Editors' view

How it works

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Today's clinicians can turn to a number of resources to learn more about the drugs they prescribe. They are encouraged to use treatment guidelines or formularies to select drug therapy. If no algorithm exists, they are expected to use evidence-based medical practices to determine the most appropriate treatment. A search of the available literature about a new drug entity will result in numerous articles about the drug's effectiveness and its place of therapy, the likelihood of adverse effects compared to standard of care, or perhaps the pharmacokinetic profiles in genetically diverse populations. Even the *Journal* is heavily populated with pharmacoepidemiological data. So where is information that will satisfy our need to understand pharmacological mechanisms of drug action?

Perhaps society has progressed so far that this understanding is deemed irrelevant in today's results-oriented society. However, one could argue that a patient's hope that he or she will achieve the expected drug effects is the same now as when a patient in ancient Egypt approached his or her local alchemist centuries ago. Sadly it appears that those that purport to study medicine are no different. Scientists cling to statistics hoping they can elucidate that which is true. To illustrate the timelessness of this argument, the curators at the Boerhaave Museum in Leiden, the Netherlands recently uncovered a report of the educational process by two different professors at Cecilia Hospital in Leiden in 1637. Professor Screvelius communicated 'to his students the prescriptions for agreeable and powerful medicine, tested by years of experience, after he had examined the patients and established a convalescence plan' [1]. In contrast, after he presented a case, Professor Heurnius initially attempted to have the students determine appropriate therapy. Yet, this method of teaching had to be abandoned as most of the students did not like this way of teaching. They preferred when he 'gave his diagnosis and ideas for treatment, without first questioning his students' [2].

But the fact is, we as clinical pharmacologists have been fascinated with how a drug works for several centuries. Paracelsus has been credited for introducing science into

the former realm of alchemic mysticism. He worked to combine chemistry with medicine, ultimately deducing that that everything was a poison, it just depended on the dose that was given. But it was Felix Fontana's meticulous descriptions of how viper venom affects muscle tissue that presented the concept that most closely resembles the pharmacological mechanism of action. He believed that it was possible to know how an active component of a product worked on a specific part of the body to elicit an effect. Francois Magendie and Claude Bernard then subsequently established modern pharmacology by systematically demonstrating that drugs had a particular mechanism by repeatedly exhibiting the effects on a specific part of the body.

The current issue introduces *Journal* readers to a new series which will draw attention to recently licensed medicines with entirely new mechanisms of action.

The purpose is to update readers on new pharmacological discoveries. With a focus on *how* the drug works in contrast to how *well* the drug works. The series concentrates on the proposed mechanisms of action in contrast to the epidemiological evidence of its usefulness. Thus, publication does not imply endorsement of use in clinical practice but acknowledgment of the discovery of a unique pharmacological entity.

The drugs to be highlighted will be new drugs (approved within the last year), that have new mechanisms. The so-called 'me-too' drugs will not be considered. Table 1 lists a handful of drugs recently approved by either the Food and Drug Administration (FDA) or European Medicines Agency (EMEA). Examples of drugs deemed appropriate or otherwise for the new drug mechanism series are tabulated below. Detailed discussions of the therapeutic value of these new agents will not be included. The focus of the series will be to illustrate how the mechanism of a product can influence biological processes.

In this series we have chosen to combine drawing with textual information to describe the mechanisms of the new agents. The *Journal* has adopted the format of the Teaching Resource Centre (TRC) Pharmacology Program which is used to teach medical and biomedical sciences

Figure 1A

Icon language of various commonly used receptors

Figure 1B

TRC Pharmacology illustration of ziconotide

Drug name	Appropriate for review?	reason
abatacept	Yes	Inhibitor of APC mediated T-cell activation
clevipidine	No	Non-novel mechanism: Calcium channel blocker
eculizumab	Yes	Complement C5 antibody
etravirine	No	Non-novel mechanism: non-nucleoside reverse transcriptase inhibitor
iacosamide	No	Non-novel mechanism: Sodium channel blocker
raltegravir	Yes	Inhibitor of the catalytic activity of the integrase enzyme
sugammadex	Yes	New approach to removal of drug from the body even though no new pharmacological mechanism related to human physiology

students at the University of Leiden. The TRC has been illustrating pharmacological mechanisms of action in the context of physiological process since 2000 [3]. The TRC program is a database of over 600 graphics and text explanations of pharmacological and physiological mechanisms. The aim is to enhance the reader's understanding of the mechanisms beyond that of being able to simply recognize the 'breed' of drug (e.g. that propranolol is a beta-blocker).

Each drawing makes use of the TRC icon language. These icons are simple graphics of pharmacological characteristics that are standardized throughout the program.

Figure 1A shows some of the icons used in the system and Figure 1B is an example of a mechanism.

Although the copyright for these images remains with the University of Leiden, the images can be freely used. The TRC Pharmacology program can be accessed via a search of 'TRC' the Dutch medical education portal www.medicaleducation.nl. Use of the site is free after providing registration information. Besides offering deeper understanding of newly approved drugs, the *Journal* believes these images can be useful in providing unbiased information that can easily be incorporated into presentations and education about the fascinating and diverse ways medicines work.

REFERENCES

- 1 Kyperus quoted by G.C.B. Surgingar in 'Stichting der school voor klinische onderwijs te Leiden', in *Nederlands Tijdschrift voor Geneeskunde*, 1862, no. 6, pp. 518–519: [. . .] na het onderzoek der lijder en de vaststelling van het geneesplan, de voorschriften van aangename, krachtige en door langdurige ervaring beproefde geneesmiddelen aan zijne leerlingen mede te delen.
- 2 Lindeboom GA. 'Medical Education in the Netherlands 1575–1750' in O'Malley CD a.o., *History of Medical Education*, p. 205.
- 3 Benjamins E, van Gerven JMA, Cohen AF. Uniform visual approach to disseminate clinical pharmacology basics in medical school. *IUPHAR Pharmacol Int* 2000; 55: 6–7.