.

Combined Deficiencies and Other Immunodeficiency Syndromes

These deficiencies (Table III) represent a heterogeneous group with patients showing severe to mild disease. Totally 46 patients (12.4%) are registered with 20 persons living

giving a prevalence of 0.45 per 100,000 individuals. Seventeen of the deceased children belonged to this group including 9 of 12 children with severe combined immunodeficiency (SCID). Five related patients with Omenn syndrome originate from a small area in the south of Norway. Seven other SCID patients were reported, including two with verified X-linked SCID. Overall incidence of SCID in Norway has been 8.9 (1.5–9.3) per million live births over the last two decades (Table VII).

Other well-defined deficiencies include syndromes such as DiGeorge anomaly with immunodeficiency ($n = 8$), ataxia telangiectasia (AT) ($n = 17$), and Wiskott–Aldrich syndrome ($n = 8$). The incidences per million live births of WAS and AT are calculated in Table VII. There were two pairs of siblings in the AT group. DNA mutation analysis and genealogical search have shown that eight other patients with AT are distantly related, having one specific Norwegian variant of AT mutation in common (32). Nine patients with AT died as young adults, six reached their 20s, but all six died before 26 years of age. One adult patient with an isolated T-cell deficiency also was reported.

Complement Deficiencies

A large group of patients (Table IV) with hereditary angioedema (HAE) and C1-inhibitor deficiency (CINH)

Table III. Characteristics of T-Cell Defects, Combined Deficiencies, and Other Well-Defined Immunodeficiency Syndromes

Designation	N	Male	Female	Children	Adults	Living	Deceased
Combined immunodeficiencies ^a							
Omenn syndrome	5	1	4	5	0	1	4
X-linked SCID ^b	2	2	0	2	0	1	1
Other SCID	5	3	2	5	0	1	4
Predominantly T-cell Defects							
Primary CD4 T-cell deficiency	1	0	1	0	1	1	0
Immunodeficiency syndromes							
Wiskott–Aldrich syndrome	8	8	0	7	1	5	3
Ataxia-telangiectasia	17	7	10	6	11	7	10
DiGeorge anomaly with immunodeficiency	8	5	3	8	0	4	4
Total	46	26	20	33	13	20	26

^aX-linked hyper-IgM syndrome; see Table II, antibody deficiencies.

^bVerified X-linked SCID caused by IL-2 receptor gamma chain defect (IL2RG).

Table IV. Characteristics of Complement Deficiencies

Complement deficiencies	N	Male	Female	Children	Adults	Living	Deceased
C1 inhibitor deficiency	67	31	36	18	49	67	0
C2 deficiency	7	3	4	3	4	7	0
C4 deficiency	1	0	1	0	1	1	0
C5 deficiency	2	1	1	0	2	2	0
C8B deficiency	1	1	0	0	1	1	0
Total	78	36	42	21	57	78	0

($n = 67$) has been reported from one research group located in Bodø, in the northern part of Norway (33). These investigators have actively searched for affected family members in their local area and in other parts of the country. Other complement disorders were C2 deficiency ($n = 7$), C4 deficiency ($n = 1$), C5 deficiency ($n = 2$), and C8 beta deficiency ($n = 1$) (34–36). A total of 78 patients (21.0%) are registered with complement deficiencies. All these patients were alive in January 1999, giving a prevalence of 1.75 per 100,000 individuals.

Phagocytic Disorders

Twenty-five patients (6.7%) with phagocytic disorders have been registered (Table V) with the following distribution: Severe congenital neutropenia ($n = 3$), cyclic neutropenia ($n = 8$), and idiopathic neutropenias ($n = 7$). Half the patients with cyclic and idiopathic neutropenia lived in the same county. The other phagocytic disorders are chronic granulomatous disease (CGD) ($n = 4$), leukocyte adhesion defect (LAD 1) ($n = 1$), and interferon gamma receptor 1 deficiency (IFNGR1) ($n = 2$). Three patients with phagocyte deficiency are dead: one child with IFNGR1 (37) and two adults with severe congenital and idiopathic neutropenia, respectively. As 22 patients are living, the total prevalence of phagocytic disorders can be calculated to 0.50 per 100,000 individuals.

