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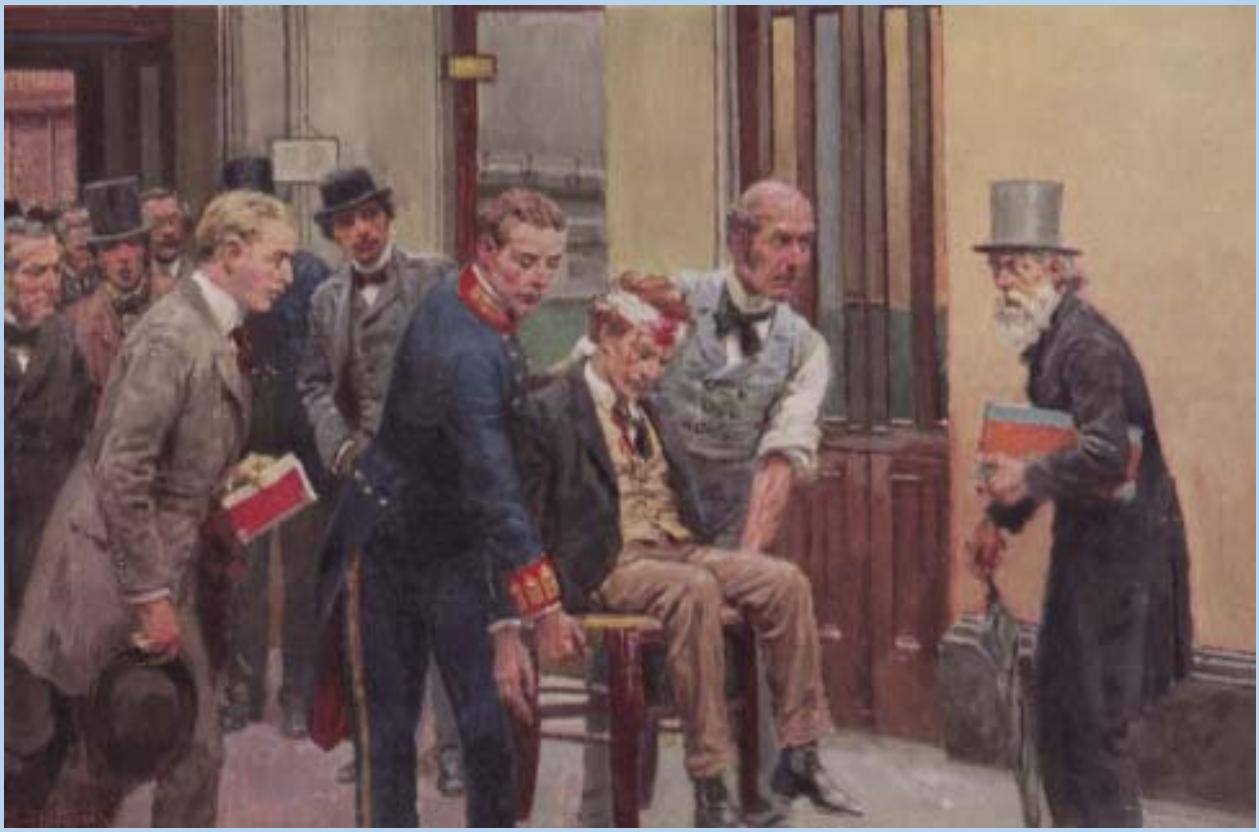

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Telephones + 94 11 2320356-9
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Cover picture

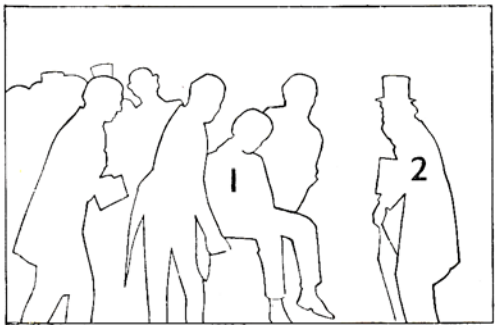
Algernon Charles Swinburne (1837-1909)

As that eminent poet and critic, and for a long time assistant in the Department of Printed Books at the British Museum, Sir Edmund Gosse, approached the Reading Room one day, he was met by two attendants silently carrying out in a chair an inert and corpse-like figure, its eyes closed, its arms dangling loosely, and its face stained with drops of blood. As he stood aside to allow them passage, he had no difficulty in recognizing the massive head and flaming-red mane which contrasted so violently with the deathly-white countenance and the puny limbs; for photographs of Algernon Charles Swinburne, extravagant songster of youth who shocked the mid-Victorians, were to be seen then in almost every shop-window. While working in the Reading Room, Swinburne had fallen in an epileptiform fit and had cut his forehead on the iron staple of his desk. Gosse was relieved to hear a few days later that he had quite recovered.

