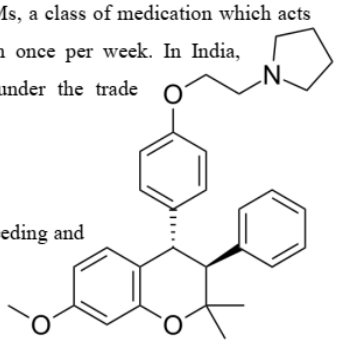
Non steroidal contraceptives

Birth control, also known as **contraception** and **fertility control**, is methods or devices used to prevent pregnancy. Planning, provision and use of birth control is called family planning. Birth control methods have been used since ancient times, but effective and safe methods only became available in the 20th century. Some cultures limit or discourage access to birth control because they consider it to be morally, religiously, or politically undesirable.

Ormeloxifene

Ormeloxifene (also known as **centchroman**) is one of the selective estrogen receptor modulators, or SERMs, a class of medication which acts on the estrogen receptor. It is best known as a non-hormonal, non-steroidal oral contraceptive which is taken once per week. In India, ormeloxifene has been available as birth control since the early 1990s, and it is currently marketed there under the trade name **Saheli**. Ormeloxifene has also been licensed under the trade names **Novex-DS**, **Centron** and **Sevista**.



Medical uses

Ormeloxifene is primarily used as a contraceptive but may also be effective for dysfunctional uterine bleeding and advanced breast cancer.

Birth control

Ormeloxifene may be used as a weekly oral contraceptive. The weekly schedule is an advantage for women who prefer an oral contraceptive, but find it difficult or impractical to adhere to a daily schedule required by other oral contraceptives.

For the first twelve weeks of use, it is advised to take the ormeloxifene pill twice per week. From the thirteenth week on, it is taken once per week. The consensus is that backup protection in the first month is a cautious but sensible choice. A standard dose is 30 mg weekly, but 60 mg loading doses can reduce pregnancy rates by 38%.

It has a failure rate of about 1-2% with ideal use which is slightly less effective than found for combined oral contraceptive pills.

Other indications

- Ormeloxifene has also been tested in experimental setting as a treatment for menorrhagia.
- Use in treatment of mastalgia and fibroadenoma has also been described.

Adverse effect

There are concerns that ormeloxifene may cause delayed menstruation.

Mode of action

Ormeloxifene is a SERM, or selective estrogen receptor modulator. In some parts of the body, its action is estrogenic (e.g., bones), in other parts of the body, its action is anti-estrogenic (e.g., uterus, breasts.) It causes an asynchrony in the menstrual cycle between ovulation and the development of the uterine lining, although its exact mode of action is not well defined. In clinical trials, it caused ovulation to occur later than it normally would in some women, but did not affect ovulation in the majority of women, while causing the lining of the uterus to build more slowly. It speeds the transport of any fertilized egg through the fallopian tubes more quickly than is normal. Presumably, this combination of effects creates an environment such that if fertilization occurs, implantation will not be possible.

Marketing

Ormeloxifene is only legally available in India as of 2009.

Ormeloxifene has been tested and licensed as a form of birth control, as well as a treatment for dysfunctional uterine bleeding.

- It was first manufactured by Torrent Pharmaceuticals, and marketed as birth control under the trade name **Centron**. Centron was discontinued.
- A new license for ormeloxifene was issued to Hindustan Latex Ltd., which now manufactures ormeloxifene as birth control under the trade name **Saheli**, **Novex** and **Novex-DS**.
- Torrent Pharmaceuticals has resumed manufacture of ormeloxifene under the trade name **Sevista**, as a treatment for dysfunctional uterine bleeding.

Antibiotics

Antibiotics or **antibacterials** are a type of antimicrobial used in the treatment and prevention of bacterial infection. They may either kill or inhibit the growth of bacteria. Several antibiotics are also effective against fungi and protozoans, and some are toxic to humans and animals, even when given in therapeutic dosage. Antibiotics are not effective against viruses such as the common cold or influenza, and may be harmful when taken inappropriately.

