



# PAIN MANAGEMENT FOR KNEE REPLACEMENT



Dr Keith Holt

*Managing pain after knee replacement is key to obtaining better function and earlier recovery from that surgery. With this in mind, it is important to realise that everyone has different degrees of pain post surgery and, even within that range of experiences, individuals can interpret pain very differently. For this reason, everyone needs to have a regime tailored to his or her personal needs and, despite modern pharmacological science, this frequently cannot be done other than by trial and error.*

*For most people, the best way is to start on a standardised regime, then to modify this to suit. For some however, there are known sensitivities to various drugs that can make this more difficult. In these situations, there are other regimes and medications that can be used but, unfortunately, the choice is ultimately finite. Understanding the drugs that can be used is helpful when developing an individual pain control program. This document is designed to help you understand what each of the various medications do, how they are normally used, and what the alternatives are. This review is not intended to be read as a whole document. Try to focus on understanding the drugs that you are on.*

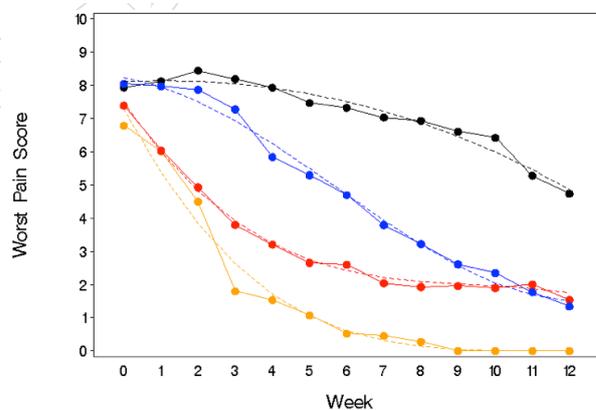
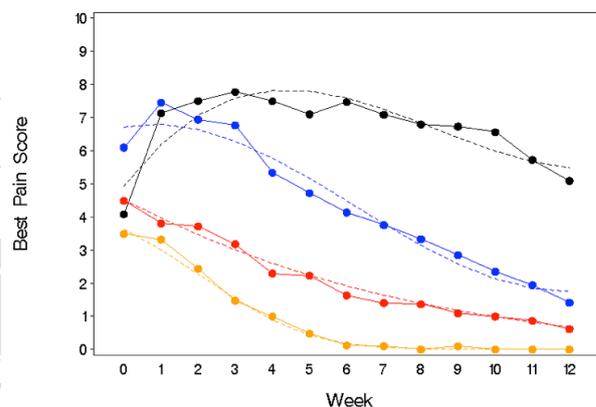
## Pain after knee replacement

*Pain Relief is, for most people, the single biggest reason to consider replacement: and results of the larger series do indeed show that the vast majority are pain free, or have minimal aches and pains, in the longer term. Overall however, it must be said that a knee replacement is not quite as pain free as say a hip replacement, and it certainly does not recover as fast. This may be due to the fact that the knee is relatively superficial and not surrounded by muscle like the hip. It may also be because of the complexity of this joint in comparison to a hip. Either way, the results, at least in the short term (the first year), are not quite as good as a hip replacement. After that however, the results do approach that of hip replacement, though the percentage of unsatisfactory results, for one reason or another, always remains higher in the longer term.*

*Achieving good long term pain relief begins at the time of surgery, and perhaps even before then. Establishing and maintaining control of pain after surgery is one of the keys to longer term success and, without doubt, post operative pain control is the most important. The duration of post-operative pain is variable but, for some, it may go on for over 3 months: that is twice as long as for a hip replacement. This is best illustrated by looking at the graphs shown opposite, which are derived from pain studies published under the title:*

### **Knee pain during the first three months after unilateral total knee arthroplasty. A multi-centre prospective observational cohort study.**

Morze, C, Johnson, N, Williams, G, Moroney, M, Lamberton, T, McAuliffe, M.



*Of concern with knee replacement are, the group that have difficulty managing their pain (~10% overall), and the group who still have 5 out of 10 'best pain' scores at the 3 month mark. In the first 6 weeks, with simple analgesics, this latter*

group are barely better than they were in the first week post surgery. More recently however, various strategies have evolved to improve this group, and these are now being used where indicated. Unfortunately, only time will tell if they are effective, particularly noting that other factors such as prosthetic design, limb alignment, and ligament tension also play a role in this. The issue is complex.

There is another group who, in complete contradistinction to the group mentioned above, have almost no pain by 6 - 8 weeks (~10%). The reasons for this are unknown, and it does not always seem to relate directly to swelling, stiffness or other operative factors, albeit that these may be the cause of some of this problem. One of the indicators for being in either the best or the worst group, is the degree and extent of arthritis that exists pre-operatively. We know for instance, that those people who have tolerated a really bad knee for a long time, will tolerate a knee replacement: and hence are expected to do well. On the other hand, those who come to replacement with significant on-going pain, and yet do not have a particularly arthritic knee, generally will not do so well. Obviously this has something to do with pain tolerance, but other factors are almost certainly at play as well: and the above guide is not always reliable. In any event, a lot of work is being done to try and improve the short term figures and make the initial few weeks better.

**Depression** is a major factor which needs to be mentioned. There is good evidence that those who are depressed will find pain relief hard to achieve. Pain tolerance can be significantly reduced, the individual's focus may be shifted to the pain rather than to the achievement of function, and all the analgesics seem less effective. If untreated, it seems that this problem will be worse. In addition, post-operative pain that is difficult to control will, in turn, make the depression worse: hence leading to a spiral of problems that can be very difficult to treat.

With the above in mind, if there is an on-going problem of depression, then this should be treated. The modern drugs are very effective for this, they work reasonably quickly, and they are relatively well tolerated. If this is an issue that needs looking at, your GP should be consulted, and this should be arranged prior to surgery.

### **Pre-operative measures**

**Exercise** has been shown, at least in some series, to help with recovery from surgery: but the advantages may not be huge, and more recent studies are less clear on the advantages. What seems to be relevant is general fitness, and this is more important than fitness relating to the area being operated on. In addition, it is important not to make the arthritic or damaged area sorer by trying to stretch or exercise it. That does not help. Thus, if you are having your knee replaced, pool exercise or upper body exercise may be helpful. The degree to which this is helpful however, will be variable, and it is certainly not essential to recovery.

**Weight Loss** has been shown to help with pre-operative symptoms from osteoarthritis, but there is less evidence for its role in reducing post-operative pain. The improvement gained by weight loss, prior to replacement, can be easily explained by a reduction of weight (force) on a sore, damaged, joint. In the post-operative phase however, this is no longer the case. When the joint has been replaced, it is no more painful if increased forces are put across it. The pain is the same. From a pain perspective therefore, there is no evidence that the overweight (high BMI - body mass index) do any worse in the first 3 months than the normally thinner (low BMI) morphologic types.

What weight reduction does do, is to make the surgery easier: hence giving rise to less complications. Unless the weight change is very significant however, the reduction in difficulty caused by weight loss is not enough to make it worth while. Also, large and rapid drops in weight can lead to some relative malnutrition, and this, in itself, can lead to some weakness in the immune system which, in turn leads to increased complications. Substantial weight loss therefore, whilst beneficial, needs to be done well ahead of time, and the body needs to have stabilised to the changes before surgery is performed. This stabilisation will often take about 3 months to occur, particularly if the diet change is one of a reduction in carbohydrates and an increase in fats.

