

Complete recovery from epilepsy?

Discontinuation of anti-epileptics after five or more seizure-free years

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Patients in whom epilepsy has been diagnosed are often told that they will have to take medication as long as they live. This statement is unnecessarily discouraging. It is quite right to impress on the patient that he must carefully take his medication for years, but the perspective of a recovery should not be taken away from him.

Introduction

Complete recovery from epilepsy is not rare: a few recent studies have shown that medication can be discontinued in over 50 percent of patients who have been seizure-free for years. Since 1973 we have – hesitantly at first but subsequently more and more often – discontinued medication of patients who had been free from epileptic symptoms five years or longer. This was always done on a voluntary basis. All patients were followed up for two years after medication was discontinued.

This article discusses how medication can be gradually discontinued, which problems can arise, which information the patient and his family should receive, and what can be done in the case of a relapse. The results obtained in various types of epilepsy are also discussed. Motives to discontinue medication are briefly considered to begin with.

Motives

The patients involved are often young people with a life expectancy of forty to fifty years; unnecessary medication during so many years is to be avoided if at all possible.

Unnecessary medication is especially undesirable for pregnant women because anti-epileptics can have a teratogenic effect, if only occasionally. There has recently been some concern about the question whether some anti-epileptics reduce male fertility (*Christiansen and Lund*).

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Successful discontinuation of medication psychologically benefits the patient and is a social advantage, e.g. in applying for a job and at medical fitness examinations.

Information

It is imperative that the patient and his family receive detailed information before one starts to reduce medication. In a long interview with the patient and his (her) marital partner we provide the following information:

- it is impossible to predict whether a relapse will or will not occur;
- after five seizure-free years it is more often possible to discontinue than necessary to continue medication; an exception are patients with primary generalized epilepsy who have had tonic-clonic seizures (*table 1*);
- if a relapse occurs, this usually happens quickly upon reduction or after discontinuation of medication;
- in the event of a relapse, the seizures can always be suppressed again by the same medication (this is the most important bit of information for the patient);
- in a few cases it may then be advisable

Table 1. Types of epilepsy in the 151 patients studied.

Type of epilepsy	Recovery	Relapse	Total
Primary generalized epilepsy	32	25	57
Partial epilepsy	35	19	54
Secondary generalized epilepsy	8	3	11
History of fewer than three seizures	11	–	11
Benign epilepsy of childhood with points Rolandiques	10	–	10
Unclassifiable epilepsy	6	2	8
Total	102	49	151

to give a more modern drug, e.g. sodium valproate (Depakine) in primary generalized epilepsy;

– once a person has remained seizure-free for two years without medication, the risk of a relapse is small and he no longer has to report back for follow-up. When this information had been given, the patient was asked what he thought of an attempt to discontinue medication. The reactions to this question varied widely.

The validity of the driving license was likewise discussed. The fact that the driving license becomes invalid for two years after an epileptic seizure prompted so many patients to forgo an attempt to discontinue medication that we raised this problem with the Central License Board. It was agreed that the driving license should remain valid after a relapse if it were certified that the attempt to discontinue medication had been initiated by the attending physician because the patient had been seizure-free for at least five years; furthermore that the patient had reported back to the clinic and resumed his former medication.

It is advisable to have the marital partner present during this informative interview because he (or she) is likewise concerned and requires information and instructions. Some have in fact never witnessed the partner in a seizure. Moreover, their presence is required to check possible attempts at dissimulation on the part of the patient.

Selection of patients

Before a patient can be considered to have been seizure-free for five years, very careful questions have to be asked regarding even the slightest epileptic symptoms (and these questions should not be asked solely of the patient!). Minimal symptoms prove to occur sporadically in a by no means negligible number of apparently seizure-free patients – usually in the form of auras which last a few seconds. Apparently,

focal epileptic attacks can remain confined for years to auras in stabilized patients. On the other hand, a decreased level of consciousness can sporadically occur, or absences during a few menstrual periods, or symmetrical twitches in both arms in the early morning hours. No attempt to discontinue medication was made for patients with such minimal epileptic symptoms.

For various reasons we refrained from an attempt to discontinue medication in twenty-four cases. Some patients were afraid of a relapse and others were irregular in reporting back to the clinic so that a responsible program for gradual reduction of the medication was impossible. In three instances we considered the patient too old for an attempt. These patients were older than 70, and one of them had a pacemaker. The oldest patient was 82 when he had his last psychomotor (partial complex) attack with automatisms. He subsequently remained seizure-free for seven years; apparently a patient need never give up the hope of becoming seizure-free!

Before an attempt was made to reduce medication, an EEG was requested. The attempt was forgone if the EEG revealed epileptic activity. This was the case in twenty-two patients, that is some 10 percent of the patients who had been seizure-free for five years. Whether this decision was correct remains debatable.

