A. Introduction

In epilepsy research, animal models serve a variety of purposes. First, they are used in the search for new antiepileptic drugs. Second, once the anticonvulsant activity of a novel compound has been detected, animal models are used to evaluate the possible specific efficacies of the compound against different types of seizures or epilepsy. Third, animal models can be used to characterize the preclinical efficacy of novel compounds during chronic administration. Such chronic studies can serve different objectives, for instance, evaluation of whether drug efficacy changes during prolonged treatment, e.g. because of the development of tolerance, or examination of whether a drug exerts antiepileptogenic effects during prolonged administration, i.e. is a true antiepileptic drug. Fourth, animal models are employed to characterize the mechanism of action of old and new antiepileptic drugs. Fifth, certain models can be used to study mechanisms of drug resistance in epilepsy. Sixth, in view of the possibility that chronic brain dysfunction, such as epilepsy, might lead to altered sensitivity to drug adverse effects, models involving epileptic animals are useful to study whether epileptogenesis alters the adverse effect potential of a given drug. Seventh, animal models are needed for studies on the pathophysiology of epilepsies and epileptic seizures, e.g. the processes involved in epileptogenesis and ictogenesis (Lothman 1996a).

Not all animal models of seizures and/or epilepsy can be used for all of the above described purposes. Furthermore, the intention of the experiment is essential for selection of a suitable animal model. For instance, simple seizure models such as the maximal electroshock seizure (MES) test, allowing testing of high numbers of compounds for anticonvulsant activity in a relatively short time, will be preferred to more complex models in screening approaches to anticonvulsant drug development. The use of animal models in the search for new anticonvulsants is dealt with in Chapter 6 of this volume. Nevertheless, in order to review the most important animal models currently used in epilepsy research, it will be necessary to characterize their pharmacological and predictive profile in terms of clinical types of seizures or epilepsy.

Most animal models used in epilepsy research are models of epileptic seizures rather than models of epilepsy. Since epilepsy is characterized by
spontaneous recurrent seizures, a test such as the maximal electroshock seizure test, in which an acute seizure is electrically induced in a normal non-epileptic animal, cannot represent a model of epilepsy. On the other hand, there are true models of epilepsy, for instance animal mutants or transgenic animals with spontaneously recurrent seizures, which are obviously more closely related to human epilepsy than mere seizure models. Furthermore, epileptogenesis resulting in spontaneous recurrent seizures can be induced by chemical or electrical means. Unfortunately, many researchers do not differentiate between animal models of epilepsy and animal models of epileptic seizures, although the difference may be important in the interpretation of data obtained with such models. Of course, models of epilepsy, e.g. mutant animals with inherent epilepsy, can be used as models of seizures, e.g. in anticonvulsant drug potency studies, whereas a pure seizure model in a non-epileptic animal cannot be used as a model of chronic epilepsy.

An ideal animal model of epilepsy should fulfil the following requirements: (1) development of spontaneously occurring recurrent seizures; (2) seizure type(s) similar in clinical phenomenology to seizure types occurring in human epilepsies; (3) paroxysmal EEG alterations similar to EEG alterations occurring in the respective seizure types in humans; (4) a high seizure frequency to allow acute and chronic drug efficacy studies; (5) pharmacokinetics (particularly the rate of elimination) of antiepileptic drugs which allow the maintenance of effective drug levels during chronic treatment; (6) effective plasma (and brain) concentrations of antiepileptic drugs similar to those required for control of the relevant seizure types in epileptic patients. Although no model at present meets all these criteria, there are several so-called genetic animal models of epilepsy, i.e. species or strains of laboratory animals with “inborn” epilepsy, which resemble idiopathic epilepsy in humans more closely than any other experimental model (Löscher 1984, 1992). However, out of practical reasons, the most commonly used animal models in anticonvulsant drug development are not models of chronic epilepsy but models of single epileptic seizures, in which seizures are induced in small laboratory animals (rats, mice) by simple chemical or electrical means.

Innumerable models of epilepsy and epileptic seizures have been described in the literature, so that it is not possible to review all these models in this chapter. In this respect, the interested reader is referred to previous reviews or volumes on this topic (Purpura et al. 1972; Koella 1985; Löscher and Schmidt 1988; Fisher 1989; Engel 1992). The various animal models can be assigned to different categories, e.g. models with spontaneously occurring seizures versus chemically or electrically induced seizures, models with recurrent seizures versus models with single seizures (i.e. chronic versus acute models), models with partial seizures versus models with generalized seizures, models with convulsive seizures versus models with non-convulsive seizures, screening models versus models for a more advanced phase of the screening procedure (“secondary screening”), mechanism-related models (i.e. with