Clearly, arthritic joints can make exercise very difficult to undertake, thus making weight loss hard to achieve. For a number of people therefore, it is sometimes best to just get on and replace the joint with a view to losing weight with the increased activity that should be possible in the post operative phase. In the long term, weight reduction is good for the prosthesis which, after all, is just a mechanical device. As such, it is subject to wear and tear like any other mechanical device. Hence, weight reduction has been shown to be associated with increased longevity of the prosthesis.

**Bariatric surgery**, be that gastric banding or gastric sleeve, is designed to change eating habits and absorption of food. The latter of the procedures is the more complicated, but also the most powerful, procedure. These procedures, particularly the latter, have significant complications, both in the short and the long term and, accordingly, need to be well considered. For most overweight people they are probably unnecessary but, occasionally, they do seem indicated. If needs be therefore, a recommendation can be provided to help find an appropriate Bariatric Surgeon.

The long term results of weight loss surgery remain unknown but, needless to say, there are some complications beginning to show up that were not anticipated when these procedures were first contemplated and designed. In particular, some changes to the bone structure, making it hard and brittle, has led to a fracture that is seen in the upper femur, just below the hip, occurring some 5 or so years out. This fracture shows resistance to healing because the bone in the region becomes so hard and brittle that it damages its own blood vessels and

dies. It then becomes an extraordinarily difficult problem to fix.

Other problems of weight loss surgery, including long term mal-nourishment, are also seen. This can then lead to excessive weight loss, with an inability to eat adequate amounts of food, or an adequate range of food types. The usual cause of these serious problems is a sleeve procedure, where the stomach volume has been considerably reduced, and the area left for absorption is small or inadequate. Unlike gastric banding however, this procedure cannot be reversed. For this reason, it should be undertaken only when all else has failed, and only then by experienced Bariatric Surgeons.

**Age and Sex** both influence pain and recovery. In deference to what you might think however, it is the young fit males who do worst, and the little old ladies who do best. Firstly, older people seem to get less pain than the younger ones. Whether that is purely an age related phenomenon, or whether that generation is just tougher, having seen wars and their consequences, is unknown. Either way, it is a well documented observation.

The second consideration is that younger people heal better than old. This might seem advantageous but, in a procedure like knee replacement, this can mean more scar, more tissues sticking to each other, and more swelling: hence - more pain and less movement. This also seems to be worse in males.

The third factor relating to this, comes down to rehabilitation and how hard the knee is pushed. Ideally, the aim is to gradually get the range of motion past 90° before leaving hospital. It does not have to occur on day 1, and more exercise is not better. As the primary aim of the recovery period is to get maximal range of motion, there is an optimal rate of achievement that is to be aimed for. Essential for this process is swelling reduction, which means rest is required, and for some weeks to months following surgery. Early on, excessive walking should be avoided, the leg should be elevated for long periods of time, and the knee range should be achieved in the easiest way possible; and not done too often. Simple hanging the knee over the edge of a chair, 3 times a day for short periods, may be enough. There is no need to bend the knee a harder way when the result is the same. This just aggravates the situation.

Similarly, the initial aim is not to get fit. Being fit and strong does not help. So, whilst some water work may make the knee feel good, and may help the bending, excessive walking and exercising, either in or out of a pool, may undo those benefits. It is always to be remembered that, the primary aims are to reduce swelling, and to maximise the range of motion. It is not a competition to see who can do the most soonest: an attitude that is more common amongst males than the females, and more common in the young. The simple mantra is that 'More is not Better'.

**Adequate iron stores** are helpful for surgery. Not because they help the pain or function, but because they decrease the risk of transfusion, and hence, the risk of transfusion caused

infection. If there is some doubt about your iron levels, if there is or has been some anaemia present, then these should be checked pre-operatively so that the situation can be remedied. This is now easy to do, either with oral iron (if the stores are just slightly low), by intra-muscular injection (if more iron is required), or by an intravenous iron infusion (if time is short). If in doubt about this, you can have your GP (or Dr Holt) measure your iron levels for you.

**Pre-medication** is now rarely used by Anaesthetists. Sometimes they will use sedation as a means of relieving nervousness, but the older techniques of routine pre-operative medication have now been abandoned because of the increased risk of nausea and other problems.

**Pre-operative pain modifying agents** such as Pregabalin (Lyrica - see below for details) are sometimes used, and there is some evidence for these, albeit that the evidence suggests that it may not be necessary to start these pre-operatively. Indeed, the result may be the same if commenced in the post-operative period, a practice that is more common.

### **Intra-Operative Measures**

**Minimal tourniquet use** is helpful from a pain perspective. There is no doubt that the use of the tourniquet is very helpful when performing a procedure such as knee replacement. To a degree it reduces blood loss, it significantly aids visualisation of the joint, and it allows the bone to be drier at the time of cementation of the prosthesis. Unfortunately, leaving a tourniquet on for an hour whilst the procedure is being performed, can cause significant pain in the upper thigh region where the tourniquet is applied.

Pain occurs not only due to the direct pressure of the tourniquet and the resultant loss of blood supply to that section of muscle during the procedure, but because the tourniquet traps muscle underneath it and, as the knee is taken through to full flexion to allow insertion of the prosthesis, that muscle gets stretched underneath the tourniquet causing injury to that muscle (albeit usually minor).

Although only a few people complain of significant pain in the upper thigh region after knee replacement, both evidence, and personal experience, would suggest that it is more common than suspected. We now know that knee replacements performed with minimal use of the tourniquet have less pain, require less analgesia, and get home earlier than when a tourniquet has been used for the entire procedure.

At present, Dr Holt tries to restrict tourniquet use to the minimum possible time. Usually this means for the first 5 to 10 minutes of the procedure during which time the knee is exposed and the navigation rods inserted. By the time this has been done a lot of the bleeding blood vessels have sealed themselves off, thus meaning that when the tourniquet is released, the resulting amount of bleeding is limited. If significant bleeding occurs thereafter, the tourniquet may be

re-inflated, either to finish the procedure with reduced blood loss, or to allow optimised cementation of the prosthesis. Where possible however, tourniquet use will be minimised.

Using a tourniquet for the first 5 to 10 minutes of the procedure does not seem to produce significant extra pain, and results seem directly comparable to performing the procedure with no tourniquet throughout.

**Local Anaesthetic Instillation** directly into the joint, at the end of the procedure, is usual. A large volume of long acting local anaesthetic can be placed into the joint via a small catheter that is placed in-situ prior to closing the knee. The catheter is put in from inside the knee to the outside so that nothing passes through the skin and into the joint: this method hopefully preventing skin organisms from being pushed into the joint.

The local anaesthetic is generally used along with Tranexamic Acid, which helps decrease bleeding within the joint. This combination reduces pain in the immediate post-operative period (18 - 24 hours), and is usually complimented by an adductor canal (saphenous nerve) block, or similar.

**Direct Wound and Capsule Infiltration** is not needed in knee replacement that often, given how good the other techniques have proven to be. Whilst this is advocated by many in the literature, there is no evidence that the effect lasts any longer than the length of action of the local anaesthetic. To get a better result from this technique, most enthusiasts advocate the addition of cortisone to the mixture. This makes the local anaesthetic last longer, and it provides better control of inflammation; but it lowers local immunity, and thus increases the infection risk. Given that infection is the most difficult of all the long term complications of knee replacement to deal with therefore, the author does not advocate this, and instead, he prefers the safer alternative of systemic cortisone (beginning at induction) in association with local joint instillation and nerve blocks (particularly adductor canal blocks).