That Swinburne suffered from true epilepsy is a matter of some doubt. There was no hereditary tendency to the disease in either his father's or his mother's family. Epilepsy generally begins in childhood or early adolescence, while Swinburne was twenty-six when he had his first fit. In his case there was no progressive degeneration of the mental faculties, nor was there any mention of the suffused face or the foaming lips which are the characteristic features of an epileptic seizure. But given the poet's weakness for alcohol-since his undergraduate days at Balliol he had been seemingly intent on drinking himself into an early grave it is more probable that Swinburne's epileptiform fits were brought on by chronic alcoholic toxaemia. Such fits, when they begin in adult life, are almost indistinguishable from true epilepsy.

Swinburne's seizures were usually precipitated by excitement or emotion, and naturally they were a source of embarrassment and anxiety to his acquaintances. Once he threw a fit in Whistler's studio in Paris; another time he collapsed at Lord Houghton's breakfast table, and on several occasions his father, Admiral Swinburne, was hastily summoned to find him in what appeared to be final collapse. But, as exuberant and extravagant as his poetry, the patient always seems to have recovered rapidly and to have been, if anything, better physically and more mentally alert for his experience.

*Key to Illustration



1. Algernon Charles Swinburne
2. Sir Edmund Gosse

Antidepressants: how they act and how to select

Antidepressants are some of the commonly prescribed medications worldwide. Data from National Health Service (NHS) Digital UK indicate that 70.9 million prescriptions for antidepressants were issued in 2018, compared to 36 million in 2008 [1]. The efficacy, acceptability, convenience of administration and affordability of antidepressants makes them one of the main treatment options in depression.

The first antidepressants; iproniazid and imipramine were introduced in the early 1950s. Iproniazid a monoamine oxidase inhibitor (then used in the treatment of tuberculosis) and imipramine a tricyclic antidepressant both made two essential contributions to the development of psychiatry. First, they changed the psychiatric care of depressed patients and allowed patients to be offered medication instead of non-evidence based stigmatizing physical treatments. Secondly these agents have paved the way for imperative research on psychopharmacology, culminating in the introduction of the aetiopathogenic hypothesis, which continues to be the putative theory of depression today [2]. Since the early medications, over 20 different antidepressants belonging to different classes have been introduced into clinical practice. Majority of them alter neurotransmission in the serotonin, norepinephrine and dopamine pathways in the brain.

Mechanism of action

The different classes of antidepressants work in slightly different ways. Majority of the antidepressants act by increasing serotonin (5-hydroxytryptamine; 5-HT) or norepinephrine (NE) or both at the synapse. Selective Serotonin Reuptake Inhibitors (SSRIs) act by increasing 5-HT availability at the synaptic cleft by inhibiting 5-HT reuptake by the presynaptic cleft. Serotonin Norepinephrine Reuptake Inhibitors (SNRIs) block both 5-HT and NE reuptake thereby increasing their levels at the synapse. Atypical antidepressants such as bupropion act by inhibiting the reuptake of both NE and Dopamine (DA) at the presynaptic cleft. Agomelatine acts by potentiating melatonin receptors while blocking serotonergic receptors (5HT2C) and promoting DA and NE availability. Tricyclic antidepressants (TCAs) are thought to act by inhibiting the reuptake of 5-HT and NE [3].

Selecting an antidepressant

The management of depression follows a bio psycho social model. The clinical history and mental state examination will dictate which arm or arms in the model will take more prominence in the management. While some patients with mild depression may benefit from psycho social interventions alone there are specific circumstances where antidepressant medications should be offered, and that can be life saving. Antidepressants are considered first line treatment for moderate and severe depression in adults irrespective of environmental factors and symptom profile. It is also first line in depression of any severity that has persisted for 2 years or more [4]. Special considerations are made when antidepressants are offered to specific groups such as the pregnant or breastfeeding mothers, children and adolescents, those with neurocognitive disorders and patients with medical comorbidities. Prescribing to these special groups is done by a careful analysis of the benefit risk ratio. Antidepressants are also indicated for patients who have responded well to drug treatment during previous episodes of depression and also when psychological therapies are inaccessible or unaffordable to patients.