In 1928, Alexander Fleming identified penicillin, the first chemical compound with antibiotic properties. Fleming was working on a culture of disease-causing bacteria when he noticed the spores of little green mold in one of his culture plates. He observed that the presence of the mold killed or prevented the growth of the bacteria.

Classes of antibiotics

Antibacterial antibiotics are commonly classified based on their mechanism of action, chemical structure, or spectrum of activity. Most target bacterial functions or growth processes.[24]

Those that target

- the bacterial cell wall (penicillins and cephalosporins) or
- the cell membrane (polymyxins), or
- interfere with essential bacterial enzymes (rifamycins, lipiarmycins, quinolones, and sulfonamides) have bactericidal activities.

Those that target protein synthesis (macrolides, lincosamides and tetracyclines) are usually bacteriostatic (with the exception of bactericidal aminoglycosides).[25]

Further categorization is based on their target specificity. "Narrow-spectrum" antibacterial antibiotics target specific types of bacteria, such as Gram-negative or Gram-positive bacteria, whereas broad-spectrum antibiotics affect a wide range of bacteria.

Following a 40-year hiatus in discovering new classes of antibacterial compounds, four new classes of antibacterial antibiotics have been brought into clinical use in the late 2000s and early 2010s:

- Cyclic lipopeptides (such as daptomycin),
- Glycylcyclines (such as tigecycline),
- Oxazolidinones (such as linezolid), and
- Lipiarmycins (such as fidaxomicin).

Production

With advances in medicinal chemistry, most modern antibacterials are semisynthetic modifications of various natural compounds. These include, for example, the beta-lactam antibiotics, which include,

- ✓ The penicillins (produced by fungi in the genus *Penicillium*),
- ✓ The cephalosporins, and
- ✓ The carbapenems.

Compounds that are still isolated from living organisms are the aminoglycosides, whereas other antibacterials—for example, the sulfonamides, the quinolones, and the oxazolidinones—are produced solely by chemical synthesis.

Many antibacterial compounds are relatively small molecules with a molecular weight of less than 2000 atomic mass units.

Since the first pioneering efforts of Florey and Chain in 1939, the importance of antibiotics, including antibacterials, to medicine has led to intense research into producing antibacterials at large scales. Following screening of antibacterials against a wide range of bacteria, production of the active compounds is carried out using fermentation, usually in strongly aerobic conditions.

Administration

Oral antibiotics are taken by mouth, whereas intravenous administration may be used in more serious cases,[*citation needed*] such as deep-seated systemic infections. Antibiotics may also sometimes be administered topically, as with eye drops or ointments.

The topical antibiotics are:

- Erythromycin

- Clindamycin
- Gentamycin
- Tetracycline
- Meclocycline
- (Sodium) sulfacetamide

While topical medications that act as Comedolytics as well as antibiotics are:

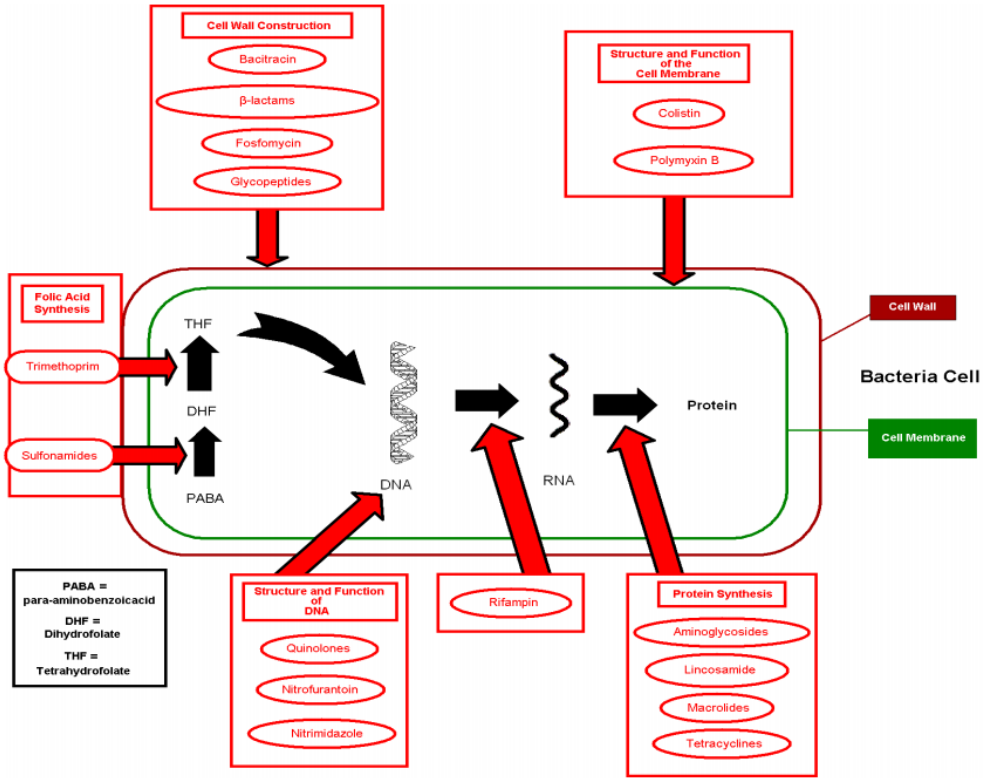
- Benzoyl peroxide
- Azelaic acid

Side Effects

- Antibiotics are screened for any negative effects on humans or other mammals before approval for clinical use, and are usually considered safe and most are well tolerated. However, some antibiotics have been associated with a range of adverse side effects. Side-effects range from mild to very serious depending on the antibiotics used, the microbial organisms targeted, and the individual patient. Safety profiles of newer drugs are often not as well established as for those that have a long history of use.
- Adverse effects range from fever and nausea to major allergic reactions, including photodermatitis and anaphylaxis.
- Common side-effects include diarrhea, resulting from disruption of the species composition in the intestinal flora, resulting, for example, in overgrowth of pathogenic bacteria, such as *Clostridium difficile*.
- Antibacterials can also affect the vaginal flora, and may lead to overgrowth of yeast species of the genus *Candida* in the vulvo-vaginal area.
- Additional side-effects can result from interaction with other drugs, such as elevated risk of tendon damage from administration of a quinolone antibiotic with a systemic corticosteroid.
- Some scientists have hypothesized that the indiscriminate use of antibiotics alter the host microbiota and this has been associated withchronic disease.

Resistance Mechanisms

Resistance may take the form of biodegredation of pharmaceuticals, such as sulfamethazine-degrading soil bacteria introduced to sulfamethazine through medicated pig feces. The survival of bacteria often results from an inheritable resistance, but the growth of resistance to antibacterials also occurs through horizontal gene transfer. Horizontal transfer is more likely to happen in locations of frequent antibiotic use.



Antibiotics such as penicillin and erythromycin, which used to have a high efficacy against many bacterial species and strains, have become less effective, due to the increased resistance of many bacterial strains