**Major Nerve Blocks** are an excellent way of relieving immediate post-operative pain, and are frequently performed in procedures such as knee replacement when more proximal (spinal or epidural) blocks have not been used. By using the newer, longer lasting, local anaesthetics, it is now frequently possible to obtain nearly 24 hours of pain relief with these techniques. It is to be understood however, that by blocking major nerves such as the femoral nerve or the sciatic nerve, not only are the sensory nerves that carry pain blocked, but the motor nerves that supply the muscles are also blocked. This means that, whilst the pain is relieved, the quadriceps (in a femoral nerve block, or other muscles in a sciatic nerve block) may also be paralysed. When the nerve recovers however, full function should return.

If the femoral nerve alone has been blocked, then standing should not be initiated until quadriceps function has returned. If the sciatic nerve has been blocked as well, not only does the above apply, but the limb needs to be more carefully

looked after to make sure that no pressure areas develop in the anaesthetised areas that are at risk. This particularly means the heel, where it is necessary to protect against pressure areas with special pads and supports (which the nursing staff provide). For all the above reasons, these blocks are now rarely used by Dr Holt's Anaesthetists.

**Adductor Canal Blocks** are an attempt to anaesthetise only the sensory branches of the femoral nerve that cross the knee area, without paralysing the quadriceps. Essentially, these block the saphenous branch of the femoral nerve in near isolation from the rest of the femoral nerve. It can only be done under ultrasound control, and it is something that Dr Holt's Anaesthetists now do routinely for knee replacement and similar procedures. When performed as a single injection, it provides excellent pain relief for close to 24 hours. However, if a small catheter is left in situ so that an anaesthetic infusion pump can be used, it can provide relief for 3 - 4 days. These infusion pumps generally contain low concentration local anesthetic (usually 0.2% Ropivacaine) which for most people is adequate, particularly if the rate of infusion is high enough. Sometimes however, this still does not provide adequate relief. If this is the case, the block can be topped up with higher concentration anaesthetic (0.75% Ropivacaine), something that is easily done as a bolus injection into the catheter.

This method has proven a revolution in post operative pain control for this sort of surgery: and thus, the use of an adductor canal catheter with an infusion pump is now part of standard protocol (where possible) for Dr Holt's patients.

The problem with adductor canal catheters, is that the position of the catheter, as it enters the skin, coincides with the site of the tourniquet. Hence, the tourniquet (if used) is inflated over the top off this. This means that the tip of the catheter may move far enough away from the nerve to be ineffective. Fortunately however, this is uncommon and, if it does happen, the catheter can be easily replaced on the ward by the Pain Management Physician (who is also an Anaesthetist).

**Complications of nerve blocks** are not uncommon but, fortunately, usually not permanent. All nerve blocks have a small potential for nerve damage which, in the sensory distribution, is usually in the form of prolonged dysesthesias (numbness, funny pains, burning feelings, and/or tingling along the course of the nerve). In almost all cases this fully resolves, but it may take 3 - 12 months to do so. If only a sensory nerve has been blocked however (as in an adductor canal block), then no weakness ensues. Thus, the benefits out-way the potential risks, particularly in the elderly.

When a major nerve (femoral or sciatic) has been blocked, there may be an associated motor nerve problem leading to a delay in the recovery of muscle strength and function: and hence some residual weakness. This problem seems to be less common now that Anaesthetists are injecting the local anaesthetic under ultrasound guidance rather than just

by nerve stimulation techniques, but it does not abolish it completely. Often it is mild and clinically undetectable, but we know that a femoral nerve block in the elderly will double the likelihood of a fall in the subsequent 3 months when compared to those not having a block. On the other hand, that risk needs to be balanced against the benefits of reduced levels of narcotic analgesia, and the subsequent confusion that it can create, during the period of hospitalisation.

The other concern with major nerve blocks, more particularly when ultrasound guided injection was not available, was the potential to damage the major vessels of the limb. Both the femoral nerve where it lies in the groin, and the saphenous nerve where it lies in the adductor canal, pretty much lie next to, or lie on, the femoral artery and vein. Hence, there is a potential for injury to these vessels, albeit a remote one.

With the more recent adoption of ultrasound guidance for these blocks, this would now be considered a rare event. In addition, it is one that would most likely be observed in real time, and thus could be dealt with immediately. Any leakage of blood from a vessel can be seen whilst scanning and, if such occurred, treatment by pressure application could be instigated until bleeding stopped: hence, straight forward.

Late problems, such as a false aneurysm (a balloon like swelling) of a vessel due to damage of the vessel wall, are very rare. They may however, take months to cause symptoms or be detected. Even when they occur and are detected however, they are not always problematic: and therefore may not need any active treatment.

**Epidural Anaesthesia** is often used as an accessory to general anaesthesia. Most usually, this was used when both knees were replaced at the same time. This is now done less commonly than previously because Anaesthetists are becoming better at adductor canal blocks.

Epidural catheters sit in the epidural space. That is the space that is outside the dura (which is the sheath around the spinal cord). The local anaesthetic that is instilled therefore, bathes all the nerve roots that pass out from the spinal cord below a given level. The more anaesthetic that is put in, the more the space fills up, hence the block gets higher. The result of a rising block is increasing numbness, and a progressively rising numbness which can move up towards the waist or even higher. This is something that needs to be watched and, if noticed, reported to the nursing staff so that they can decrease the amount of anaesthetic that is pumped into the space.

When it works, epidural anaesthesia provides very good pain relief. The problem with epidural anaesthesia however, is that it is not always reliable. It often affects one leg more than the other, and it can be difficult to get it to spread to the side where it is required. To try and correct the spread, and to get it to an area of need, may require being rolled right onto your side for a while so that the anaesthetic will move across the space. This can help. There are however, a percentage of cases where the technique proves inadequate, and other

options may then need to be explored.

Another problem with epidural anaesthesia is that the catheter can only be left in for a maximum of 3 nights. The catheter leads directly to the spinal canal, and hence, there is a potential for skin organisms to pass along the catheter and infect the epidural space. Accordingly, the catheter is electively removed on day 3 to prevent that happening. When this is done, any prophylactic blood thinning is missed out so that bleeding into the epidural space does not occur; something that is always a potential problem when needles and catheters are introduced into this area.

**Epidural bleeding** is the complication, albeit rare, that is most feared from this technique. It is usually venous bleeding, and hence at low pressure. The space is large, so that it may take a long time to bleed into it to the extent that the pressure in the space starts to rise. This means that the onset may be slow or very delayed, and the initial signs may be minimal. Potentially however, weakness or paralysis can ensue. The diagnosis can be very difficult to make early on, and indeed, may only be suspected when precipitous events occur. Also, the only way of excluding or confirming this complication is with an MRI scan, something that takes time to obtain: and the only treatment is surgical decompression, something that may take considerable time to arrange.

Although rare, it is the risk of this complication that makes anyone with a bleeding diathesis, or who is on a long term blood thinner, unsuitable for an epidural anaesthetic. It can however, be used with the controlled low dose anti-coagulation that is routinely used for most knee replacements, albeit that a dose may need to be missed out on day 3 to allow safe removal of the catheter.

**Spinal Anaesthesia** is slightly different to epidural anaesthesia. With this form of anaesthesia, the local anaesthetic is placed inside the dural space rather than outside it. This then puts it directly in contact with the spinal cord. This makes this much more reliable than epidural anaesthesia but, because of its location, no catheter can be inserted. This means that this is a once only form of anaesthesia, usually given just prior to sedation or a general anesthetic, and not topped up or repeated. It provides complete and reliable anaesthesia, and can be used with just sedation rather than a general anaesthetic if needs be. It usually lasts for many hours post surgery, depending on the nature of the anaesthetic material used.

