Ten Drugs That Changed The World

I have been thinking about this topic for a long time. How does one choose ten drugs? Is acne cream less important than adrenaline? I suppose it depends whether you have spots or a cardiac arrest. So, I have stepped over the precipice with a selection. In true Alan Freeman style (for those of you who remember Pick of the Pops), I shall do it from 10 to 1.

10 PROPRANOLOL

Actually I would like to choose all β-blockers but propranolol has been with me all my practising life.

They are immensely important. They were first discovered over one hundred years ago when it was realised that adrenaline and nor-adrenaline sites could be blocked. Pronethalol, the first β-blocker was discovered in 1960.

James Black, who received the Nobel prize for medicine in 1988, discovered propranolol working at ICI in 1962 and research progressed apace through the 60s to the 80s. Atenolol was introduced in the early 70s and a large number of other similar drugs have been released since then.

Black’s work was to find a treatment for angina pectoris but these drugs are also used for heart rhythm irregularities, congestive cardiac failure, raised blood pressure, tremors, migraine, heart attack, anxiety, hyperthyroidism and a host of other problems.

They may cause dizziness, blurred vision, cold extremities, loss of sex drive and nightmares but, when they were first released, they made possible treatments for previously untreatable problems.

Nearly sixty years on they are still very widely used.

9 ASPIRIN

In a crude form, aspirin has been used for two-and-a-half thousand years and is therefore the oldest of my top ten drugs.

It was originally obtained from the leaves of the willow tree. The active ingredient, acetylsalicylic acid, was first made by Gerhardt in 1853 and Bayer improved and launched it at the turn of the twentieth century.

One hundred billion tablets are still used every year.
Its principal use is in the treatment of pain; headache, viral muscle aches, toothache and period pain. It is also an antipyretic (lowers temperature) and is used in colds and ‘flu.

At low doses it has an anti-platelet effect. That means that the blood is less sticky and the result is that blood clots are less likely to form within blood vessels.

Patients taking aspirin may experience increased bleeding from lacerations, at periods or following tooth extractions.

Aspirin is also prescribed in heart attacks, strokes, some types of arterial disease and in some types of vascular surgery where clotting may be a problem.

It can cause problems such as gastric bleeding from ulcers, indigestion and abdominal pain.

Some people are allergic to aspirin, resulting in a range of symptoms from a rash to a full-blown anaphylaxis.

Aspirin is now used much less routinely and has been replaced by paracetamol and Nurofen (ibuprofen) but it remains hugely valuable.

Zidovudine (also known as azidothymidine AZT), first described in 1964, is a key drug in the treatment of HIV/AIDS.

It owes its discovery to the theory that retroviral infections actually caused cancers, a view which had been held since the early 1900s.

It is one of a number of anti-viral drugs and was the first drug to be used in the treatment of HIV in 1986. Its introduction heralded the realisation that HIV was not a death sentence.

Zidovudine did not cure HIV patients but it slowed the disease down and it became the first of a series of drugs that became the cornerstone of the battle against HIV/AIDS.

Zidovudine causes serious and even life-threatening side effects including allergic rashes, muscle weakness and blood disturbances including anaemia and low white cells.

It also causes liver damage which, if severe, may be fatal.

The drug and its successors have resulted in a sharp decline in AIDS deaths in the last twenty-five years.

Simvastatin lowers blood cholesterol and has considerably reduced the incidence of stroke and other vascular-based diseases and disorders.

The first statins, mevastatin and iovastatin were isolated from fungal cultures. During research on iovastatin, scientists at the pharmaceutical company Merck derived a synthetic form called simvastatin.

Simvastatin was first released in 1992. Statins, normally taken daily before bed, are a lifetime medication and are used as part of an overall strategy of risk reduction in cardio-vascular disease.

Smoking cessation, exercise, limiting alcohol and eating well also reduce cholesterol.

Simvastatin may cause muscle weakness and damage and some forms of statin may interact with grapefruit juice which should

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be avoided. Overall only one patient in every 10,000 suffers a serious effect with a statin.