Immunodeficiency Associated with Other Diseases

A total of 34 patients (9.1%) had immunodeficiency in combination with another congenital disease or an immunodeficiency syndrome. As of January 1999, 28 were alive giving a prevalence of 0.63 per 100,000 individuals.

One patient with a deletion of chromosome 18 and one with Turner's syndrome, both having an antibody deficiency, were reported to the registry. In addition, one girl with mental retardation and immunodeficiency and a boy with X-linked lymphoproliferative syndrome are included (Table VI). Three infants with primary asplenia representing Ivemark's syndrome with situs inversus and major cardiac defects have been registered. There also were three boys from the same family with an unclassified severe immunodeficiency (38), and only the youngest boy grew old enough to also receive the diagnosis of anhidrotic ectodermal dysplasia.

Two other syndromes are included in this group: hyper-IgE syndrome (39) ($n = 1$) and chronic mucocutaneous candidiasis ($n = 23$). Three siblings have chronic mucocutaneous candidiasis associated with hypothyroidism. Sixteen patients have autoimmune–polyendocrinopathy–candidiasis–ectodermal dystrophy (APECED) (40, 41), comprising ten patients in four families. The last four of the 23 with chronic mucocutaneous candidiasis probably have the dominant type

Table V. Characteristics of Phagocytic Disorders

Phagocytic disorders	N	Male	Female	Children	Adults	Living	Deceased
Functional defects							
Chronic granulomatous disease	4	4	0	1	3	4	0
Interferon gamma receptor 1 deficiency	2	2	0	2	0	1	1
Leukocyte adhesion defects (LAD1)	1	1	0	1	0	1	0
Congenital neutropenias							
Severe congenital neutropenia	3	2	1	2	1	2	1
Cyclic neutropenia	8	3	5	1	7	8	0
Idiopathic neutropenia	7	1	6	1	6	7	1
Total	25	13	12	6	19	22	3

Table VI. Immunodeficiencies Associated with or Secondary to Other Congenital or Hereditary Conditions

Immunodeficiencies associated with or secondary to other diseases	N	Male	Female	Children	Adults	Living	Deceased
Chromosomal defects							
Turner syndrome ^a	1	0	1	0	1	1	0
Deletion chromosome 18 ^a	1	0	1	0	1	1	0
Immunodeficiency with dermatological defects							
Probably anhidrotic ectodermal dysplasia with severe immunodeficiency	3	3	0	3	0	0	3
Other							
Hyper-IgE syndrome	1	0	1	1	0	1	0
Chronic mucocutaneous candidiasis ^b	23	11	12	10	13	23	0
Ivemark syndrome	3	3	0	3	0	1	2
X-linked immunoproliferative disease	1	1	0	1	0	0	1
Unclassified							
Syndrome of mental retardation and immunodeficiency ^a	1	0	1	1	0	1	0
Total	34	18	16	19	15	28	6

^aPredominantly antibody deficiency.

^bChronic mucocutaneous candidiasis included autoimmune–polyendocrinopathy–candidiasis–ectodermal dystrophy (APECED).

without endocrinopathy, and they are all from the same family (42).

DISCUSSION

This is the first epidemiological study of PID in Norway. A total of 372 patients representing 33 different diagnoses are registered. The age and sex distribution is 117 children and 255 adults and 162 females and 210 males. Since 303 are alive, the prevalence of PIDs is 6.82 per 100,000 inhabitants, with a regional variation from 2.31 to 7.82 per 100,000 inhabitants. In our material the proportion of males compared to females among children is almost 2:1, due to the X-linked diseases, which is in agreement with other reports (1, 5, 6, 11, 26). The majority of boys is even more evident among the dead children, where the proportion is exactly 3:1.