In both epidural and spinal anaesthesia, local anaesthetic can be mixed with a narcotic, be that morphine, fentanyl or whatever. This is quite a useful adjunct, and allows the use of quite a low dose of narcotic compared to when it is given systemically (into a muscle or vein). Hence, side effects such as nausea, itching, and so forth are much less common. The limitation of adding a narcotic to the local anaesthetic in these situations however, is that the body becomes temporarily sensitized to that narcotic. This means that, until the spinal

effect of the narcotic has worn off, systemic administration of these drugs has to be limited. Generally this is not a big problem, but occasionally it limits the options somewhat.

The use of spinal (intra-thecal) narcotic alone, without adjunctive local anaesthetic, is reasonably popular. It has advantages of good analgesia without numbness or paralysis of the muscles. It can also be used with adjunctive blocks, and with direct instillation of local anaesthetic into the joint. Thus, it can be regarded as complimentary to a standard post-operative, analgesic protocol.

### **Tranexamic Acid**

This is a drug that stops clot being dissolved quite as easily as is normal. It thus decreases bleeding, which in turn lessens pain and swelling. In addition, it lessens the chance of needing a blood transfusion, particularly when both knees are being replaced simultaneously. This is, in turn, important, because transfusion is known to be associated with an increased infection rate. In addition, transfused blood is, by its nature, both foreign and old. Hence, it gets removed by the body fairly quickly. Any advantage therefore, is somewhat short lived. This then makes its indications limited and, in most cases, it is better to wait for the body to make up the short fall rather than to proceed to transfusion.

Tranexamic acid can be given intravenously or by tablet. It can also be put directly into the knee, thus providing a high local dose with equal efficacy to intravenous use (based on several studies). It has also been shown that there is some additive benefit to using a combination of both intravenous, and intra-articular, tranexamic acid: hence, this combination is now part of Dr Holt's standard protocol when performing a knee replacement.

### **Post-Operative Measures**

**Patient Controlled Analgesia (PCA)** was once, before the advent of adductor canal blocks, the commonest of all the post operative methods of pain control. It involves having a pump which can be activated by pressing a button on a hand control. This then leads to the delivery of a set amount of narcotic which goes directly into the vein. The amount of narcotic delivered is set by the Anaesthetist. What is also set, is a restriction on how often the button can be pressed (usually a 5 minute lockout), such that overdose is unlikely.

**Fentanyl** is the commonest drug used for this and, for most people, provides reasonable analgesia without too many side effects. For some however, this does not provide adequate analgesia. In this situation, the best option is usually to change the drug to one of the other narcotics (such as morphine, pethidine or hydromorphone), which are stronger analgesics. The downside to this is that there may be an increase in the side effects related to the stronger narcotic, albeit that this is not always the case. Indeed, because the dose required is lower, the side effects may actually be less rather than more.

**Morphine** is perhaps, still the most significant pain relieving

drug available. Although not used as much as previously, it can provide excellent pain relief in the situation where something like a fentanyl PCA is proving inadequate.

**Hydromorphone**, a derivative of Morphine, is 5 times more potent on a weight for weight basis than Morphine itself, but seems to have less side effects. It is therefore a good choice when morphine sensitivity is an issue. In addition, it comes in tablet form, and hence it can be continued after the PCA (with the intravenous line) has been removed (usually day 2-3). It is often used by anaesthetists both during the procedure, and for immediate pain control in the recovery room.

**Pethidine**, a totally synthetic opioid, often provides excellent analgesia with few side effects. Again therefore, it may be a good choice when morphine leads to nausea or other problems. It is currently out of fashion, whereas it was once the mainstay of all post-operative analgesia. It is a very effective drug and has relatively low levels of side effects. By preference however, it should not be used as a PCA in children and adolescents where it can sometimes cause convulsions.

Note that pethidine is actually considered safe in the younger age groups, including children, but only when it is given by intramuscular injection, where the dose is fixed, and release into the system is slow. It is only with intravenous administration (including PCAs) that problems occur in this age group.

**Other drugs** can be incorporated into PCA's, just like they can be included in epidural and spinal anaesthetics. The commonest one that is used is Ketamine which, on its own, is actually a general anaesthetic. In lower dose however, there is some evidence that it helps modify pain in some people when used in conjunction with a narcotic. Our experience with this however, is that it often leads to confusion and a feeling of being 'spaced out'. Whilst Anaesthetists sometimes prescribe this therefore, in practice it seems to have very limited value: and it often has to be removed from the mixture.

**The advantage of PCA techniques** is that they are 'on demand' and work quickly. The disadvantage is that, if the button is needing to be pushed as often as every 5 minutes or so, then one has to be awake to control the pain adequately. This then makes it difficult to get some sleep without a flare up of the pain. In this situation, it is generally better to change drugs to one that is stronger, and/or one which will give more long lasting pain relief. This will be needed in about 1 case in 3 where Fentanyl has been the first choice of analgesic. Changing it is simple to do, just requiring a change in the infusion fluid, which is pre-prepared with the narcotic already in it.

Alternatively, an oral, slow release, background narcotic can be used in conjunction with a PCA. This is a common additive to post operative analgesic regimes using drugs such as Oxycodone, Hydromorphone or Tapentadol (see below for further information on these drugs).

PCA's can be made to give a constant infusion of narcotic, which can then be added to by pushing the on-demand button. A constant infusion PCA is not used very often because of the risk of overdose, particularly when sleeping. Such overdose may lead to respiratory depression, meaning that it decreases breathing rate and depth which, if sustained, can lead to problems including loss of consciousness. This therefore, is generally not as good an option as changing up to a stronger analgesic drug to be used under direct patient control.

**Complications of Opioid Analgesics** are usually avoidable or treatable. In general, all opioids cause respiratory depression with higher doses, hence PCA's (Patient Controlled Analgesia) are programmed to have dose limits. Both the dose, and the duration between doses, can be programmed into the pump so that overdose does not occur. There is therefore, a balance to be struck between too much and not enough, and this may take a day or so too fully sort out. The ward staff however, are very experienced at this. There are also dedicated Acute Pain Service Nurses in the hospital who help to look after both adductor canal blocks and narcotic related problems.

As well as respiratory depression, all opioids can cause nausea and vomiting which will require treatment, possibly including a change of drug. Sometimes however, a better dosage regime, providing a lower dose of the same drug but more often, is also effective.

All narcotics, can cause intense itchiness, usually most marked on the nose and face. This is not an allergic reaction, but is a direct result of the narcotic. Often it settles with an anti-histamine such as Promethazine (Phenergan), but occasionally, the drug needs to be changed.

**Anti-inflammatory drugs** can be of significant benefit when combined with narcotics. In general they work best when given immediately pre-operatively or at the time of surgery. Generally the Anaesthetist will make that decision depending on what other drugs he is planning to use. All of the anti-inflammatory drugs have been shown to help, no matter which group is used. The more established and older NSAID's (non steroidal anti-inflammatory drugs) such as Nurofen, Voltaren, Naprosyn, Indocid, Feldene etc., all work well. The newer NSAIDs (the COX-2 inhibitors) which include Celebrex and Mobic, are perhaps not quite as good anti-inflammatories as the older NSAID's, but seem to have at least similar, if not slightly better, pain relieving qualities. Hence, these drugs are often chosen as part of a regular post-operative protocol.

Whilst these agents are reasonable adjuncts, they need to be taken with food so as to decrease the chance of stomach upsets, including ulceration and bleeding. These gastric complications can limit their usefulness, particularly in the elderly who are most prone to them. If needs be, NSAID's can be given along with a gastric acid inhibitor (which decreases the stomach side effects) but, if any abdominal symptoms develop, they should be stopped altogether.