In the UK there are now five formulations of statin.

The others are atorvastatin, fluvastatin, pravastatin and rosuvastatin.

One of my abiding memories of hospital practice in the seventies was working on old style nightingale wards with stroke patients down one side and heart attack patients down the other side.

Statins have provided a major contribution to reducing the morbidity associated with the cardiovascular diseases and those lines of patients have now gone.

CHLORPROMAZINE

It is said that the introduction of the tranquilliser chlorpromazine in the 1950s represented a turning point in psychiatry.

Indeed it was the drug that resulted in a psycho-pharmacological revolution. To a generation of doctors in the seventies and beyond, it was known as Largactil.

It was discovered by the chemist Charpentier in 1950 and was introduced in 1953.

The first drug of its type, it quickly became the standard for the treatment of psychotic disorders such as schizophrenia, bipolar disorder and ADHD and it even worked in the treatment of intractable hiccups.

Its existence provided the foundation for the development of a host of drugs used for anxiety and depression and across the whole spectrum of psychiatry. Equally importantly, its effects on neurotransmitters shone a light into the previously obscure nature of how electrical impulses passed from neurone to neurone in the brain.

It had a lot of side effects and tolerance to the drug developed, resulting in the use of higher and higher doses. Withdrawal of the drug, particularly if done too quickly, was associated with acute symptoms and relapse.

However, despite the difficulties associated with its use, it provided the first of a large number of treatments where previously there were none.

NITROGEN MUSTARD

This may be regarded perhaps as a little ‘left field’ but the derivatives of nitrogen mustard had a profound effect.

In 1917 the horrific and appalling mustard gas was first used on British troops by the Germans in Ypres. It produced blistering of the skin, eroding sores and severe itching.

Men coughed up and vomited blood. It took up to six weeks to die.

Several countries stockpiled nitrogen mustard again in the second world war but it was never used.

In the 1940s the chemical was studied by Goodman and Gilman (authors of the famous textbook of pharmacology) at Yale University.

It was realised that the gas resulted in a reduction in circulating lymphocytes (a type of white blood cell) and it resulted in the creation of the drug mechlorethamine (mustine) which was introduced for the treatment of lymphomas.
Mustine was the first chemotherapy drug. It was very toxic and its use has been phased out but the discovery stimulated a huge amount of research and has resulted in the chemotherapeutic agents that are used today.

Such drugs include cyclophosphamide, chlorambucil and melphalan.

The success of chemotherapeutic medicine in cancer today can be traced back to that appalling episode in history during World War I.

This is a good example of where something used to fight mankind was found to be more valuable and better suited to the fight against cancer.

**QUININE**

Malaria is still a desperately serious and commonly fatal disease in those areas where it is endemic.

Better treatments are now being produced as well as more effective mechanisms for eliminating the malarial parasite and the mosquitoes which are its vector.

The first anti-malarial was quinine which has a long history in Peru where the cinchona tree was found to be a source of the crude chemical which could treat the disease.

Indeed it is still used to this day. In therapeutic doses it is quite toxic and was gradually replaced by its less toxic successor, chloroquine which was, until relatively recently the safest and most widely used of all anti-malarials.

Of course the management of the disease is now much better understood. Such drugs are now commonly used in combination to avoid the development of resistance to any one and a range of newer treatments such as mefloquine, sulpha drugs and pyrimethamine are now used.

However, it must not be forgotten that that Peruvian tree started the whole process of eliminating the disease.

**Enovid**

This is probably not a name that means much to most people, yet it signalled a change which was to have profound global effects.

Enovid was the first Oral Contraceptive and was trialled in Puerto Rico in 1957.

It was originally introduced for menstrual disorders but was released in the United States as a contraceptive.

Its release in the United Kingdom occurred a year later in 1961 although, at that time, it was available through the National Health Service only for married women.

The government did not want to be seen to be encouraging promiscuity or ‘free love’.

The pill contains an oestrogen and a progestogen to suppress ovulation and to produce a withdrawal bleed mimicking a period.