The choice of antidepressant for a particular patient is based on many factors (Box 1). The evidence states that the efficacy profile of different antidepressants vary only slightly within a drug class and there may be a small change between classes [5]. Theoretically, antidepressants that target multiple neurotransmitter systems (SNRIs, TCAs) are more efficacious than an antidepressant that targets one system; concurrently the adverse effect profile also tends to be more troublesome when multiple neurotransmitter systems are involved. In practice, a medication with high tolerability and good efficacy should be used in mild to moderate depressive disorder as the first option. Ease of switching should be considered as there is a high possibility that the first antidepressant may not lead to full remission [5]. In most guidelines (National Institute of Clinical Excellence 2020, British Association of Psychopharmacologists 2015, Maudsley prescribing guidelines 2020) SSRIs are considered first line for this reason. In contrast, for patients with a complicated depressive episode the main consideration should be efficacy over tolerability. TCAs and SNRIs are recommended for severe depressive episodes. Adverse effects are one of the commonest reasons for medication non compliance in psychiatry. Knowledge about these effects and communicating them to patients have been shown to improve adherence. The commonest reported adverse effects of antidepressants are related to the gastrointestinal tract. A meta-analysis in 2021 indicated escitalopram and

sertraline as the least tolerated antidepressants among 15 antidepressants studied with, nausea, vomiting, diarrhea, abdominal pain, dyspepsia and anorexia being the commonest reported GI effects. Mirtazapine, a noradrenergic and specific serotonergic antidepressant (NaSSAs) was shown to be the best tolerated being only associated with increased appetite [6]. Of the commonly prescribed antidepressants TCAs and NaSSAs are implicated in pronounced weight gain; central nervous system adverse effects such as sedation and agitation are commonly seen with TCAs, NaSSAs and MAOIs; sexual adverse effects such as erectile problems, ejaculatory problems and changes in libido have shown to be prominent with SSRIs, SNRIs, and TCAs [5]. Antidepressants with the lowest rate of sexual adverse effects are considered to be bupropion, mirtazapine, viladozone (serotonin partial agonist and reuptake inhibitor), vortioxetine (a multimodal agent enhancing serotonin activity) and agomelatine.

Box 1: Factors to consider when selecting an antidepressant

Efficacy vs tolerability

Subtype of depression

Safety in overdose

Co-morbid medical illnesses and drug interactions

Patient and clinician preference

Matching an antidepressant to the sub type of depression warrants careful consideration. Patients with co-morbid anxiety are known to benefit from SSRIs and moclobemide. The favored antidepressant in severe depression with prominent psychomotor retardation are TCAs, SNRIs, vortioxetine and MAOIs. Preferred antidepressants in depression with prominent anhedonia and demotivation are SSRIs, SNRIs, agomelatine and reboxetine. Duloxetine (an SNRI) or TCAs are considered a good choice for patients with co-morbid chronic pain syndromes. In fact these medications are approved for the treatment of chronic neuropathic pain, independent of depression [5]. Vortioxetine has shown promising results in the treatment of cognitive deficits in major depressive disorder [7].

The safety profile of an antidepressant becomes important when a risk of overdose is anticipated. TCAs can be fatal in overdose due to their narrow therapeutic window. This property of TCAs becomes a limitation factor when prescribing to patients with severe depression and high suicide intent.

Drug interactions are also common with antidepressants as most drugs commonly inhibit and some potentiate the cytochrome system. Increased risk of serotonin toxicity is seen when SSRIs are combined with St. John's wort (a herbal remedy used to treat depression), Monoamine Oxidase Inhibitors (MAOIs) and tramadol. SSRIs are also implicated in platelet dysfunction leading to abnormal bleeding in patients on antiplatelet medication. Clinically significant bradycardia has been reported when co-administering SSRIs with metoprolol or propranolol [7].

Medication non-compliance is a major challenge in treating patients with depression. Adherence is shown to improve when patients are involved in the decision making process on which treatment to take [5]. An open discussion on the expected benefits and adverse effects will not only keep the patient better informed but will also allow to dispel myths regarding antidepressants.

Recent advances in therapy

After a hiatus in antidepressant drug development the FDA approved ketamine, under the name esketamine for treatment-resistant depression in 2019. This led to a lot of excitement as ketamine targeted novel receptors in depression. Ketamine is a non-competitive antagonist at NMDA receptors. However, ketamine's mechanism of action is more complex than NMDA antagonism. The antidepressant action of ketamine involves a cascade of events culminating in the augmentation of synaptic plasticity and synaptic strength. Part of the excitement with esketamine is its ability to improve depressive symptoms fast and its capacity to alleviate suicidal ideation [9]. There are several antidepressant medications being developed based on ketamine's mechanism of action and also medications acting on glutamatergic targets.