Slightly different to the usually prescribed COX 2 inhibitors, but of that class, is a drug called Ketorolac (Toradol). This is by far the best analgesic of the anti-inflammatories, and can be given by both intra muscular injection and tablet. It is said to have nearly 50 times the analgesic effect of Naproxen (an NSAID) and, for a good number of people, it provides excellent analgesia without the side effects of narcotic analgesia. The problem with this drug is that it is potentially toxic to the kidney. This means that if renal function is not normal, and certainly in the older population group where this is a possible problem, it cannot be used safely. Even in the younger population with healthy kidneys, where it can be used, there are limitations: and this means 3 times a day for 3 - 5 days maximum. If used with these provisos however, Ketorolac can be an excellent adjunct to standard narcotic analgesia.

Because of its potential for renal problems, Ketorolac tends to be used on lower than maximal dose (10mg rather than 30mg), and it cannot be used if another background anti-inflammatory is being used because of the additive effect. It is therefore, sometimes preferable, not to use a background anti-inflammatory, just so that this drug can be utilised. This may be the case where all the stronger analgesics are not being well tolerated.

### **Cortisone and related drugs**

Cortisone (a corticosteroid) is a naturally occurring steroid that is made by the body, and is essential for life and well being. It is a glucocorticoid, and therefore is not anabolic. This means that it will not help muscle development, strength or fitness. What it does do however, is to help maintain body functions, including regulation of glucose metabolism (where it opposes insulin), and others. When used in higher doses it becomes a very strong anti-inflammatory agent, being much more powerful than the ones described above. In this role, it reduces both swelling and pain. In addition, it reduces scar formation, which means that it can decrease the amount of abnormal scarring around a joint: hence, helping to keep it mobile and thus to increase the range of motion of that joint.

All of the above has been shown by various studies, but it is only recently that Cortisone and related compounds have been used on a broader basis to help post-operative recovery. The reason for this has always been a concern about the increase in the risk of infection. One of the ways in which cortisone acts is to reduce immuno-globulin action, and hence the bodies defences. Indeed, this is one of the mechanisms that it uses to decrease inflammation and scarring. Despite this, if cortisone is used systemically, rather than in or around the surgical site, the increased infection risk appears to be negligible.

There are studies available that have reviewed the effects of Cortisone that has been used locally, having been injected into the joint capsule, or the wound edges, at the time of surgery. These seem to show very favourable results in

terms of pain control but, we know from the studies done using these techniques for simple knee arthroscopy, that the infection rates are definitely higher. In other words, the locally injected cortisone seems to reduce immunity at the wound or joint site, and this seems to be important. For this reason therefore, we do not use Cortisone in this way. Instead, we restrict it to systemic use, given by injection, and then by tablet when needed.

When using Cortisone in this way, it is important that it is started before the surgery. We therefore get the anaesthetist to do this at the time of induction of the anaesthetic, just prior to commencement of the procedure. This then gets cortisone into the tissues that are being operated on before surgery is commenced. This initial intravenous dose is then (usually) followed by 5 or so days of cortisone taken in tablet form.

By using Cortisone in knee replacement, we have found that pain levels are lower, narcotic use is lower, swelling is reduced, and range of motion is better. Studies concur with this, in that, they show significantly lower levels of inflammatory markers in the blood (and hence inflammation at the surgical site) after surgery when Cortisone is used in the peri-operative period. The down side of Cortisone however, is that it cannot be used on a prolonged basis. If used for more than a week or so, it may have to be reduced slowly. This is because it suppresses the bodies own production of cortisone, and this manufacture then needs to start up again. In addition, when used in moderate doses for longer periods of time, it leads to fluid retention and loss of calcium from the bones (osteoporosis). As previously mentioned, it also opposes the effect of insulin, essentially raising blood glucose levels. For this reason it has to be used with caution in diabetics, particularly insulin dependent diabetics where, if used, the insulin dose may have to be increased.

The usual regime in knee replacement is to give 4 - 8mg of Dexamethasone (a powerful synthetic corticosteroid) at induction, then to follow this up with a 4mg dose at 24 hours post surgery. Thereafter, a 25mg tablet of Prednisolone (the body makes the equivalent of about 5 - 7mg of prednisolone per day) is used each day for 5 - 7 days. It is taken in the morning because it has some propensity to keep people awake. Only in unusual circumstances would this be continued past the one week mark, a time frame after which it can be safely stopped without any tail off or dose reduction being required.

## **Oral agents**

What is helpful with any of the above techniques, is to institute a regime of oral analgesia, including both slow release and quick release drugs. The slow release tablets can provide a constant level of background analgesia, with a fast release option being used to control any break through pain.

**Paracetamol** is a drug that is generally used as low dose background analgesic. It is common for it to be used in addition to whatever other drugs are being prescribed.

The advantage of Paracetamol is that, in low dose, it is well tolerated and can be continued for long periods of time without addiction. It produces very little in the way of nausea, and thus, can be used in situations where other drugs are not tolerated. Also, it does not affect the bowel like codeine and the narcotics, so it does not cause constipation.

The down sides of Paracetamol are firstly, that it is not a very powerful pain killer, and secondly, that it has a low threshold of toxicity. If more than 4gm per day (8 standard 500mg tablets) is used, the chance of liver failure becomes real. This therefore limits its use as an isolated analgesic in the early post-operative period.

Note that Panadol-Osteo is just Paracetamol that is released at a slightly slower rate than normal Paracetamol. It does not contain any other agent for pain relief. By being slow release it has a slower rate of onset but, on the other hand, it only needs to be taken 3 times per day because it enables the use of a slightly bigger dose (2 x 665g tablets = 1330mg, 3 times per day: i.e. ~4g per day) than the normal 4 times per day Paracetamol (2 x 500mg tablets = 1gm, 4 times per day: i.e. 4g per day).

**Paracetamol / Anti-Inflammatory combinations** have been found to be very useful in that: they are generally well tolerated, do not cause significant nausea or constipation, and, in some studies, have been shown to provide analgesia equivalent to some of the narcotics such as those described below. For this reason, such a combination is generally used after most surgery.

With the banning of codeine as an over the counter medication, there has been an emergence of freely available Paracetamol / Anti-Inflammatory combination tablets. Such drugs as Nuromol (Paracetamol 500mg with Ibuprofen 200mg per tablet), Mersynofen (Paracetamol 500mg with Ibuprofen 200mg per tablet), and Maxigesic (Paracetamol 500mg with Ibuprofen 150mg per tablet) are now all over the counter medications for which the recommended dose is 2 tablets, 4 times per day. The limit on the daily dose is set by the Paracetamol component for which the safe maximum dosage is 4g Paracetamol per day - i.e. 8 tablets (2 tablets, taken 4 times) per day of the above combinations.

The Ibuprofen dose in these combination tablets is limited to the recommended over the counter limit of 400mg, taken 4 times per day: i.e. - 1600mg total per day. The prescription dose, and one that is safe for most adults for short to medium lengths of time, is 800mg, 3 - 4 times per day: i.e. up to 3200mg per day. If ibuprofen is used therefore, the dose can be increased by adding extra Ibuprofen tablets, be that 1 or 2 of the 200mg over the counter ones (like Nurofen or Advil) added to each of the combination tablets. This then increases the Ibuprofen dose without exceeding the safe daily limit for Paracetamol.

Other combinations exist, and perhaps the most usual is to take the Paracetamol separately (either as the usual quick

release, or as the slower release Panadol Osteo) and add in a Cox-2 selective non-steroidal anti-inflammatory drug (NSAID) such as Celecoxib (Celebrex) or Meloxicam (Mobic). For the short period of hospitalisation time these can be taken in slightly higher than the standard recommended dose (for large adults 200mg of Celebrex twice a day), but by the time of discharge this dosage should be lowered to the recommended level (100mg Celebrex twice a day). It is probably also best to take these drugs as a twice a day tablet rather than using the larger dose tablets just once a day.