The idea had originally been conceived by the Austrian scientist Haberlandt in the 1920s who established that such an approach worked in animals.

He is believed to have conducted a clinical trial in women but received criticism and opprobrium from his colleagues.

Take-up of the ‘pill’ (as it was known, though it is in fact a tablet) was quite slow.
and it was not until 1974 that Family Planning Clinics could officially use it for single women.

In the UK alone it is taken by two million women and it is estimated that 70% of women have taken it at some time.

Health scares have dogged the pill, particularly thromboses (associated with smoking commonly) and increase in breast cancer.

Advice on those women for whom the pill is inappropriate is now well established.

There are now many brands of contraceptive, including a number of ‘minipill’ brands which contain only the progestogen and no oestrogen.

The oral contraceptive has had a huge effect on the social environment. It liberated women who had previously had to rely on men for contraception and has been a significant factor in changing relationships

**INSULIN**

In 1869, Langerhans noted clumps or Islets of cells in the pancreas which now bear his name.

Over the next fifty years researchers in Europe and America recognised the association between the pancreatic islets and glucose control in the body.

By the turn of the century the pancreas and diabetes were inextricably linked. In 1920 Banting started work in the University of Toronto assisted by a medical student, later his co-researcher, Charles Best.

They isolated insulin and conducted the first clinical trial in 1922. Following the discovery they linked with the pharmaceutical company Eli Lilley. Animal sourced insulin (bovine and porcine) was the only source of insulin until the 1960s when the first synthetic insulin was developed. Biosynthetic human insulin was launched for sale in 1982.

As a footnote to history, Banting and Best are credited with discovering the hormone, working with Professor of Physiology, J. Macleod of Toronto and biochemist James Collip. However, Nicolas Paulescu, a Romanian physiologist, actually apparently beat them to it. He published the discovery a year earlier in 1921.

The incidence of diabetes and of insulin use has increased inexorably during the last sixty years as a result of a combinationm of genetics, lifestyle and environment.

3.6 million people have been diagnosed with diabetes in the UK and it is estimated that up to a million more may have it without having been diagnosed.

The NHS spends £10 billion a year on people with diabetes and one in seven hospital beds is occupied by a diabetic. Estimates suggest that up to half a million patients are now treated with insulin.

The discovery in the 1920s has saved countless lives globally and, on past developments, usage will continue to increase.

**PENICILLIN**

The introduction of penicilllin in the 1940s has been recognised as one of the greatest,
Almost everyone knows that penicillin was discovered by Alexander Fleming.

In fact the Egyptians used mouldy bread poultices to treat infected wounds but it was Fleming, in 1928, who noticed during an experiment that mould could inhibit bacterial growth.

He found that ‘mould juice’ could destroy bacteria including streptococcus, meningococcus and the diphtheria bacterium.

Fleming’s discovery was developed into a therapeutic agent by Florey and Chain at Oxford.

Penicillin was identified in 1940 and the first clinical use is recorded in 1941. The pressures of World War II resulted in considerable developments and it was soon produced in commercial quantities for use in the latter part of the war.

This miracle drug, and all the other antibiotics that have developed as a result of Fleming’s original work, have saved countless millions of lives over the last seventy-five years.

Yet we are in danger of revisiting the dark days of the 1920s again (at least in respect of bacterial infections) because indiscriminate use of antibiotics has led to the development of widespread bacterial resistance and penicillin itself has been rendered largely ineffective against many strains of bacteria.

Better control of antibiotics and more research to find new anti-bacterial agents is essential if the population is not going to succumb in large numbers to an as-yet unidentified bacterial attack.

So, there we are; my top ten. I could easily have had many more; vaccines which has eliminated or controlled so many diseases, anti-hypertensives that have reduced the incidence of stroke and cardio-vascular disease, inhalers that have considerably reduced the scourge of asthma.

And I could go on...

One thing is for sure.

Our lives today are much safer because of the work of the pharmacologists, biochemists, physicians and physical chemists who have discovered so much that has been invaluable to society.

And don’t forget the Peruvians and the Egyptians either!

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