Conclusion

Antidepressants are first line treatment options in several types of depression. A timely prescription of an antidepressant can be life saving. Choosing the "best fit" antidepressant is based on a balance between efficacy and tolerability, symptomatology of the depressive episode, safety in overdose, medical co-morbidities, drug interactions and patient preference. Antidepressants target different receptors in the brain to exert its therapeutic effect. New antidepressants target novel receptors enabling a faster onset of action and alleviating suicidal ideation.

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Dr. Suhashini Ratnatunga, MBBS, MD, *Senior Lecturer in Psychiatry and Consultant Psychiatrist, Department of Psychiatry, Faculty of Medicine, Colombo, Sri Lanka.*
E-mail: suhashini_sri@yahoo.com

Self-assessment questions on antidepressants

1. A 35- year old female complains of depressive symptoms for two weeks with functional impairment. She has had a similar episode four years ago and was prescribed fluoxetine for which she had responded well. Fluoxetine was discontinued after completing a course of six months. What is the most appropriate management for this patient?

A. Prescribe venlafaxine
B. Refer for electro-convulsive therapy
C. Restart fluoxetine
D. Reassure the patient with no active intervention
E. Prescribe a mood stabilizer

2. A 20-year old male presents following an overdose of thirty paracetamol tablets. He is now medically stable. What should be the next step in his management?

A. Admit to an inward psychiatry unit
B. Refer to a psychiatrist
C. Discharge the patient
D. Start an antidepressant
E. Perform a risk assessment

3. What is the most appropriate antidepressant for an expectant mother in her second trimester who is depressed with no psychotic symptoms?

A. Venlafaxine
B. Sertraline
C. Paroxetine
D. Imipramine
E. Mirtazapine

(Answers on page 10)

A practical approach to prescribing in adult epilepsy

Key Messages

- Choice of antiepileptic drugs (AED) in treating epilepsy is not a simple one and needs to be individualized. Patient characteristics, seizure characteristics and medication factors influence prescribing AEDs.
- Diagnosing the seizure type or epilepsy syndrome is imperative as certain AEDs are contra-indicated in certain seizure types and epilepsy syndromes.
- Co-morbidities of patients need to be considered when prescribing AEDs for patients to increase tolerability, efficacy and prevent polypharmacy.
- Prescribing AEDs for special groups such as women and the elderly needs consideration as they have unique requirements.

Preamble

Epilepsy is one of the most common neurological diseases in the world affecting 1% of the adult population. Over the last 30 years, there has been an increase in the number of antiepileptic drugs (AEDs) available for treating patients with seizures. It can be a daunting task to choose an appropriate AED for a patient with epilepsy, especially when many options are available. In this article, the current drug therapy of epilepsy in adults is briefly reviewed through some examples of case histories.

Initiating AEDs: therapeutic considerations

An appropriate AED is that, which is the most likely of all others to be truly prophylactic as monotherapy for seizures without causing undue adverse effects interfering with the everyday performance and physical and mental wellbeing of the treated individual. Hence balancing between therapeutic and toxic effects of an AED is the main objective of epilepsy management. The patient's seizure type, medical history, possible co-medication for other diseases and circumstances of the individual patient are necessary to individualize AED treatment. Some AEDs may be very effective in some epileptic seizures and syndromes, but contra-indicated in others. Certain AEDs maybe very effective in controlling seizures, but may be unsuitable for particular groups of patients because of adverse effects. Some AEDs may be effective in some but not all multiple types of seizures that a patient may have. Therefore, patient characteristics, seizure characteristics and medication factors influence selection of AEDs.

New onset seizure in adults

Case history: A 21-year-old woman presents after experiencing a convulsive seizure first-time. A friend observed the patient suddenly falling at home and convulsing for 45 seconds. Afterwards, the patient was lethargic for 15 minutes but recovered completely without residual neurologic deficit. She bit her tongue during the seizure and was incontinent of urine. What is the appropriate next step in management?

Answer: It is important to assess the risk of seizure recurrence in this patient who has experienced a new onset unprovoked seizure (information box 1). Thus, if the risk of recurrence is perceived to be high, a diagnosis of epilepsy can be made even after a single seizure according to the operational definition (condition 2) outlined in information box 1 and long term AEDs initiated. Clinical variables associated with increased risk of seizure recurrence include: a prior brain insult, an EEG with epileptiform abnormalities, a significant brain-imaging abnormality, and a nocturnal seizure [3]. Based on these it would be best to perform brain imaging and an EEG to assess the risk of recurrence. Based on the evaluation, if seizure recurrence risk is high AEDs are started.The recommended AEDs for generalized seizures are broad spectrum AEDs and for focal onset seizures narrow spectrum AEDs (Table 1). When the seizure is of unknown onset it would be prudent to initiate a broad spectrum AED.