According to our findings the frequency of PID varies significantly throughout the country. This may be partly due to diverging occurrence of these hereditary diseases, possibly related to a higher rate of consanguinity in some areas. It also may reflect underreporting and undetected PID patients, including cases where only autopsy possibly could have revealed the diagnosis. The proportion of deceased PID patients varies from 0 to 36% between the regions (Fig. 1). As for region No. 4, many of the patients reported were deceased, and then the calculated prevalence is low. This modifies the pattern but cannot explain the large differences between regions No. 1 and No. 2 compared to region No. 3. The health region served by Rikshospitalet had the highest prevalence with more than a doubled prevalence of PID compared to three of the other regions. Research activity and medical interests certainly may influence the pattern of distribution of

diagnoses. This may be the reason for the high prevalence of PID in the health region of our own hospital, Rikshospitalet, which received the patients from health region No. 2 and at least partly for the high prevalence of hereditary angioedema in the northern health region (33). Regional differences in primary, secondary, and tertiary health services including access to specialized consultants also may have influenced the number of diagnosed and reported patients.

The total number of registered PID patients in Norway is relatively high compared to the total number of ESID registered patients by July 1998 (2) from Spain ($n = 1127$), Italy ($n = 602$), and the Netherlands ($n = 611$) and equals the number of patients registered from Sweden ($n = 891$) when related to the population in each country. Improvement of and greater access to diagnostic techniques may have led to more patients being recognized and classified in most recent surveys. Also, the recent addition of new categories of PIDs to the WHO classification system and a different and more specified classification of PID diagnoses make a direct comparison with data previously published from other national registries (2–14) difficult. Prevalence and incidence of specific PID diagnoses should be used in attempts to make valid comparisons between the countries. Despite difficulties mentioned above, the distribution of the main PID diagnoses gives an impression of similarity between Norway and other countries. We have a large proportion of combined deficiencies compared to antibody deficiencies due to only a few IgA deficiencies registered and a large proportion of complement deficiencies due to many patients with hereditary angioedema. When incidence and prevalence of each specific PID is compared, our results with some exceptions correspond to other countries.

Table VII. Incidence per 10⁶ Live Birth in Norway

Designation	1961–1970		1971–1980		1981–1990		1991–1998	
	N	Incidence	N	Incidence	N	Incidence	N	Incidence
Ataxia telangiectasia	5	7.7	6	10.6	2	3.7	4	6.7
Wiskott–Aldrich syndrome	0	—	2	3.5	1	1.9	5	10.4
X-linked agammaglobulinemia	3	4.6	2	3.5	5	9.3	2	4.2
Severe combined immunodeficiency	1	1.5	1	1.8	5	9.3	5	8.3

When calculating the frequency of the severe infant diseases with high mortality, the incidence related to live births is used (Table VII). Incidence of AT earlier has been reported as 3 per 10⁶ live births (1), which corresponds to our results (3.7–10.6 per 10⁶ live births). In comparison, incidence of AT in Spain was reported as 0.04–0.05 per 10⁶ live births (1980–1994) (10) and in Switzerland reported as 1.4 per 10⁶ live births (1975–1985) (7); both reports had a shorter observation period than ours. Incidence of WAS has been estimated as ≥ 2 per 10⁶ individuals (1), while our calculations are related to live births and cannot be directly compared. When comparing the results from Spain (10) of 0.01–0.04 WAS per 10⁶ live births (1980–1994), the incidence found in Norway is high (1.9–10.4 WAS per 10⁶ live births, 1971–1998). However, our retrospective observation period is longer, permitting additional patients with mild WAS to be reported (43). The XLA incidence previously has been reported as 5.4 per 10⁶ live births in Switzerland (1975–1985) (7), and our study shows a similar incidence ranging from 3.5 to 9.3 per 10⁶ live births. In contrast, XLA in Spain was reported as only 0.05–0.11 per 10⁶ live births (10). Incidence of SCID in other studies suggests 2–20 per 10⁶ live births, with half the cases representing X-linked SCID in reports from the United States (1, 26). SCID incidence in Switzerland was 24.3 per 10⁶ live births (1975–1985) (7) and in Sweden 14 per 10⁶ births (1974–1979) (5). In comparison our SCID incidences have been lower, ranging from 1.5 to 9.3 per 10⁶ live births over the last three decades, with only a few X-linked SCID patients. As Norway and Sweden are neighboring countries, the frequency of SCID should be relatively similar. The differences may be due to infant deaths not verified as caused by SCID.