All NSAIDs have cardiovascular side effects if taken for prolonged periods with up to a 35% increase in major events being reported for Celebrex. In addition, they have a relatively high incidence of gastric side effects, including bleeding and perforation. They also cost 5 times as much as Ibuprofen, and some studies would suggest that the pain relieving effects are similar. Clearly therefore, these drugs are not meant for prolonged use.

**Paracetamol / Codeine combinations** are quite useful where other stronger analgesics are not well tolerated. They increase the effectiveness of the Paracetamol by providing the addition of some Codeine. Codeine, like some of the below agents, is a morphine derivative. In low dose however, it rarely causes nausea but, like the other related compounds, it can cause constipation, particularly when used in higher doses.

This combination of drugs comes in a variety of sizes, each of which can be taken 4 times per day. As each combination contains Paracetamol, it must not be taken with any other Paracetamol or Paracetamol containing tablet for fear of overdose and liver damage.

The combinations available are as follows, albeit noting that there is more than one brand of each combination, others having a different brand name to the one listed:

Paracetamol 500mg / Codeine 8mg (Panadeine)  
Paracetamol 500mg / Codeine 15mg (Panadeine Extra)  
Paracetamol 500mg / Codeine 30mg (Panadeine Forte)

Each can be taken up to a maximum dosage of 2 tablets, 4 times a day - the limit being the same as for Paracetamol. Although increasing the Codeine amount does increase the analgesic effect, the difference between Panadeine Extra and Panadeine Forte is not all that great so, generally, the former is preferred given its lower constipation rate. All codeine containing drugs now require a prescription.

**Oxycodone** is the commonest oral agent that is used post surgery. As a quick release drug (Endone, Oxynorm) it comes in 5mg, 10mg and even bigger doses. It works fast, provides quite good levels of analgesia, and can be repeated often. One of the advantages of this drug is that it is relatively non-toxic. This means that, unlike something like Paracetamol, the dose can be increased as needed without too much concern about toxicity. Indeed, in some instances, it can be taken every 2 hours if needs be.

If tolerated, then Oxycodone can also be given as a slow release tablet (Oxycontin, Targin) which leaches out over 12 hours. When used, any fall off in pain relief can then be dealt with by using the quick release version to fill in the gaps. The slow release version of choice used to be Oxycontin. This however, is now used less often than the newer alternative, which is Targin. The latter not only contains slow release Oxycodone (similar to Oxycontin), but it also contains a narcotic inhibitor (Naloxone). Essentially, the inhibitor counteracts the effect of the Oxycodone in the gut. As it is de-activated by the liver before it gets into the systemic circulation, the Naloxone does not effect the systemic analgesic quality of the Oxycodone. By reducing the effect on the gut however, constipation and loss of bowel function is reduced, which is advantageous.

Unfortunately, the effect of the Naloxone does not persist as long as the effect of the slow release Oxycodone, and hence, the effect on the gut is not perfect. It is however, better than when slow release Oxycodone (Oxycontin) is used alone. For this reason, we try and start this drug early on in the post-operative period, particularly if the Anaesthetist has provided a PCA. This then provides not only a continuous background pain relief, but it also helps lessen the constipating side effect that all the narcotics (including the PCA delivered ones) have.

**Targin (Oxycodone with Naloxone)** comes in many sizes. For most people we start at a dose of either 10mg/5mg (10mg of Oxycodone and 5mg of Naloxone) or 5mg/2.5mg being given twice a day. If tolerated, this dose can then be increased, albeit rarely exceeding 20mg/10mg twice a day.

Like all narcotics, Oxycodone is potentially addictive. For this reason we like to get people off the drug by 2 months post knee replacement. By this stage, a few people may show some signs of addiction, but most do not. Unfortunately, addiction may not be clear until the drug is ceased, giving rise to shaking and shivering etc. ('cold turkey' if you like). The only way past this is to stop the drug. Trying to reduce the dose, or to wean of this slowly, does not work. Rather, it just prolongs the problem and makes it worse. Sometimes, giving a related drug (such as Codeine) is helpful in that it seems to reduce the side effects of withdrawal and, in itself, such a drug is much less addictive. Hence, something like Panadeine Forte (Codalgin Forte etc.), which has quite a bit of codeine in it, can be used.

**Hydromorphone.** When Oxycodone causes nausea or dizziness, Hydromorphone is often a good alternative. Although this is also a Morphine derivative, it seems to have less side effects than either Morphine or Oxycodone. It is similar in its analgesic effect, and it is relatively non-toxic. The dose can therefore be increased for short periods without too much risk of problems developing. This drug comes in a 2mg quick release form (Dilaudid) and an 8mg, once a day, slow release form (Jurnista). Like Oxycodone, the quick release form can be taken every 2 - 4 hours if needs be.

The 8mg slow release tablet (Jurnista) is usually best taken in the evening so that the effect lasts all night, this being the hardest time to control pain. This formulation however, does last pretty close to 24 hours, and its level in the blood stream is remarkably constant throughout this period. It is however, only once a day drug, and should not be repeated 12 hours later. Larger dose formats, including 16mg and above, do exist if required. This is however, uncommon after surgery such as knee replacement.

Like oxycodone, it is advantageous to try and get off this drug by 2 months post surgery, and sooner is better from an addiction point of view.

**Tramadol (Tramal).** This is an unusual drug which, whilst still regarded as an opioid, is not a morphine derivative: indeed, it is classed as a Benzenoid and it acts somewhat differently from them. Like the other opiates, it binds to the  $\mu$ -opioid receptor to provide its analgesic effect, but it also acts as an SNRI (Serotonin–Noradrenaline Re-uptake Inhibitor). Most modern anti-depressants are SSRIs (Selective Serotonin Re-uptake Inhibitors), but some versions are SNRIs: hence there is a potential problem if any of these anti-depressants are used at the same time as Tramadol. In addition, if physical dependence occurs (something that WHO - the World Health Organisation - would suggest is actually a low risk when it is used for short periods of time only) then withdrawal may come as a combination of opiate withdrawal and SSRI withdrawal.

Tramadol is quite a strong analgesic and, like Oxycodone and Hydromorphone, comes in both quick and slow release versions. Tramadol has some activity in its own right, but some of it gets converted in the liver to desmetramadol which is a much more active metabolite (700x more active at the  $\mu$ -opioid receptor site).

Tramadol has a recommended dose limit of 400mg per day. Studies in cancer patients however, have suggested both efficacy and safety up to 600mg per day in normal size adults. A true upper limit has not been established. It comes as a 50mg immediate release capsule, and as 50mg, 100mg, 150mg and 200mg slow release capsule. It is a drug that has less effect on the bowel than the morphine derivatives and, because of its decreased addictiveness, it can be used for a longer period of time post surgery.

The down side to this drug is that 1 person in 3 seems to get some nausea with it. For the rest however, it seems to give very little in the way of side effects. This then makes it a very useful drug for those people.

The nausea and vomiting is thought to be due to activation of (but it does not bind to) the 5-HT<sub>3</sub> receptor which produces increased serotonin levels. Thus: Metoclopramide (Maxolon), a 5-HT<sub>3</sub> receptor antagonist, can be used to treat tramadol-associated nausea and vomiting. On the other hand, Ondansetron (Zofran), a commonly used anti-emetic, and also a 5-HT<sub>3</sub> receptor antagonist, may partially reverse

the analgesic effect of Tramadol by that same mechanism.

Tramadol is often used with concomitant Paracetamol therapy, a combination that has been shown to increase its efficacy.