Information Box – 1

Definitions

The following are definitions required when considering AEDs for patients.

What is a seizure?

An epileptic seizure is a transient occurrence of signs and/or symptoms due to abnormal excessive and synchronous neuronal activity in the brain [1]. These signs take the form of motor, sensory, autonomic manifestations occurring in isolation or in combination. The clinical characteristics of a seizure are the result of the area of the brain that is abnormally stimulated.

What is epilepsy?

Epilepsy is a disease characterized by an enduring predisposition to generate epileptic seizures [2]. It is a disease of the brain which is defined by fulfilment of any one of the following 3 conditions:

1. At least 2 unprovoked seizures occurring > 24 hours apart.
2. One unprovoked seizure and a probability of further seizures similar to the general recurrence risk after 2 unprovoked seizures, (≥ 60%) occurring over the next 10 years (Eg:- If a seizure occurs beyond 1 week from the onset of a stroke, the said person runs the risk of > 60% of having a recurrent seizure over the next 10 years, thus the person would be diagnosed to have epilepsy after a single seizure).
3. Diagnosis of an epilepsy syndrome. An epilepsy syndrome is defined by a group of features usually occurring together. Patients of each epilepsy syndrome can share the same clinical features, seizure type(s), age of onset, family history, EEG findings, effective treatment and prognosis. Examples of such epilepsy syndromes in adolescents and adults are: juvenile absence epilepsy (JAE), juvenile myoclonic epilepsy (JME), epilepsy with generalized tonic-clonic seizures alone and progressive myoclonic epilepsies.

Acute symptomatic (provoked) seizure

A seizure that occurs during the time of a systemic insult or in close temporal association with a documented brain insult (Eg:- seizures within 1 week of stroke, traumatic brain injury, anoxic encephalopathy, intracranial surgery or seizures within 24 hours of a severe metabolic derangement, drug or alcohol intoxication and or withdrawal or exposure to epileptogenic drugs).

Remote symptomatic (unprovoked) seizure

Unprovoked seizures occur in the absence of a potentially responsible clinical condition as mentioned above or beyond the interval estimated for the occurrence of acute symptomatic seizures.

Generalized seizures

Generalized epileptic seizures are conceptualized as originating at some point within, and rapidly engaging, bilaterally distributed networks within the brain (Eg:- tonic-clonic (GTC), clonic, tonic, myoclonic, atonic, absence seizures). Individual seizures may have an apparently localised onset but location and lateralisation are not consistent from one seizure to another.

Focal seizures

Focal epileptic seizures are conceptualized as originating within networks limited to one hemisphere. There may be more than one epileptogenic network and more than one seizure type in an individual but each has a consistent site of onset within the brain.

Table 1.

Narrow spectrum AEDs	Broad spectrum AEDs
Carbamazepine	Valproate
Oxcarbazepine	Topiramate
Phenytoin	Lamotrigine
Lacosamide	Levetiracetam
*Phenobarbitone	***Clobazam
**Pregabalin	
**Gabapentin	

* Not considered first line due to adverse effect profile

** Not considered first line therapy due to reduced efficacy compared to other AEDs

*** No data to support use as first line therapy

Importance of syndromic diagnosis

Case history: A thinly built 14-year old boy comes with his first generalized tonic-clinic (GTC) seizure. On further inquiry he complains of "lightening jerks" especially in the morning and he often drops things as a result of this. His EEG demonstrated generalized poly-spike and wave discharges which had a fronto-central emphasis and a frequency between 4 and 6 Hz. What AED would one choose for this patient?

Answer: Myoclonic jerks without loss of consciousness occurring on or after awakening and associated with typical generalized epileptiform EEG abnormalities, with an age of onset between 10 and 25 are typical for a diagnosis of Juvenile myoclonic epilepsy (JME) and fulfills the 3rd operation definition in diagnosis of an epilepsy syndrome (information box 1). For this syndrome the recommended AEDs include: lamotrigine, topiramate, valproate and levetiracetam. Valproate is unquestionably the most efficacious and drug of first choice in men, thus recommended in this patient. AEDs best avoided include: vigabatrin, gabapentin, pregabalin, phenytoin, oxcarbazepine, and carbamazepine, as these worsen seizure control, especially myoclonic and absence seizures.