In our study, antibody deficiency, especially CVID, is the most frequent diagnosis among adults, and prevalence of CVID was 21 per 10⁶ population January 1999. Reports from most other European countries (3–10) demonstrate significantly lower prevalence, with some exceptions: Prevalence of CVID in United Kingdom (1998) was 18.7 per 10⁶ population for males and 14.7

per 10⁶ population for females (4). In direct comparison, the prevalence of CVID in Norway (January 1999) was 22.3 per 10⁶ population for males and 20.0 per 10⁶ population for females.

Prevalence of IgAD presented in this study is extremely low compared to the expected 1 per 600 in Caucasians (1). The reason for this is probably that our patients with IgAD were tested and diagnosed because they presented with various clinical signs and symptoms, and consequently our registration, unlike many others, was not based on screening investigation of the general population. In PID registries of other European countries, the proportion of IgA deficiencies is higher than that of CVID (9, 10). There may be patients with IgAD, IgG subclass deficiencies, or CVID that are cared for by private practitioners without referral to a medical center, but this is not very likely for patients treated with immunoglobulins.

The high prevalence of hereditary angioedema in Norway (15.1 per 10⁶ population) is unique and due to large families with many affected members, most of them living in the northern part of the country. Moreover, as the research group reporting their data en bloc to us has actively searched for and tested relatives, the large number reported is a consequence of this high research activity. In contrast, the other complement deficiencies seem to be rare, and surprisingly nobody is reported as deceased. Others also have found a low prevalence of deficiencies of late-acting complement factors in the Norwegian population (34, 35); however, there still may be many undiagnosed patients.

The prevalence of CGD is low compared to Sweden (44). It is probable that more Norwegian patients are undiagnosed, especially patients with autosomal recessive CGD, since only X-linked CGD was reported. The prevalence of severe congenital neutropenia, based on surveys from other countries, has been estimated to be 1–2 cases per 10⁶ population (24), which is higher than our result (0.5 per 10⁶ population). The prevalence of cyclic neutropenia previously has been estimated to be 0.5–1 case per 10⁶ population (24), which is lower than

the 1.8 per 10⁶ population we found. The prevalence of idiopathic neutropenia previously has been reported as 2–4 cases per 10⁶ population (24), not far from our results of 1.6 cases per 10⁶ population. The idiopathic as well as the cyclic neutropenias may be underreported. Half the reported patients with neutropenia live in the same county and are treated by the same hospital.

Collecting patient data using a questionnaire, as in the present survey, has certain limitations and pitfalls. The success depends on the good will and collaboration of the participating physicians. Only a minority of Norwegian hospitals was able to retrieve patient diagnoses (ICD-9) electronically for longer than a few years back. This possibility has improved during the last years and may simplify the search for similar patient data in the future. The more recent international classification of diseases (ICD-10) and subsequent improved successors may permit better search possibilities for patients with a particular PID diagnosis.

Our study provides data that permit a more correct estimation of the resources needed for PID patients from the Norwegian National Health Service. The data also may form the basis for national plans for various treatment modalities in PID such as immunoglobulin treatment and bone marrow transplantation. With continuous PID registering in Norway, it will be possible to obtain population based knowledge of the natural course of patients with PID as part of an increasing international research effort.

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