Like Tapentadol (see below), it has been shown to reduce the seizure threshold. Hence it has to be used with caution, or not at all, in epileptics. It can also lead to serotonin syndrome (see below) in those taking other serotonin re-uptake inhibitors - usually the SSRIs used for depression.

The other factor to be considered, is that this drug is currently categorised differently to the morphine derived narcotics. This means that the quick release version can be prescribed with repeats, unlike Oxycodone or Hydromorphone. The slow release version cannot however, and only 1 box (20 tablets) at a time can be supplied.

**Tapentadol (Palexia),** like Tramadol, is an opioid analgesic of the Benzenoid class. Like Tramadol, it binds to the  $\mu$ -opioid receptor to provide its analgesic effect, and it also acts as an NRI (Noradrenaline Re-uptake Inhibitor). Unlike Tramadol however, it has minimal activity as an SRI (Serotonin Re-uptake Inhibitor). It is also a significantly more potent opioid and does not have any active metabolites. It has an analgesic effect similar to Oxycodone, but with a lower incidence of side effects. A 50mg dose of Tapentadol is roughly equivalent to 3mg of Morphine.

Tapentadol comes in both IR (immediate release) and SR (slow release forms) and, unfortunately, unlike hydromorphone, the trade name is the same (Palexia), albeit followed by the letters IR or SR (or CR for continuous release which is the same as SR). Hence, some care needs to be taken when looking to see which drug is being taken.

Tapentadol, like Tramadol, is limited in its daily dosage. The recommended starting dose is 50mg SR taken twice a day, with a maximum total daily dosage being no more than 600mg. This can be achieved by slowly working up to say: a 150mg SR dose taken twice a day plus a 50mg IR dose taken every 4 hours. This will give the maximum dose of 600mg. Alternatively, one could take a 250mg SR tablet twice a day, leaving 2 x 50mg IR tablets for emergency extra cover.

Tapentadol comes as 50mg, 75mg and 100mg IR (immediate release), and 25mg, 50mg, 100mg, 150mg, 200mg and 250mg SR (slow release) tablets.

The big advantage of Tapentadol is that it seems to cause less nausea than Tramadol, and hence it is better tolerated. Like Tramadol however, it decreases the seizure threshold, so should not be used in epileptics. In addition, these drugs should be used with caution with alcohol as their plasma level is raised when alcohol is imbibed. This can cause respiratory depression which, as a worst case scenario, can lead to respiratory arrest. It is a serotonin re-uptake inhibitor like tramadol, albeit to a much lesser degree. Hence, while it can also lead to serotonin syndrome in patients taking other

re-uptake inhibitors such as SSRIs for depression, it is perhaps less likely to do so.

The TGA classify Tapentadol as S8, similar to Oxycodone, Hydromorphone and Morphine, based on the potential for recreational abuse. There are recommendations from world bodies to reduce this to a wait and see mode due to low levels of incidence, but currently it requires a separate script; and repeats on that script are not permitted.

**Duration of therapy.** Once the 8 week mark post surgery has been reached, if Oxycodone or Hydromorphone are still being used, it is a reasonable option to try and come off these drugs, and change to Tramadol or Tapentadol. This then usually provides adequate on-going analgesia, but with less toxicity: and a potential for more prolonged use if necessary.

In the majority, it would be expected that all moderate strength analgesics will have been ceased by about the 3 month mark. By then, either complete cessation of all analgesics, or a reduction to just the lower level ones like Paracetamol (or Panadol-osteo, the slow release version), with or without an adjunctive anti-inflammatory, would be expected.

**Serotonin Syndrome.** Of note with Tramadol and (to a lesser degree) Tapentadol, is that they have a tendency to raise serum serotonin. By itself this is not harmful. When used with an SSRI (Selective Serotonin Re-uptake Inhibitor) anti-depressant however, that combination can sometimes, albeit rarely, lead to a condition called serotonin syndrome. This is usually manifest as an uncontrollable rise in temperature in the first instance, but can progress and become more serious thereafter. Immediate treatment is required for this.

Fortunately this syndrome is rare, even when these drugs are used in combination: and certainly it would be unlikely if the dose of the SSRI is low. In line with this however, general advice is not to use Tramadol or Tapentadol if there is concurrent use of an SSRI. It is important therefore, that we (the medical community involved in your care) know if you are on such a drug, so that concurrent use will not occur.

**Combination therapy.** It is to be noted that if analgesics work differently, they can be taken together. Thus, Tramadol or Tapentadol can be taken at the same time as Oxycodone or Hydromorphone, Panadeine Forte or Paracetamol. Similarly, an anti-inflammatory can be used at the same time as well. Ideally however, it is better to try and optimise the analgesics that are being taken, raising or lowering doses to an appropriate level, rather than using too many different analgesic drugs at the same time.

## Patches

Various drugs come as slow release patches. These are usually narcotics, and have the benefit of leaching out a constant supply of analgesia over a long period of time. They tend to be lowish dose, so they are not suitable for everyone. In addition, they are addictive just like their injectable and tablet

counterparts, so their use is still limited to the early weeks after surgery. The drugs most commonly used are Fentanyl (Durogesic) and Buprenorphine (Norspan). They come in various doses, and the patches need to be changed every 3 - 5 days or so (depending on the type of patch used). In general, they are not as effective as oral medication, so they are not used in the post operative situation all that often. On the other hand, if the stronger oral medication leads to nausea or other intolerance, then a patch may be a reasonable option to consider. On the positive side, they provide a constant background level of analgesia which does not require reminders every few hours to make sure it is taken. This is particularly helpful in the elderly.

**Fentanyl** is a synthetic opioid, which has a rapid onset and short duration. It is thus favoured by most anaesthetists for initial peri-operative pain, usually being delivered intravenously by a PCA pump (see above). It also comes as a patch however (Durogesic), and hence is sometimes used where other analgesics are not tolerated. It has moderate analgesic effects in this format, with varying strengths being available.

**Buprenorphine** is a semi-synthetic opioid which is slightly stronger than fentanyl, but it is also more addictive and more prone to side effects. For this reason it has largely been abandoned as an injectable drug. As a patch however, it (Norspan) seems to work much better, and thus it tends to be used a moderate amount for chronic pain control. This includes post operative pain control in some instances.

Buprenorphine also comes as a sub-lingual medication which is useful post surgery for breakthrough pain. It has a fairly rapid onset of action and can achieve good analgesia without the need for injection. Hence, it is sometimes used instead of a PCA. It is not recommended for longer term use as it is moderately addictive.

## Pain modifying agents

These can be very useful as adjuncts to any of the above drugs. Perhaps the most commonly used one now is Pregabalin (Lyrica). This is usually classified as an anti-epileptic. Nobody is exactly certain as to how it works as a pain modifying agent but it does block various calcium channels. Even in low dose it can make a big difference to some people's pain, but that improvement cannot be predicted ahead of time.

Sometimes these drugs are started pre-operatively, but more commonly, immediately post surgery. It has been shown that, for most people, Pregabalin can reduce the narcotic use for the first 48 hours. After that though, there is no difference in usage, hence, this drug is usually discontinued at that juncture. There is also some evidence that the use of post operative Pregabalin can reduce chronic residual pain after surgery. Whether this is the case when it has been used in the first few days, or with the use of better local anaesthetic techniques, remains to be seen. For the moment however, the indications to continue its use for longer periods post

operatively are outweighed by the side-effects and the potential for withdrawal problems.

Sometimes, if the pain post-operatively is not settling, a trial of Pregabalin is worth undertaking. For some people it can turn the pain around and thereby reduce the need for other analgesics. This effect is sometimes quite dramatic.