Epilepsy in women

Case history: A 17-year old female student attends a general practice with generalized seizures. She has a diagnosis of JME. Her seizure frequency is highest around the days of menstruation. What AED would one choose?

Answer: About half of women with epilepsy are in the reproductive age group (15-49 years). The possibility of pregnancy should be considered in any woman of childbearing age with epilepsy, as the treatment of epilepsy is often long term. Valproate is not recommended for women of childbearing age with focal epilepsies and best avoided in generalized epilepsies due to its teratogenic effect (highest of all AEDs). For generalised epilepsy, lamotrigine and levetiracetam are preferred as pregnancy registry data suggest that these have the lowest teratogenicity [4]. While lamotrigine is effective in controlling GTC and absence seizures, there are few reports of exacerbation of myoclonic seizures which may be a caveat. Often the patient is counselled to look for worsening of myoclonic seizures before initiation. Thus, lamotrigine and or levetiracetam seem reasonable choices for the above patient.

This patient may have catamenial epilepsy which is when the periodicity of the exacerbation of seizures is associated with the menstrual cycle. This is due to progesterone deprivation and/or a relative increase in oestradiol/ progesterone ratio in serum. There are 3 recognized seizure patterns; perimenstrual (day -3 to +3), periovulatory (day 10 to 13) and during the entire luteal phase in anovulatory cycles (day 10 to 30) [4]. Quick acting clobazam is widely used during exacerbations. Progesterone only tablets as

an adjuvant treatment along with AEDs, seems to be effective as well.

Importance of considering co-morbidities

Case history: The above patient with JME is now 18 years and has a body mass index (BMI) of 29 kg/m². She has severe migraine as a result of stress of appearing for the advanced level examination and is clinically depressed. What treatment option would one choose?

Answer: Several co-morbidities need to be considered in this case which include migraine, high BMI and depression. AEDs associated with weight gain are gabapentin, pregabalin, valproate, vigabatrin and possibly, carbamazepine. Topiramate is associated with weight loss. Weight neutral AEDs are lamotrigine, levetiracetam and phenytoin. It would be useful if an AED which either causes weight loss or is weight neutral is prescribed in the above case.

AEDs such as barbiturates, levetiracetam, vigabatrin and topiramate have shown associations with occurrence and worsening of depression and thus would be counter intuitive to prescribe in the above patient. Alternatively, AEDs such as lamotrigine, carbamazepine, and valproate have evidence supporting their role as long-term mood stabilizers. One of the main advantages of lamotrigine is that it causes less cognitive impairment or overt sedation compared with other AEDs. Lamotrigine is reported to increase the subjective sense of well-being, and reported to be a positive psychotropic medication. Lamotrigine appears to inhibit uptake of serotonin, dopamine, and noradrenaline explaining its efficacy in the maintenance phase of treatment for bipolar disorder. It has been shown to significantly increase the time between major mood episodes.

Topiramate and valproate have demonstrated efficacy in migraine prophylaxis. Thus considering the fact that lamotrigine is weight neutral and has a positive effect on depression, it may be the best choice in the above patient though it is not recommended in the prevention of migraine in general. Some reports however, suggests a role in treating specifically migraine with aura. Topiramate due to its negative effect on depression and valproate due to its teratogenic effect seem less favourable options.

Drug-drug interactions and contraception

Case history: Now the patient described previously is 22 years. She is not planning to conceive in the near future. Her JME diagnosed 5 years earlier is controlled on lamotrigine. She is asking for contraceptive advice. What options are available for her?

Answer: The potential for drug interactions is extremely important in choosing an AED. Older AEDs such as phenytoin, phenobarbitone, and carbamazepine are enzyme-inducers, and valproate is an enzyme inhibitor. These increase the likelihood of interactions with other medications. Newer AEDs with few or no interactions, such as lamotrigine and levetiracetam, may be more suitable especially when co-administering multiple drugs. Thus alternative forms of contraception or higher doses have to be considered in patients using hormonal contraception and enzyme-inducing AEDs to prevent contraceptive failure. However, medroxyprogesterone acetate depot injection is a hormonal contraceptive option unaffected by enzyme-inducing AEDs and is an option for women on enzyme-inducing AEDs. Therefore, the following: medroxyprogesterone acetate depot injection, intrauterine devices or barrier method are contraceptive options for patients on enzyme inducing AEDs.