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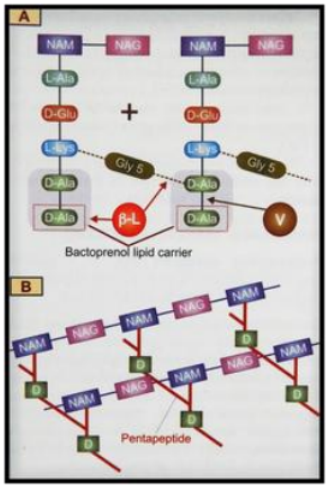
Several molecular mechanisms of antibacterial resistance exist. Intrinsic antibacterial resistance may be part of the genetic makeup of bacterial strains. For example, an antibiotic target may be absent from the bacterial genome. Acquired resistance results from a mutation in the bacterial chromosome or the acquisition of extra-chromosomal DNA. Antibacterial-producing bacteria have evolved resistance mechanisms that have been shown to be similar to, and may have been transferred to, antibacterial-resistant strains. The spread of antibacterial resistance often occurs through vertical transmission of mutations during growth and by genetic recombination of DNA by horizontal genetic exchange. For instance, antibacterial resistance genes can be exchanged between different bacterial strains or species via plasmids that carry these resistance genes. Plasmids that carry several different resistance genes can confer resistance to multiple antibacterials. Cross-resistance to several antibacterials may also occur when a resistance mechanism encoded by a single gene conveys resistance to more than one antibacterial compound.

Example – 1: Penicillin

Penicillin (**PCN** or **pen**) is a group of antibiotics which include penicillin G (intravenous use), penicillin V (oral use),procaine penicillin, and benzathine penicillin (intramuscular use). They are derived from *Penicillium* fungi. Penicillin antibiotics were among the first medications to be effective against many bacterial infections caused by staphylococci and streptococci. Penicillins are still widely used today, though many types of bacteria have developed resistance following extensive use. All penicillins are β-lactam antibiotics. About 10% of people report that they are allergic to penicillin; however, up to 90% of this group may not actually be allergic. Serious allergies only occur in about 0.03%.

Penicillin was discovered in 1928 by Scottish scientist Alexander Fleming. People began using it to treat infections in 1942. There are several enhanced penicillin families which are effective against additional bacteria; these include the antistaphylococcal penicillins, aminopenicillins and the antipseudomonal penicillins.

Mechanism of action of penicillin



All beta-lactum antibiotics interfere with bacterial cell wall synthesis. The bacteria synthesize UDP-N acetylmuramic acid pentapeptide called 'Park Nucleotide' and UDP-N acetyl glucosamine. The peptidoglycan residues are linked together forming long strands and UDP is split off. The final step is cleavage of terminal D-alanine of the peptide chains by transpeptidases; the energy so released is utilized for the establishment of cross linkage between peptide chains of the neighboring strands. This cross linking provides rigidity and stability of the cell wall. The penicillin inhibits the transpeptidases so that cross linking does not take place. These enzymes and related proteins constitute the *Penicillin Binding Proteins* (PBPs) which have been located in the bacterial cell wall.

When susceptible bacteria divide in the presence of beta-lactum antibiotic-cell wall deficient (CWD) forms are produced. Because interior of bacterium is hyperosmotic, the CWD forms swell and burst causing bacterial lysis. This is how beta0lactum antibiotics exert antibacterial action. Lytic effect of these antibiotics may also be due to depression of bacterial autolysins which normally function during cell division.

Rapid cell wall synthesis occurs when bacteria are multiplying rapidly; beta-lactum antibiotics are more lethal in this phase. Blood, pus and tissue fluids do not interfere with antibacterial action of these drugs.

Bacteria constantly remodel their peptidoglycan cell walls, simultaneously building and breaking down portions of the cell wall as they grow and divide. *β*-Lactam antibiotics inhibit the formation of peptidoglycan cross-links in the bacterial cell wall; this is achieved through binding of the four-membered *β*-lactam ring of penicillin to the enzyme DD-transpeptidase. As a consequence, DD-transpeptidase cannot catalyze formation of these cross-links, and an imbalance between cell wall production and degradation develops, causing the cell to rapidly die.

The enzymes that hydrolyze the peptidoglycan cross-links continue to function, even while those that form such cross-links do not. This weakens the cell wall of the bacterium, and osmotic pressure becomes increasingly uncompensated—eventually causing cell death (cytolysis).

