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Original Contribution

Psychiatric Hospitalizations in a Cohort of Danish Polio Patients

Nete Munk Nielsen[1], Klaus Rostgaard[1], Henrik Hjalgrim[1], Dorthe Askgaard[2], Peter Skinhøj[2], and Peter Aaby[1,3]

[1] Department of Epidemiology Research, Statens Serum Institut, Copenhagen, Denmark.
[2] Department of Infectious Diseases, National University Hospital, Copenhagen, Denmark.
[3] The Bandim Health Project, Bissau, Guinea-Bissau.

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Although previous polio infection remains a considerable cause of long-term morbidity worldwide, few studies have examined the psychiatric consequences of poliomyelitis. The authors followed 4,660 polio patients hospitalized at the primary infectious disease hospital in Copenhagen, Denmark, between 1922 and 1954 as well as 19,017 age- and gender-matched Danes for psychiatric hospitalizations from January 1, 1977, to December 31, 1993. Incidence rates of all psychiatric disorders combined and of separate diagnostic groups of psychiatric diseases in the two cohorts were compared, yielding the incidence rate ratio, a measure of relative risk. Overall, polio patients had a 40% increased risk of being hospitalized for a psychiatric disorder (incidence rate ratio = 1.43, 95% confidence interval: 1.23, 1.66). Apparently, the overall increased risk of psychiatric hospitalizations could not be confined to specific groups of psychiatric disorders but seemed to be explained by slightly increased risks of several different disorders, especially milder psychiatric disorders. Finally, psychiatric morbidity did not differ between paralytic and nonparalytic polio patients. History of hospitalization for polio might be associated with subsequent risk of hospitalization for psychiatric disorders. The underlying mechanism for this association remains uncertain.

Denmark; hospitalization; mental disorders; poliomyelitis

Abbreviations: CI, confidence interval; ICD-8, *International Classification of Diseases*, Eighth Revision; IRR, incidence rate ratio.

Chronic and life-threatening diseases are known to be accompanied by increased risk of anxiety, depression, and suicide (1–7). It has furthermore been suggested that certain medical conditions such as childhood infections of the central nervous system could subsequently increase the risk of psychosis and schizophrenia (8–10).

Poliomyelitis may cause a very serious central nervous system infection, which may be accompanied by paralysis of the limbs, trunk, or respiratory system (11, 12). Although many of the persons who contracted poliomyelitis during the large epidemics in the 1940s and 1950s recovered completely, thousands were left with lifelong disabilities (13), which makes poliomyelitis an important contributor to the burden of chronic diseases.

Three to four decades after the acute infection, many polio patients experience new signs of neuromuscular dysfunction, the so-called *post-polio syndrome* defined by new muscle weakness, pain, atrophy, and fatigue (13, 14). What remains uncertain is whether polio survivors are also at risk of psychiatric sequelae. Some studies have shown elevated depression and distress scores among polio patients (15–17), whereas other studies have shown normal levels (18–20). However, previous studies have been limited by few participants, self-reported symptoms, use of different depression scale systems, and inclusion of selected groups of polio patients, often paralytic polio patients seeking help for other symptoms (15–20).

In the present study, we took advantage of historical medical archives on patients hospitalized for poliomyelitis in

Correspondence to Nete Munk Nielsen, Department of Epidemiology Research, Statens Serum Institut, Artillerivej 5, 2300 Copenhagen S, Denmark (e-mail: nmn@ssi.dk).

Copenhagen, Denmark, between 1922 and 1954 and of the nationwide Danish Psychiatric Central Research Register to assess the risk of being hospitalized for a psychiatric disorder among patients with a history of polio.

MATERIALS AND METHODS

Patients treated for poliomyelitis between 1922 and 1954 at the Blegdamshospital, the main infectious disease hospital in Copenhagen, were identified as described previously (21). Data for all cases with a discharge diagnosis of paralytic polio, nonparalytic polio, or primary lymphocytic meningitis were included in the analysis. Primary lymphocytic meningitis was generally considered nonparalytic polio after other possible viral infections such as mumps were excluded (22).