Other medication may interact with AEDs affecting their efficacy. The combined oral contraceptive pill may reduce the blood concentration of lamotrigine by 40%-60%, which can result in poor seizure control and needs consideration especially when introducing the pill to a patient whose seizure control is good. Thus medroxyprogesterone acetate depot injection, intrauterine devices and barrier method are contraceptive options for this patient.

Prescribing in elderly

Case history: A 68-year old male patient comes with spells that are described as episodes in which he goes blank and has repetitive grasping movements of the left hand. He is confused for 2 hours following these episodes. He has been diagnosed with Alzheimer's disease and is on rivastigmine and is also on warfarin for atrial fibrillation. What is the choice of AED?

Answer: Cognitive impairment is common in elderly patients, hence AEDs with cognitive adverse effects (ie:- topiramate) are not optimal choices [5]. Valproate may be associated with a higher risk of cognitive problems and parkinsonism in the elderly. Osteoporosis is a co-morbidity in the elderly and enzyme-inducing AEDs, as well as valproate have been shown to increase the rate of bone loss, leading to increased risk of fractures and other bone injuries. As of yet there is little evidence linking newer

AEDs to impaired bone health. Reduction in serum albumin levels seen in the elderly leads to reduction in protein binding and increase in free fraction of AEDs that are highly protein bound such as phenytoin, carbamazepine, and valproate. Most AEDs are metabolized by the liver, particularly by the cytochrome P450 enzyme complex. The functional capacity of this system progressively decreases after age 40. Thus the elderly have a narrower therapeutic window and lower maximal tolerated concentration. Considering these factors and to minimize the risk of adverse effects, one needs to "start low and go slow" when prescribing. Due to the said factors and the minimal risk of drug-drug interactions, newer AEDs such lamotrigine and levetiracetam seem optimal choices for the above patient.

Conclusion

Choice of AED in treating epilepsy needs careful consideration. AEDs can adversely affect quality of life of the patient which is often under recognized due to emphasis on seizure control.

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Dr. I K Gooneratne, MBBS, MD, *MRCP (UK), Consultant Neurologist, District General Hospital, Hambantota, Sri Lanka.*
E-mail: kishig@gmail.com

Self-assessment questions on antiepileptic medication

1. **A 88-year-old man is referred for evaluation of recurrent seizures. Five months ago, he began to experience recurrent attacks of altered awareness. He had stereotyped mouthing movements with a blank expression, and was unresponsive for several minutes at times extending for half an hour. He was started on levetiracetam 500mg bd without response or adverse effects. He was diagnosed to have prostate carcinoma, managed conservatively. He was on insulin therapy for diabetes without recent dose modification. His serum creatinine was 2.3 mg/dl and this was 1.3 mg/dl a few months back. Brain imaging was normal. What is your next step in the management?**

   A. Increase dose of levetiracetam as this dose is a moderate one.

   B. Switch to another AED such as lamotrigine

   C. A diagnostic video EEG to better characterize events

   D. Check serum ionized calcium

   E. Check blood sugar during an event

2. **A 67 year old male comes to the ward with a right motor seizure involving the right arm which progresses to a tonic-clonic seizure. He has had a history of stroke involving the left middle cerebral artery territory several months ago. He has diabetes and hypertension. His initial metabolic screen is negative. Which of the following is the best course of action?**

   A. Do nothing as this patient does not fulfill the criteria to diagnose epilepsy.

   B. Perform a MRI brain and EEG to assess the risk of recurrence.

   C. Start the patient on an AED as this patient fulfills the diagnosis of epilepsy.

   D. Refer to a cardiologist to look for an arrhythmia as this patient's seizures are more likely to be anoxic seizures.

   E. Reassure the patient as seizure most like represents a provoked seizure and thus does not require AEDs.

3. **Which of the following statements regarding epilepsy in women is/are correct**

   A. Levetiracetam as an antiepileptic drug, is a good choice for women with childbearing potential.

   B. Women with epilepsy who are on lamotrigine are likely to experience a decrease in seizure frequency when using combined oestrogen plus progesterone hormone replacement therapy.

   C. There is a long-term risk to the cognitive and behavioural development of a child exposed in utero to sodium valproate.

   D. Catamenial epilepsy can be due to a relative increase in oestradiol/progesterone ratio in the blood.

   E. Lamotrigine dosage may have to be increased in pregnancy as maternal plasma concentrations can markedly decline as pregnancy progresses, affecting seizure control.