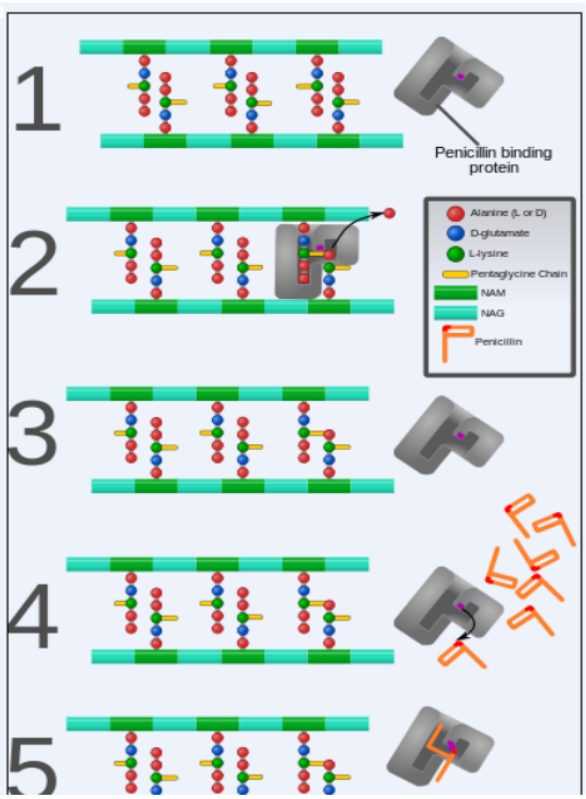
In addition, the build-up of peptidoglycan precursors triggers the activation of bacterial cell wall hydrolases and autolysins, which further digest the cell wall's peptidoglycans. The small size of the penicillins increases their potency, by allowing them to penetrate the entire depth of the cell wall. This is in contrast to the glycopeptide antibiotics vancomycin and teicoplanin, which are both much larger than the penicillins.

Gram-positive bacteria are called protoplasts when they lose their cell walls. Gram-negative bacteria do not lose their cell walls completely and are called spheroplasts after treatment with penicillin.

Penicillin shows a synergistic effect with aminoglycosides, since the inhibition of peptidoglycan synthesis allows aminoglycosides to penetrate the bacterial cell wall more easily, allowing their disruption of bacterial protein synthesis within the cell. This results in a lowered MBC for susceptible organisms.

Penicillins, like other *β*-lactam antibiotics, block not only the division of bacteria, including cyanobacteria, but also the division of cyanelles, the photosynthetic organelles of the glaucophytes, and the division of chloroplasts of bryophytes. In contrast, they have no effect on the plastids of the highly developed vascular plants. This supports the endosymbiotic theory of the evolution of plastid division in land plants.

The chemical structure of penicillin is triggered with a very precise, pH-dependent directed mechanism, effected by a unique spatial assembly of molecular components, which can activate by protonation. It can travel through bodily fluids, targeting and inactivating enzymes responsible for cell-wall synthesis in gram-positive bacteria, meanwhile avoiding the surrounding non-targets.



Penicillin can protect itself from spontaneous hydrolysis in the body in its anionic form, while storing its potential as a strong acylating agent, activated only upon approach to the target transpeptidase enzyme and protonated in the active centre. This targeted protonation neutralizes the carboxylic acid moiety, which is weakening of the β-lactam ring N–C(=O) bond, resulting in a self-activation. Specific structural requirements are equated to constructing the perfect mouse trap for catching targeted prey.

Production

- Penicillin is a secondary metabolite of certain species of *Penicillium* and is produced when growth of the fungus is inhibited by stress. It is not produced during active growth. Production is also limited by feedback in the synthesis pathway of penicillin.
  - α-ketoglutarate + AcCoA → homocitrate → L-α-aminoadipic acid → L-lysine + β-lactam
- The by-product, L-lysine, inhibits the production of homocitrate, so the presence of exogenous lysine should be avoided in penicillin production. The *Penicillium* cells are grown using a technique called fed-batch culture, in which the cells are constantly subject to stress, which is required for induction of penicillin production. The available carbon sources are also important: Glucose inhibits penicillin production, whereas lactose does not. The pH and the levels of nitrogen, lysine, phosphate, and oxygen of the batches must also be carefully controlled.
- The biotechnological method of directed evolution has been applied to produce by mutation a large number of *Penicillium*strains. These techniques include error-prone PCR, DNA shuffling, ITCHY, and strand-overlap PCR.
- Semisynthetic penicillins are prepared starting from the penicillin nucleus 6-APA.