A total of 4,660 patients (paralytic: $n = 1{,}903$ (including 67 persons admitted for polio sequelae); nonparalytic: $n = 2{,}202$; primary lymphocytic meningitis: $n = 555$) were alive and residing in Denmark on January 1, 1977. For each patient, four persons were identified in the Danish Civil Registration System, matched on sex, age, and geographic residence as of January 1, 1977. Both cohorts have previously been included in a study of the incidence of somatic diseases among polio patients for the period 1977–1999 (21). By means of the unique personal identification number assigned to all Danish citizens, the exposed (poliomyelitis) and the unexposed cohorts were linked with the Danish Psychiatric Central Research Register, which, since 1970, has registered electronically all admissions to Danish psychiatric hospitals and to psychiatric departments at general hospitals. Day admissions were included in the register in 1974 (23). From 1969 until December 31, 1993, psychiatric diseases were coded according to the *International Classification of Diseases*, Eighth Revision (ICD-8). Beginning on January 1, 1994, *International Statistical Classification of Diseases and Related Health Problems*, Tenth Revision (ICD-10) codes were used. Because the ICD-10 and ICD-8 codes are not easily comparable, follow-up ended on December 31, 1993. The study was approved by the Danish Data Protection Agency.

Outcomes

As outcomes, we looked at first hospitalization (date of admission) for any psychiatric disorder and each of the specific psychiatric disorders in the list below, with the further requirement that it should be the worst outcome so far according to the hierarchy. The latter requirement reflects the probability that later psychiatric disorders could be manifestations of earlier, more severe psychiatric disorders and thus not really incidence outcomes. Accordingly, psychiatric diagnoses for each patient were arranged in a hierarchy (24) in the following order modified from Lynge et al. (25):

1. Organic disorders: ICD-8 codes 290, 292, 293, 294, 309
2. Schizophrenia: ICD-8 code 295
3. Manic-depressive psychosis: ICD-8 code 296
4. Other psychosis: paranoid states, ICD-8 code 297; reactive psychosis, ICD-8 code 298; unspecified psychosis, ICD-8 code 299
5. Neurosis: ICD-8 code 300
6. Personality disorder: ICD-8 code 301
7. Substance or alcohol abuse: ICD-8 codes 291, 303, 304
8. Other nonpsychotic mental disorders: transient maladaptation, ICD-8 code 307; other diagnoses, ICD-8 codes 302, 305, 306, 308

Thus, if a person was diagnosed with a neurosis, he or she would still be at risk of subsequently developing diseases in group 1–4 but no longer at risk of developing diseases in group 6–8. The present article deals with primary and auxiliary diagnoses among all inpatients, including day and night patients. We considered only those psychiatric diseases categorized as either psychoses, neurosis, personality disorders, or other nonpsychotic mental disorders (ICD-8 codes 290–309).

Members of the cohorts were followed from January 1, 1977, until the date of outcome considered, disappearance, emigration, death, a more severe outcome (in the disease-specific analysis), or December 31, 1993, whichever occurred first. To avoid prevalent cases of psychiatric diseases, patients diagnosed with any psychiatric disorder before January 1, 1977, were excluded from the analyses.

Statistical methods

The incidence rate for each outcome in the cohorts was calculated as the number of persons experiencing the outcome during follow-up, divided by the total follow-up time in person-years for that outcome in the respective cohorts. The ratio of incidence rates in the exposed and unexposed cohorts, the incidence rate ratio (IRR), served as a measure of the relative risk. Ninety-five percent confidence intervals for the IRR were estimated from Wald's test assuming a Poisson distribution of the observed cases. Whenever the exposed cohort was divided, to maintain confounder control, the unexposed cohorts were defined as the individually matched controls for the exposed individuals. All tests of statistical significance were two-sided, likelihood-ratio tests.