(Answers on page 11)

Answers for self-assessment questions on antidepressants

Question 1: Answer C

This is a recurrent depressive disorder. If there is a functional impairment associated with the depressive episode it is prudent to start medication early. The most appropriate medication choice is the medication the patient has responded to previously. Often a higher dose than the initial dose as well as a longer duration of treatment is required for a relapse.

Question 2: Answer E

Every deliberate self harm attempt warrants a careful risk assessment. This is possible at a primary care level. If the risk is thought to be moderate to high then referral to a specialist psychiatry unit is recommended. Antidepressants are prescribed when there is an underlying depressive/anxiety disorder.

Question 3: Answer B

Sertraline is considered relatively safe in pregnancy. Imipramine can also be prescribed for more severe forms of depression in pregnancy. However, prescribing psychotropic medication in pregnancy is done after a careful risk:benefit analysis.

Answers for self-assessment questions on antiepileptic medication

Question 1: Answer E

It is important to consider the possibility of provoked seizures, as the treatment of such seizures is focused on the aetiology and does not require long-term AED therapy. In this case vignette the risk of hypoglycaemia increases since there has been a decrease in eGFR without a concurrent dose reduction of insulin (insulin is metabolized by the kidneys). Thus it is imperative to exclude provoked seizures occurring due to hypoglycaemia in this particular case!

Question 2: Answer C

If a single unprovoked seizure has a recurrence risk of at least 60% over the next 10 years a diagnosis of epilepsy can be made. The risk of recurrence of a seizure occurring after 1 week from the onset of the stroke is approximately 70% over the next 10 years and thus fulfills the diagnosis of epilepsy. Hence the best possible answer is to start an AED in the above patient as he has a diagnosis of epilepsy. It is important to note that if a seizure occurs within 1 week of stroke then it is considered a provoked seizure according to the guidelines provided by the International League Against Epilepsy (ILAE). These patients do not require long-term AEDS.

Question 3: TFTTT

AED teratogenicity should be considered during drug selection for all women of childbearing potential, as many pregnancies are not planned, and most women with epilepsy cannot stop AED treatment due to the danger that seizures present to both mother and foetus. Lamotrigine and levetiracetam are preferred AEDs in women in the childbearing age group due to its low incidence of teratogenicity. Overall, the highest malformation rates are seen for valproate. Furthermore, large prospective cohorts indicate that there is a longer term risk to the cognitive and behavioural development of the child exposed in utero to sodium valproate. One needs to review lamotrigine dosage as combined oral contraceptive pill may reduce the blood concentration of lamotrigine potentially leading to breakthrough seizures. Lamotrigine plasma concentrations can decline during gestation to as much as 30% or less of prepregnancy values. Oestradiol has long been known to decrease seizure threshold, and make women more vulnerable to seizure. This is the basis of catamenial epilepsy.

Current information about drug registration

Generic name	Brand name	Dosage form	Manufacturer	Importer	Therapeutic class / use(s)
Afatinib	Xovoltib	Tablet, 40 mg, 30 mg, 20 mg	Boehringer Ingelheim, Germany	Hemas	Protein kinase inhibitor
Diosmin + Hesperidin	Daflon	Tablet, 450 mg + 50 mg	Servier, France	Hemas	Venous circulation disorders
Eplerenone	Epnone	Tablet, 25 mg, 50 mg	MSN, India	Axia	Aldosterone antagonist
Lenvatinib	Lenvanix	Tablet, 10 mg, 4 mg	Beacon, Bangladesh	Emerchemie	Protein kinase inhibitor
Lenvatinib	Lenvima	Tablet, 10 mg, 4 mg	Eisai, Japan	Baurs	Protein kinase inhibitor
Lenvatinib	Levat	Tablet, 10 mg, 4 mg	Julphar, Bangladesh	Tabrane Healthcare	Protein kinase inhibitor
Thalidomide	Thalijo	Tablet, 100 mg, 50 mg	Jodas, India	Softcare	Immunosuppressant
Tofacitinib	Tofanib-XR	Tablet, 11 mg	Globe, Bangladesh	Tabrane Healthcare	Immunosuppressant
Tofacitinib	Tofanib	Tablet, 5 mg	Globe, Bangladesh	Tabrane Healthcare	Immunosuppressant
Tofacitinib	Tofatin	Tablet, 5 mg	Ziska, Bangladesh	Tabrane Pharmaceuticals	Immunosuppressant

Compiled by **Ms Chinta Abayawardana**

For further information please contact Professor Rohini Fernandopulle, Secretary, Medicines Evaluation Committee, National Medicines Regulatory Authority, No. 120, Norris Canal Road, Colombo 10.