Therapeutic hormones towards human system

Insulin (medication) is the use of insulin and similar proteins as a medication to treat disease. Insulin comes in a number of different types including short acting (such as regular insulin) and long acting (such as NPH insulin). Insulin is used to treat a number of diseases including diabetes and its acute complications such as diabetic ketoacidosis andhyperosmolar hyperglycemic states.[3] It is also used along with glucose to treat high blood potassium levels.[3] Side effects may include: low blood sugar levels, skin reactions at the site of injection and low potassium levels among others.[3] Insulin was first used as a medication in Canada by Charles Best and Frederick Banting in January 1922.

Types

Medical preparations of insulin are never just 'insulin in water'. Clinical insulins are specially prepared mixtures of insulin plus other substances including preservatives. These delay absorption of the insulin, adjust the pH of the solution to reduce reactions at the injection site, and so on.

Slight variations of the human insulin molecule are called insulin analogues, (technically "insulin receptor ligands") so named because they are not technically insulin, rather they are analogues which retain the hormone's glucose management functionality. They have absorption and activity characteristics not currently possible with subcutaneously injected insulin proper. They are either absorbed rapidly in an attempt to mimic real beta cell insulin, or steadily absorbed after injection instead of having a 'peak' followed by a more or less rapid decline in insulin action, all while retaining insulin's glucose-lowering action in the human body. However, a number of meta-analyses, including those done by the Cochrane Collaboration in 2002, Germany's Institute for Quality and Cost Effectiveness in the Health Care Sector [IQWiG] released in 2007, and the Canadian Agency for Drugs and Technology in Health (CADTH) also released in 2007 have shown no unequivocal advantages in clinical use of insulin analogues over more conventional insulin types.

Choosing insulin type and dosage/timing should be done by an experienced medical professional working closely with the diabetic patient.

The commonly used types of insulin are:

- Fast-acting: Includes the insulin analogues *aspart*, *lispro*, and *glulisine*. These begin to work within 5 to 15 minutes and are active for 3 to 4 hours. Most insulins form hexamers which delay entry into the blood in active form; these analog insulins do not, but have normal insulin activity. Newer varieties are now pending regulatory approval in the U.S. which are designed to work rapidly, but retain the same genetic structure as regular human insulin.
- Short-acting: Includes *regular* insulin which begins working within 30 minutes and is active about 5 to 8 hours.
- Intermediate-acting: Includes *NPH insulin* which begins working in 1 to 3 hours and is active 16 to 24 hours.
- Long acting: Includes the analogues *glargine* and *detemir*, each of which begins working within 1 to 2 hours and continue to be active, without major peaks or dips, for about 24 hours, although this varies in many individuals.
- Ultra-long acting: Currently only includes the analogue *degludec*, which begins working within 30–90 minutes, and continues to be active for greater than 24 hours.
- Combination insulin products – Includes a combination of either fast-acting or short-acting insulin with a longer acting insulin, typically an *NPH insulin*. The combination products begin to work with the shorter acting insulin (5–15 minutes for fast-acting, and 30 minutes for short acting), and remain active for 16 to 24 hours. There are several variations with different proportions of the mixed insulins (e.g. Novolog Mix 70/30 contains 70% aspart protamine [akin to NPH], and 30% aspart.)

Yeast-based

In late 2003, Wockhardt commenced manufacture of a yeast-based insulin costing $3.25 in India claiming it eliminated the risk of contracting diseases such as BSE and CJD associated with insulin derived from pigs and cattle. However, the company continues to manufacture insulin derived from pigs and cows in the United Kingdom under the Hypurin/CP Pharmaceuticals brand name.