So far, however, nine of these twenty-two patients have had a relapse, even though the medication was continued. All patients had been seizure-free at least five years counting back from 1st January 1976; that is to say that their last seizure had occurred prior to 1st January 1971. In other words: their last seizure had occurred in 1970 or earlier. This is why sodium valproate plays no role in this study.

Reduction of medication

In some 90 percent of patients who had been seizure-free five years or longer, the EEG no longer revealed epileptic activity. In these cases the medication was reduced step by step. This was done as follows; the dosage of one of the drugs was gradually halved; whereupon an EEG was registered. The dosage of the drug in question was then further reduced and finally discontinued altogether, whereupon another EEG was requested. This procedure was then repeated with a second drug. The gradual reduction of medication with three drugs (a, b en c) therefore took the

following course: EEG; a-b- $\frac{1}{2}$ c. EEG; a-b. EEG; a- $\frac{1}{2}$ b. EEG; a. EEG; $\frac{1}{2}$ a. EEG; -. EEG.

Much has in recent years been written about patient compliance. I am therefore under no illusion that the prescribed medication was always taken by everyone. Some patients took it upon themselves to reduce or discontinue their medication, e.g. by taking their drugs twice daily instead of three times a day. Sometimes they forgot to take their medication for one or a few days. If a relapse then occurred, it was counted as such. In such cases it seemed likely that the patient could not yet do without the medication. On the other hand, when a patient had himself discontinued medication without undue consequences, it was assumed that the medication could indeed be stopped.

Which drug is best reduced first? Nothing very sensible can be said about this. Generally, the administration of so-called second-choice drugs was stopped first. When gingival hyperplasia developed as a result of phenytoin medication, this drug was eliminated before carbamazepine (Tegretol) was stopped. Phenytoin was also stopped before carbamazepine was when its serum concentration was far less than 10 mg/l (in which case little therapeutic effect can be expected according to modern views).

The rate at which medication can be reduced is still uncertain. In many of our patients it took several years before medication was entirely stopped.

Inevitably, the medication must have come to have a placebo effect in some patients; drugs have had this effect always and everywhere. In patients subject to this placebo effect, reduction of medication was followed by, for example, complaints about protracted dizziness, an uncertain feeling or a sensation of light-headedness. Some of them resumed their former medication voluntarily.

In the event of a relapse the patient should resume his penultimate medication and report back to the clinic as soon as possible. This is reiterated at every follow-up in order to minimize possible damage. We have recently even

increased the dosage of the penultimate medication after a relapse has occurred. The underlying argument is: at the time when the medication has been so much reduced that a relapse may occur, this does not necessarily always happen immediately. The medication may since have been further reduced (this may be the case especially in primary generalized epilepsy with its low seizure frequency).

Results

An attempt to discontinue medication was made in 156 cases. Forty-nine patients suffered a relapse; 102 remained seizure-free for at least two years without medication. In five cases, no conclusion can (yet) be reached: in four, further reduction of medication was forgone because the EEG showed a return of primary generalized epileptic activity; in the fifth, medication was indeed discontinued but the follow-up is still less than two years.

Of the forty-nine relapses, twenty-eight occurred while medication was being reduced and twenty-one after discontinuation of medication. The relapse nearly always consisted of a tonic-clonic seizure, but sometimes this could not be confirmed by witnesses. The patient might have woken up tired in the morning and had bitten on his tongue; or he might suddenly have lost consciousness on his way to work. In a few cases brief episodes of unconsciousness returned, with or without automatisms. In three cases there was only a return of auras lasting a few seconds, and identified by the patient as precisely the same in sensations as previous auras. In only one case did absences return. In no case did status epilepticus occur.

Patients with primary generalized epilepsy should be divided into those with exclusively absences and those with (in addition) clonic-tonic attacks; the latter group showed a much higher relapse incidence than the former (*table 2*).

Nearly all patients suffering solely from absences were older than 18 years when we started to reduce the medication; they were receiving prophylactic

Table 2. Manifestations in the 57 patients with primary generalized epilepsy.

Manifestations	Recovery	Relapse	Total
Only absences	12	1	13
Absences and tonic-clonic seizures	10	10	20
Only tonic-clonic seizures	10	14	24
Total	32	25	57

Table 3. Number of seizure-free years in the 44 patients suffering from primary generalized epilepsy with tonic-clonic seizures

Number of seizure-free years	Recovery	Relapse	Total
5 - 9	6	10	16
10 - 14	9	12	21
15 - 19	5	1	6
20 - 24	–	1	1
Total	20	24	44

therapy against tonic-clonic attacks. Experience has shown that patients with absences who develop no tonic-clonic attacks before age 18, usually do not develop such attacks later. Fortunately, this also proved to be the case after discontinuation of medication: only one relapse occurred, and this was confined to absences.