RESULTS

Persons included in the study were on average age 38.9 years on January 1, 1977 (median, 34.8 years; interquartile range, 29.8–46.7 years) and were followed for an average of 15.4 years, yielding a total of 365,773 person-years of follow-up. Patients contracted poliomyelitis between 1922 and 1954, the majority (60 percent) between 1950 and 1953, at an average age of 11.3 years (median, 7.4 years; range, 14 days–59.2 years).

Overall, history of poliomyelitis was associated with a 40 percent increased risk of being hospitalized for a psychiatric disorder (IRR = 1.43, 95 percent confidence interval (CI): 1.23, 1.66) (table 1). Similar risks were observed among the three groups of polio patients. The risk of psychiatric hospitalization tended to be highest before age 45 years (IRR = 1.82, 95 percent CI: 1.50, 2.20 vs. IRR = 1.02, 95 percent CI: 0.79, 1.30; $p < 0.01$) (table 1) and was slightly higher among those hospitalized for polio before age 7 years (preschool children) (IRR = 1.71, 95 percent CI: 1.38, 2.09 vs. IRR = 1.19, 95 percent CI: 0.95,1.48; $p < 0.05$) (table 1).

TABLE 1. Risk of psychiatric hospitalization during 1977–1993 in a Danish cohort of polio patients treated at the Blegdamshospital, 1922–1954

	All polio cases			Paralytic polio cases			Nonparalytic polio cases			Primary lymphocytic meningitis cases		
	Obs* no.	IRR*	95% CI*	Obs no.	IRR	95% CI	Obs no.	IRR	95% CI	Obs no.	IRR	95% CI
All†	232	1.43	1.23, 1.66	84	1.27	0.99, 1.61	113	1.51	1.21, 1.87	35	1.69	1.13, 2.48
Age (years) at psychiatric hospitalization												
<45	152	1.82	1.50, 2.20	51	1.52	1.09, 2.08	82	1.92	1.47, 2.49	19	2.59	1.43, 4.56
≥45	80	1.02	0.79, 1.30	33	1.01	0.68, 1.46	31	0.96	0.64, 1.40	16	1.20	0.67, 2.04
Test for difference between age groups		$p < 0.01$			$p = 0.11$			$p < 0.01$			$p = 0.06$	
Age (years) at hospitalization at the Blegdamshospital												
<7	129	1.71	1.38, 2.09	57	1.65	1.20, 2.23	61	1.76	1.30, 2.37	11	1.71	0.81, 3.38
≥7	103	1.19	0.95, 1.48	27	0.85	0.55, 1.27	52	1.29	0.94, 1.75	24	1.68	1.03, 2.66
Test for difference between age groups		$p < 0.05$			$p < 0.05$			$p = 0.16$			$p = 0.97$	

* Obs, observed; IRR, incidence rate ratio; CI, confidence interval.
† *International Classification of Diseases*, Eighth Revision codes 290–309.

The overall increased risk of psychiatric hospitalizations could not be confined to specific groups of psychiatric disorders. Risk estimates for several of the psychiatric disorders seemed increased, but statistically significantly IRRs were observed for only organic disorders (IRR = 1.49, 95 percent CI: 1.05, 2.08) and milder psychiatric disorders such as personality disorders (IRR = 2.10, 95 percent CI: 1.56, 2.79), substance/alcohol abuse (IRR = 1.65, 95 percent CI: 1.22, 2.22), and other nonpsychotic mental disorders (IRR = 2.39, 95 percent CI: 1.39, 4.02) (table 2). This risk distribution applied equally to all three groups of patients (paralytic polio, nonparalytic polio, and primary lymphocytic meningitis).