A few people on the standard Pregabalin dose of 75mg twice a day can feel somewhat 'spaced out' or 'out of body'. This drug can sometimes be used effectively in lower doses than this however (e.g. - 25mg twice a day), which may cause less side-effects.

If needs be, the dose can be increased up to 150mg three times a day or even more. For many however, the increase in dose just causes more side effects without necessarily giving much extra pain modifying effect. For this reason, if used, one would normally start at a low dose (25 - 75mg twice a day) and only build up if necessary.

Other drugs that modify pain in the same way as Pregabalin (Lyrica) are also available. A slightly older, but similar drug, Gabapentin (Neurontin) is still in use, and may represent an alternative to Lyrica if side effects are experienced with that drug. Other anti-convulsants such as Carbamazepine (Tegretol), once the mainstay of this sort of treatment, are now rarely used in this situation. The much older tri-cyclic anti-depressants such as Amitriptyline (Endep) are now used much less often for this purpose, but still exhibit some pain modifying effect even if this is not their main role. The sedative effect of this drug however, may be helpful if used at night.

### **How long will I need to be on pain killers?**

This is very variable. Frequently however, particularly after knee replacement, most people will take something every night for at least 3 months. By the end of that period most are only taking Paracetamol, however, getting a good nights sleep can be quite difficult up until then. The pain is always worst at night, perhaps because the joint has been used during the day, exercising and so forth, and perhaps because, at night time, there is little else to distract one from the pain. Either way, night time is always the worst and, even if it is not strictly pain as such, there is often a discomfort that requires treatment. Note that discomfort is, in reality, just a different interpretation of pain, and it will therefore respond to analgesics the same as other manifestations of pain.

**Sleeping tablets.** Where the pain is not too bad, but where getting to sleep is still an issue, a sleeping tablet may prove the answer. Temazepam (Normison, Temtabs, Temaze, APO-Temazepam), is perhaps the most common one available. It tends to help one get off to sleep, and then gives reasonable sleep for 4 hours or so (but longer in some). A starting dose of one 10mg tablet is usual but 20mg can be taken. This can be done either by taking 20mg initially, or by using two 10mg tablets sequentially. If waking after 3 - 4 hours without being able to get back to sleep becomes a problem, then the latter

method may be applicable.

Temazepam (a benzodiazepine) is much preferable to a drug like Stilnox, a drug that is borderline for being taken off the market because of side effects. Although temazepam is potentially addictive, this is unlikely to happen over a 4 - 6 week period and, by 3 months, is unlikely to still be necessary.

### **Therapy**

After an operation such as knee replacement, where there is little that can be damaged, using the joint can actually help the pain. Certainly, those who get good motion early on, have less pain (and perhaps vice versa). The evidence however, is that those who push through the pain somewhat, particularly whilst in hospital, not only get better range, but have better pain scores in the short, medium and longer terms. For this reason, the physiotherapists will encourage early use of the knee and, if flexion past 90° is not being maintained after discharge, then outpatient therapy will be advised. This is not just exercise, it is critical to maintain range in the joint and not to let it stiffen up.

What has also been shown is that walking with a normal gait helps reduce pain. It is therefore important that, early on, attempts are made to use the knee properly whilst walking, aiming to restore a normal gait pattern as soon as possible. Again, the physiotherapists can help you with this, be that in hospital or thereafter.

Following discharge, pool therapy is perhaps the single best rehabilitation aid and, whilst the water makes the joint feel better, it remains important to keep the range of motion going: and this may mean supervision by a therapist to keep an eye on things, rather than just getting in the water and walking up and down on your own. Again, it is the bending that is important, not the exercise. If you get in the pool, it is to bend the knee, not to walk multiple laps.

### **Ice and Heat**

In the hospital, and in the first week or two, ice therapy can be helpful. Despite the rumours, it does not directly help swelling. In the first few days however, it causes blood vessel constriction, and hence, it reduces bleeding. This of course decreases immediate swelling, and it also decreases pain and increases function. Ice is also a good analgesic, and hence it is used after exercise and walking. On the other hand, after about 7 - 10 days, when the risk of bleeding is starting to become negligible, heat packs may provide better pain relief. This hot and cold therapy can also be alternated if needs be. Again it is a trial and error situation, and everyone has to work out what helps them and when. The important thing though, is that heat should not be used in the first week or so for fear of increasing bleeding into the knee or the wound.

### **Who will manage your pain?**

Initially, the anaesthetist is responsible for your pain management. He knows what drugs have been used during

your anaesthetic, and he can tailor a regime to take you through the first 24 hours or so based on that. By and large, these regimes will be in line with what Dr Holt normally uses but, if needs be, Dr Holt will alter them accordingly.

By the day after surgery, Dr Holt will have been around the ward to check on everybody's pain management, and to make sure that all the necessary drugs needed for the duration of the admission and discharge have been charted. After that, it is just a matter of adjusting these according to individual needs, and this will be done on a daily basis.

Hollywood hospital does have Acute Pain Service (APS) Nurses who also come around to see how things are getting on. If they have concerns, they will be in contact with Dr Holt to discuss changes to the protocols or regime. Any changes will then be instituted immediately. If there are problems with pain control, it usually happens at night time. If the night nurses cannot manage to get things back under control, you can get them to ring Dr Holt at any time, day or night, to discuss this. As stated however, during the daytime, the APS Nurse is available.

**Adductor Canal (and Epidural) Catheter management** comes under the auspices of the anaesthetic department. Often, the anaesthetist who put the catheter in, will be in some other hospital in the days that follow surgery. As an adjunct to the Acute Pain Service however, Hollywood has an anaesthetist (usually Dermott Murphy) who is full time in the hospital, and can help with these problems. If the catheter is malfunctioning, requiring an adjustment or repositioning, this will usually be done by him.

Both the nursing staff on the ward, and the APS Nurses, are used to managing these catheters. They are the prime carers of these, but they will get help if, and when, needed.

**Overall pain management** requires a team to make it work. You the patient are part of that team, and your input is vital. If things are not working out, the other team members need to know. Things can usually be changed, even if the choices are limited. For most however, pain control can be stabilised in just a few days, starting on a standard protocol, then adjusting it by trial and error. No one regime suits everyone. The aim of the team is to optimise it for each individual such that the recovery is smooth and the range of motion is maximised.

## The commonest regime

### Anaesthetic & Induction

1. General Anaesthetic
2. Intra-Venous Antibiotics, Cortisone and Tranexamic Acid given at induction

### Procedure

3. Intra-operative narcotic - usually fentanyl
4. Adductor canal block with a catheter to be left in-situ for 3 days, combined with a Local Anaesthetic infusion pump
5. Local Anaesthetic and Tranexamic Acid placed into the joint at the end of the procedure
6. Minimal use, or no use, of the tourniquet

### Post Operation

7. Regular Paracetamol as background pain relief
8. Regular NSAID - e.g. Celebrex, to augment the Paracetamol
9. Regular Targin, Hydromorphone SR, Palexia SR, or Tramadol SR, twice a day (but only once for hydromorphone), as background pain relief
10. Quick acting Oxycodone, Hydromorphone, Palexia IR, or Tramadol IR, for top-ups between SR medication doses
11. Lyrica for the first 2 - 3 days (but not in the elderly)
12. Fentanyl PCA, Sub-lingual Buprenorphine, or Morphine for breakthrough pain relief

### Other

13. Compression bandaging for 48 hours to reduce swelling
14. Follow up antibiotic dose 6 hours after surgery
15. Follow up cortisone tablets for one week
16. Ice as necessary
17. Regular Physiotherapy

## Questions and Concerns

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