The relapse incidence in patients with primary generalized epilepsy who had had tonic-clonic attacks, was found to exceed 50 percent; this applied also to patients who had been seizure-free for ten to fifteen years (table 3).

One out of three patients with partial (= focal) epilepsy had a relapse. This finding is in agreement with results reported by Juul-Jensen; and in the interview with the patient we had mentioned a risk of one in three. Medication could be discontinued in each of the eleven patients who had a life history of no more than three attacks; three of these eleven patients were suffering from primary generalized epilepsy.

Benign epilepsy of childhood (mid-temporal epilepsy, Sylvian seizures) always took a favorable course, as mentioned also in the literature. In these children, medication can be discontinued earlier: one year after the last seizure, even if the central points Rolandiques are still demonstrable in the EEG. The risk one takes is small even when the harmless attacks – with intact consciousness – recur.

Conclusion

Among the patients who had been seizure-free for five years or longer, those with primary generalized epilepsy were overrepresented. The medication in this type of epilepsy is probably more effective than that in other types; if so, then this might possibly explain the higher relapse incidence in patients with primary generalized epilepsy (more than 50 percent of those who had also had more than three tonic-clonic attacks). In view of this we now advise these patients against an attempt to discontinue medication.

No firm policy was adhered to with regard to recurrence of epileptic functional disorders in the EEG after reduction of medication. In most cases the medication of that moment was continued; in some cases the dosage was raised and in some – at the explicit request of the patient – it was further reduced, or medication was stopped altogether. In the forty-nine relapse cases, the records were studied to establish whether the EEG had previously revealed epileptic activity. This proved to have been the case in fifteen patients.

Many of the patients who developed a relapse, nevertheless received benefit from the attempt to reduce medication; in nearly all cases they received less medication after the attempt than before, and a substantial number are now on single-drug therapy.

Many data are still to be processed: age at onset of epilepsy, duration of the period with seizures, status epilepticus in the past, rate of reduction of medication, which drugs could be eliminated and which could not, which drug was the last to be reduced or stopped before a relapse occurred, the etiology of epilepsy, heredity, the patient's intelligence (oligophrenia) and previously found EEG changes. Preparations for a study of the prognostic significance of these data have meanwhile been made by the staff of the Institute for Epilepsy Control, Heemstede.

Summary. Complete recovery from epilepsy is not rare: medication can be discontinued in over 50 percent of patients after a five-year seizure-free period. Only for patients with primarily generalized epilepsy and tonic-clonic attacks is the risk high, even after ten seizure-free years. The prognosis is good for patients who had only absences and for those who have suffered no more than three seizures in the course of life.

Samenvatting. Volledig herstel bij epilepsie? Het staken van anti-epileptica na vijf of meer aanvalsvrije jaren. Volledig herstel bij epilepsie is niet zeldzaam: bij

meer dan de helft van de patiënten die vijf jaar of langer aanvalsvrij zijn, kan de medicatie gestaakt worden. Alleen bij patiënten met primair gegeneraliseerde epilepsie die tonisch-clonische aanvallen hebben gehad, is het risico hoog, zelfs als zij tien jaar aanvalsvrij zijn geweest. Voor patiënten die alleen aan absences hebben geleden, is de prognose goed, evenals voor patiënten die in hun leven niet meer dan drie aanvallen hebben gehad.

Christiansen, P. and M. Lund. Sexual potency, testicular function and excretion of sexual hormones in male epileptics. In: D. Janz (ed.). Proceedings Seventh International Symposium on Epilepsy. Thieme, Stuttgart, 1976.

Juul-Jensen, P. Frequency of recurrence after discontinuance of anticonvulsant therapy in patients with epileptic seizures. (1968) *Epilepsia (Amst.)* 9, 11-16.

Nota bene

The similarity between a scientist and an alchemist is that, when they need money, the scientist promises relevant research and the alchemist promises the philosopher's stone, the elixir of life, or a love potion. (Proposition in: A. J. M. Schoonen. Mass transport across fluid/fluid interface, release and absorption of drugs from non-polar dosage forms. *Thesis Groningen*, 1980.)

Many patients experience an alienation after admission to hospital. This is caused mainly by the marked and unnecessary changes in their daily timetable. (Proposition in: G. T. Meester. Computer analysis of cardiac catheterization data. *Thesis Rotterdam*, 1980.)

It is a misconception that children who refuse to eat, can be made to eat by starving them long enough. (Proposition in: A. P. Messer. Serious eating problems and intractable bed-wetting. [Zeer moeilijk eten en moeilijk beïnvloedbaar bedplassen.] *Thesis Leiden*, 1979.)