4. Alternative metabolic pathways that bypass the biochemical reactions that are damaged by the antibiotics.

5. Variations in cellular components, e.g. cell walls or protein making machinery, which change their structure so that they are no longer damaged by antibiotics.

HOW DO BACTERIA BECOME RESISTANT?

In-Built Resistance

For some bacteria antibiotic resistance is a built in feature that is turned on when they find themselves in an environment that contains antibiotics. For example: Resistant forms of *Staphylococcus aureus*, a notoriously nasty bacterium otherwise known as golden staph, are able to deactivate antibiotics by making an enzyme that breaks up the antibiotic molecule. However, the bacteria don't make the enzyme all the time, only when they are exposed to antibiotics. A protein in the bacterium's wall detects antibiotics and turns on the gene that codes for the enzyme. The gene is turned off in an antibiotic free environment. (Ref.2) Some bacteria turn on resistance genes in response to signals from other bacteria that have been exposed to antibiotics. (Ref.3)

Some bacteria can simply go dormant in an environment containing antibiotics. When the antibiotics are removed they become active again. This explains why some infections reappear after apparently successful treatment with antibiotics. (Ref. 4)

Biofilm Resistance

Many bacteria can organise themselves into closely packed layers called biofilms so they can attach to and live on solid surfaces. Within these biofilms the bacteria are bound together by gel-like matrix which is very difficult for antibiotics to penetrate. The bacteria also seem to change their cellular functions to a more antibiotic resistant state, even though they are genetically unchanged. If the bacteria leave the biofilm and swim around as individual cells they lose the antibiotic resistance they had in the biofilm. (Ref. 5) The bacteria have not evolved; they have simply changed from one normal physiological state to another.

Mutations

Mutations occasionally occur in the genes that control the shape of protein-making machinery in bacteria. The altered protein making machinery is less susceptible to interference by those antibiotics that work by preventing bacteria from making proteins. This may sound like evolution but it is actually degeneration. The mutated bacteria have not changed into new kinds of bacteria and are actually less efficient at making proteins than non-mutated bacteria. When antibiotics are removed from their environment the mutated bacteria remain the same inefficient bacteria and do not function as well as normal bacteria. Therefore, they only have an advantage in an environment containing antibiotics.

THE RAPID RISE OF RESISTANCE

Not all bacteria have built-in or mutated genes for antibiotic resistance, so what accounts for the enormous increase in resistant bacteria that is causing problems in hospitals today? The answer is natural selection, plus the strange ability to borrow genes, neither of which is evolution.

Selected Resistance

In any population of bacteria some forms are resistant to antibiotics and some are not. If a mixed population of resistant and non-resistant bacteria is exposed to antibiotics, many non-resistant ones will be killed but the resistant ones will survive. When the survivors reproduce, the next generation of bacteria will contain more resistant bacteria than the previous generation. If this happens many times over, the resistant bacteria eventually becomes the dominant strain in that population. Bacteria reproduce very rapidly, so this process can occur in a matter of months in an environment containing high levels of antibiotics, such as a hospital. (See diagram on next page)

Evidence that resistant “superbugs” are simply the resistant strains that have survived after antibiotics have wiped out the other strains is seen in recent research into how many different strains of bacteria cause hospital acquired infections and childhood pneumonias. Molecular biologists at Rockefeller University recently surveyed 3,000 samples of methicillin-resistant *Staph aureus* from 14 different countries and found that 70% of infections were from five strains. (There are over 4,000 known strains of this bacterium.) Almost half the drug resistant