Methods of administration

Unlike many medicines, insulin cannot be taken orally at the present time. Like nearly all other proteins introduced into thegastrointestinal tract, it is reduced to fragments (even single amino acid components), whereupon all 'insulin activity' is lost. There has been some research into ways to protect insulin from the digestive tract, so that it can be administered in a pill. So far this is entirely experimental.

Subcutaneous

Insulin is usually taken as subcutaneous injections by single-use syringes with needles, an insulin pump, or by repeated-use insulin pens with needles. Patients who wish to reduce repeated skin puncture of insulin injections often use an injection port in conjunction with syringes.

Administration schedules often attempt to mimic the physiologic secretion of insulin by the pancreas. Hence, both a long-acting insulin and a short-acting insulin are typically used.

Insulin pump

Insulin pumps are a reasonable solution for some. Advantages to the patient are better control over background or 'basal' insulin dosage, bolus doses calculated to fractions of a unit, and calculators in the pump that may help with determining 'bolus' infusion dosages. The limitations are cost, the potential for hypoglycemic and hyperglycemic episodes, catheter problems, and no "closed loop" means of controlling insulin delivery based on current blood glucose levels.

Insulin pumps may be like 'electrical injectors' attached to a temporarily implanted catheter or cannula. Some who cannot achieve adequate glucose control by conventional (or jet) injection are able to do so with the appropriate pump.

Indwelling catheters pose the risk of infection and ulceration, and some patients may also develop lipodystrophy due to the infusion sets. These risks can often be minimized by keeping infusion sites clean. Insulin pumps require care and effort to use correctly.

Inhalable insulin

In 2006 the U.S. Food and Drug Administration approved the use of Exubera, the first inhalable insulin. It was withdrawn from the market by its maker as of third quarter 2007, due to lack of acceptance.

Inhaled insulin claimed to have similar efficacy to injected insulin, both in terms of controlling glucose levels and blood half-life. Currently, inhaled insulin is short acting and is typically taken before meals; an injection of long-acting insulin at night is often still required. When patients were switched from injected to inhaled insulin, no significant difference was observed in Hb_{A1c} levels over three months. Accurate dosing was a particular problem, although patients showed no significant weight gain or pulmonary function decline over the length of the trial, when compared to the baseline.

Following its commercial launch in 2005 in the United Kingdom, it was not (as of July 2006) recommended by National Institute for Health and Clinical Excellence for routine use, except in cases where there is "proven injection phobia diagnosed by a psychiatrist or psychologist".

In January 2008, the world's largest insulin manufacturer, Novo Nordisk, also announced that the company was discontinuing all further development of the company's own version of inhalable insulin, known as the AERx iDMS inhaled insulin system. Similarly, Eli Lilly and Company ended its efforts to develop its inhaled Air Insulin in March 2008. However, MannKind Corp. (majority owner, Alfred E. Mann) remains optimistic about the concept.

Transdermal

There are several methods for transdermal delivery of insulin. Pulsatile insulin uses microjets to pulse insulin into the patient, mimicking the physiological secretions of insulin by the pancreas. Jet injection had different insulin delivery peaks and durations as compared to needle injection. Some diabetics find control possible with jet injectors, but not with hypodermic injection.

Both electricity using iontophoresis and ultrasound have been found to make the skin temporarily porous. The insulin administration aspect remains experimental, but the blood glucose test aspect of "wrist appliances" is commercially available.

Researchers have produced a watch-like device that tests for blood glucose levels through the skin and administers corrective doses of insulin through pores in the skin. A similar device, but relying on skin-penetrating "microneedles", was in the animal testing stage in 2015.

Intranasal insulin

Intranasal insulin is being investigated. CPEX Pharmaceuticals reported phase 2a clinical trial preliminary results for its intranasal drug, Nasulin, on March 19, 2010; there's no word on when it might be expected on the market.