DISCUSSION

In the present cohort study, we observed a modestly increased risk of hospitalization for psychiatric disorders among patients with a history of poliomyelitis, especially those diagnosed with polio before age 7 years. Although the IRRs of grouped psychiatric diseases did not reveal an obvious pattern, the risk of especially milder psychiatric diseases seemed to be increased.

Surprisingly, neither overall nor disease-specific psychiatric morbidity differed between paralytic and nonparalytic polio patients. Even milder polio virus infections seem to affect and damage certain areas of the cerebral cortex and centers of the brainstem, including the Reticular Activating System (26). This system is responsible for the process of attention, and it has been suggested that this damage might be associated with the difficulties in mental functioning observed among polio patients even months after acute infection (26, 27). One might therefore speculate that the central nervous system infection per se has an important influence on the risk of psychiatric disorders among polio survivors. However, a complex interaction between biologic, psychological, and sociologic mechanisms might be a more plausible explanation.

Stressful life events are considered important in the etiology or triggering of psychiatric diseases (28). For those affected, contracting poliomyelitis was a very painful and fearful event. The stringent isolation of hospitalized polio patients meant separation from parents and friends for weeks or even months and total dependence on hospital staff (12, 29). When reentering society, paralytic polio patients not only experienced all the physical problems and limitations associated with being disabled, but some of them were also exposed to social prejudice, isolation, and inappropriate parental rearing because of their disabilities (29). Interestingly, traumatic childhood events such as major illness, hospitalization, separation from parents, and physical handicaps have been suggested to be associated with an increased risk of personality disorders (28, 30). Furthermore, to survive and succeed in a society full of barriers, it is believed that polio patients acquired the highly stressful type A behavior characterized by being hard-driving overachievers and perfectionists (29, 31). Thus, the observed psychiatric morbidity among previous polio patients might be related to the traumatic experience of contracting polio, the following parental and social attitudes, and the struggle to achieve social normalcy.

TABLE 2. Risk of specific psychiatric disorders during 1977–1993 in a Danish cohort of polio patients treated at the Blegdamshospital, 1922–1954

	All polio cases			Paralytic polio cases			Nonparalytic polio cases			Primary lymphocytic meningitis cases		
	Obs* no.	IRR*	95% CI*	Obs no.	IRR	95% CI	Obs no.	IRR	95% CI	Obs no.	IRR	95% CI
Organic disorders	46	1.49	1.05, 2.08	15	1.16	0.63, 2.01	19	1.43	0.83, 2.38	12	2.62	1.24, 5.33
Schizophrenia	10	1.74	0.79, 3.55	3	1.31	0.29, 4.40	5	1.67	0.53, 4.49	2	4.16	0.50, 34.64
Manic-depressive psychosis	23	1.06	0.65, 1.64	10	1.07	0.50, 2.06	10	1.00	0.47, 1.92	3	1.25	0.28, 4.08
Other psychosis†	35	1.37	0.92, 1.99	13	1.31	0.67, 2.39	16	1.42	0.78, 2.47	6	1.39	0.50, 3.31
Neurosis	24	0.97	0.61, 1.49	7	0.59	0.24, 1.21	11	1.07	0.53, 2.02	6	2.27	0.78, 5.97
Personality disorder	70	2.10	1.56, 2.79	24	1.72	1.05, 2.75	36	2.46	1.61, 3.70	10	2.09	0.94, 4.37
Substance or alcohol abuse	60	1.65	1.22, 2.22	18	1.66	0.93, 2.82	35	1.55	1.04, 2.27	7	2.45	0.91, 6.09
Other nonpsychotic mental disorders‡	22	2.39	1.39, 4.02	9	2.74	1.13, 6.35	9	2.14	0.91, 4.70	4	2.40	0.63, 7.95

* Obs, observed; IRR, incidence rate ratio; CI, confidence interval.
† Mainly reactive psychoses.
‡ Mainly transient maladaptations.