Oral insulin

The basic appeal of oral hypoglycemic agents is that most people would prefer a pill to an injection. However, insulin is a protein, which is digested in the stomachand gut and in order to be effective at controlling blood sugar, cannot be taken orally in its current form.

The potential market for an oral form of insulin is assumed to be enormous, thus many laboratories have attempted to devise ways of moving enough intact insulin from the gut to the portal vein to have a measurable effect on blood sugar.

A number of derivatization and formulation strategies are currently being pursued to in an attempt to develop orally available insulin. Many of these approaches employ nanoparticle delivery systems and several are being tested in clinical trials.

Dosage units

One international unit of insulin (1 IU) is defined as the "biological equivalent" of 34.7 μg pure crystalline insulin. This corresponds to the old USP insulin unit, where one unit (U) of insulin was set equal to the amount required to reduce the concentration of blood glucose in a fasting rabbit to 45 mg/dl (2.5 mmol/L).

The unit of measurement used in insulin therapy is not part of the International System of Units (abbreviated SI) which is the modern form of the metric system. Instead the pharmacological international unit (IU) is defined by the WHO Expert Committee on Biological Standardization.[22]

Detection in biological fluids

Insulin is often measured in serum, plasma or blood in order to monitor therapy in diabetic patients, confirm a diagnosis of poisoning in hospitalized persons or assist in a medicolegal investigation of suspicious death. Interpretation of the resulting insulin concentrations is complex, given the numerous types of insulin available, various routes of administration, the presence of anti-insulin antibodies in insulin-dependent diabetics and the *ex vivo* instability of the drug.

Other potential confounding factors include the wide-ranging cross-reactivity of commercial insulin immunoassays for the biosynthetic insulin analogs, the use of high-dose intravenous insulin as an antidote to antihypertensive drug over dosage and postmortem redistribution of insulin within the body.

The use of a chromatographic technique for insulin assay may be preferable to immunoassay in some circumstances, to avoid the issue of cross-reactivity affecting the quantitative result and also to assist identifying the specific type of insulin in the specimen.

Combination with other antidiabetic drug

A combination therapy of insulin and other antidiabetic drugs appears to be most beneficial in diabetic patients who still have residual insulin secretory capacity.[31] A combination of insulin therapy and sulphonylurea is more effective than insulin alone in treating patients with type 2 diabetes after secondary failure to oral drugs, leading to better glucose profiles and/or decreased insulin needs.

Allergy

Allergy to Insulin products is rare with a prevalence of about 2%, of which most reactions are not due to the insulin itself but to preservatives added to insulin such as zinc, protamine, and meta-cresol.

Most reactions are Type I hypersensitivity reactions and rarely cause anaphylaxis. A suspected allergy to insulin can be confirmed by skin prick testing, patch testing and occasionally skin biopsy.

First line therapy against insulin hypersensitivity reactions includes symptomatic therapy with antihistamines. The affected persons are then switched to a preparation that does not contain the specific agent they are reacting to or undergo desensitization.[6]

Problems associated with insulin

There are several problems with insulin as a clinical treatment for diabetes:

- Mode of administration.
- Selecting the 'right' dose and timing. Usually one unit of insulin is ~15grams of CHO.
- Selecting an appropriate insulin preparation (typically on 'speed of onset and duration of action' grounds).
- Adjusting dosage and timing to fit food intake timing, amounts, and types.
- Adjusting dosage and timing to fit exercise undertaken.
- Adjusting dosage, type, and timing to fit other conditions, for instance the increased stress of illness.
- Variability in absorption into the bloodstream via subcutaneous delivery
- The dosage is non-physiological in that a subcutaneous bolus dose of insulin alone is administered instead of combination of insulin and C-peptide being released gradually and directly into the portal vein.
- It is simply a nuisance for patients to inject whenever they eat carbohydrate or have a high blood glucose reading.
- It is dangerous in case of mistake (most especially 'too much' insulin).