Nonparalytic polio patients might have been spared many of the psychological and sociologic traumas associated with suddenly being handicapped. However, a considerable proportion of nonparalytic polio patients were left with undiagnosed muscle weakness (32). One might therefore speculate that this group of so-called nonparalytic polio patients did not receive adequate treatment and attention during the acute phase of the disease and that further symptoms might have been ignored by the health authorities or considered not related to their previous polio disease. In addition, marginally disabled people tend to maladjust to a greater extent than severely disabled persons because of the more frequent role conflict (33). Obviously, severely handicapped persons are disabled, whereas those marginally disabled may act or seem to be nondisabled in a wide range of situations (33). Compared with paralytic polio patients, nonparalytic polio patients might therefore experience a greater role ambiguity and presumably a greater role conflict (33). Such circumstances might contribute to the observed increased risk of psychiatric hospitalizations among nonparalytic polio patients.

A supplementary analysis revealed that the risk of specific depressive disorders (ICD-8 codes 296.09, 296.29) was not increased among previous paralytic polio patients (IRR = 0.66, 95 percent CI: 0.22, 1.55; nonhierarchic analysis), a finding in contrast to some (15–17) but not all of the previous studies dealing with mental symptoms among paralytic polio patients (18–20) and to observations among patients suffering from other chronic neurologic diseases such as Parkinson's disease, epilepsy, and spinal cord injury (7, 34, 35).

The observed association between poliomyelitis and psychiatric disorders might, however, be influenced by different kinds of bias. An overestimation could be explained by the phenomenon that patients already in contact with the health care system are more likely to be diagnosed with another disease. However, such bias would have led to a particularly high risk of psychiatric diseases among paralytic polio patients, contrary to our observations. Underestimation could be the result of "survival" bias because only those polio patients alive on January 1, 1977, could participate in the study (beginning of follow-up). Accordingly, only the healthiest polio patients were included in the study and, furthermore, patients were on average age 39 years at the beginning of follow-up (i.e., psychiatric diseases presenting in childhood and adolescence were not included in the study). Furthermore, only those patients with major psychiatric diseases are admitted to psychiatric hospitals. Accordingly, the risk of minor psychiatric difficulties such as those treated by a general practitioner or a psychiatrist could not be investigated in the present study.

An unknown percentage of polio patients, nonparalytic (32) as well as paralytic, might develop postpolio syndrome (36, 37), which also seems to be accompanied by symptoms of anxiety and depression (36, 38, 39). Accordingly, psychiatric disorders could be misinterpreted as part of the postpolio syndrome and vice versa, leading to diagnostic ambiguity. In addition, mental symptoms associated with postpolio syndrome are probably more prone to be misinterpreted as psychiatrically relevant among nonparalytic polio patients than among paralytic polio patients with obvious signs of the previous polio infection.

Information on exposure (poliomyelitis) and outcome (psychiatric disorders) was collected independently from the historical archives of the Blegdamshospital and the Psychiatric Central Research Register. Coverage of the Psychiatric Central Research Register is high, between 95 and 100 percent (23). However, data in the Psychiatric Central Research Register were originally collected for administrative purposes and not epidemiologic research, which may affect their validity. Still, diagnoses such as schizophrenia and affective psychosis are considered to have a high validity (40). The diagnosis of personality disorders is less reliable, and substance abuse is considerably underreported (41). However, we have no reason to believe that the validity of the data should differ between the two cohorts. Accordingly, a diagnostic misclassification would be nondifferential and render our risk estimates conservative.

Finally, the diagnosis of paralytic polio, nonparalytic polio, and primary lymphocytic meningitis was based on clinical observations, which implies risk of misclassification. This is particularly true for patients without paralysis who might have suffered from infections with other viruses or other conditions. Still, this possibility would have no impact on the results obtained for paralytic patients.

To our knowledge, this is the first population-based assessment of the occurrence of psychiatric disorders among previous polio patients. The observed association merits attention and emphasizes the importance of supportive vigilance toward this group of people.

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Conflict of interest: none declared.

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