osteoarthritis.



osteoarthritis.

What is osteoarthritis ?

Arthritis is a major cause of disability and chronic pain in Australia.

More than 3.95 million Australians suffer from arthritis.

Up to two thirds of people with osteoarthritis are of working age.

Osteoarthritis is characterised by pain, loss of joint space and joint deformity.

Osteoarthritis is a progressive condition, which means it continually worsens.

Traditional treatments concentrate only on pain relief/analgesia.

At Melbourne Stem Cell Centre, we believe in the active management of arthritis.

While pain relief remains a primary objective, we use a multidisciplinary approach that aims to actively improve pain, joint movement and prevent or reduce the progression of arthritis.



What Melbourne Stem Cell Centre does

Before any treatment you will receive a thorough 'arthritis health care' consultation with one of our sports medicine physicians. Your current pain management/primary medical therapies will be optimised.

If relevant, nutritionalist/dietician and exercise rehabilitation consultations will be arranged.

Your suitability for other advanced medical therapy options will be assessed.

Formal imaging (XRays or MRI) will be arranged if required.

Your response to treatment will be monitored to maximise potential improvement.

osteoarthritis.

Osteoarthritis Treatment Plan : Options - Summary

Conservative Medical Therapy

- · Pain Relief Simple Analgesics and/or non-steroidal anti-inflammatories
- · Supplements i.e. Glucosamine Sulphate
- Exercise Exercise Physiology/Physiotherapy
- · Biomechanical Assessment Podiatry
- Weight Management Nutritionalist/Dietician

Advanced Medical Therapy

- Hyaluronic Acid / Viscosupplements
- · Cytokine Therapy (Platelet-rich Plasma and Autologous Conditioned Serum)
- Stem Cell Therapy
 - Low Dose
 - High Dose



* "Life. Be in it." campaign - a government initiative of 1975.

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conservative medical therapy.

Conservative Medical Therapy

Pain Relief

- Paracetamol
 - Non Steroidal Anti-inflammatories

*It is important to consult with your doctor before using anti-inflammatories in the treatment of arthritis.

Supplements

- · Glucosamine
 - Glucosamine is an amino-acid that forms the common 'back bone' of cartilage matrix.
 - Evidence suggests that glucosamine supplements may offer pain relief and reduce the progression of arthritis
 - Dose
 - At least 1500mg/day of Glucosamine Sulphate (NOT Glucosamine Hydrochloride)
 - + Chondroitin
 - Many glucosamine preparation have additional additives. Some evidence suggests additional benefits with Glucosamine + Chondroitin Sulphate preparations.
 - Risks
 - Allergy/anaphylaxis Glucosamine is derived from shell fish.
 - · Research :
 - McAlindon, et al. Glucosamine and Chondroitin for Treatment of Osteoarthritis Review Article, JAMA 2000, 283(11):1469-1475
- Flsh Oil / Omega 3
 - Fish oil supplements contain a large concentration of omega-3 fatty acids.
 - Evidence suggests fish oil supplements may improve pain control associated with inflammatory conditions such as rheumatoid arthritis.
 - Dose
 - 3gms/day of omega-3 fatty acid.
 - Risks
 - Bleeding / Stroke
 - may have an association with prostate cancer
 - Research :
 - Lee, et al. Omega03 Polyunsaturated Fatty Acids and the Treatment of Rheumatoid Arthritis: A meta-analysis. Archives of Medical Research 2012, 43(5): 356-362
- Tumeric/Curcumin
 - Evidence suggests tumeric supplements may improve pain control associated with inflammatory conditions such as arthritis. Curcumin is the active ingredient.
 - Dose
 - 200 1200mgs/day of curcumin.
 - Risks
 - Gastric Upset
 - · Research :
 - Julie S, Jurenka MT. Anti-inflammatory properties of curcumin, a major constituent. Alternative medicine review. 2009;14(2).







conservative medical therapy.

Conservative Medical Therapy (continued)

Exercise

- · Regular and appropriate exercise can be effective in reducing pain and disability associated with arthritis
- A structured program created and supervised by a professional rehabilitation Exercise Physiologist or Physiotherapist is recommended.
- Exercise Principles (FITT)
 - Frequency : At least three session per week for more than eight weeks
 - Intensity : Moderate Intensity
 - Type of exercise : Aerobic, resistance and load bearing
 - Time : At least 30 minute sessions
- Research :
 - Petrella, et al. Is exercise effective treatment for osteoarthritis of the knee?, BJSM 2000, 34:326-331

Biomechanical Assessment

• Podiatry assessment and relevant biomechanical adjustment can often help to take pressure off the areas of arthritis and therefore reduce pain and improve function.

Weight Management

- Increased weight is a risk factor for the development of osteoarthritis in weight bearing joints such as the hip and knee and also in non weight bearing joints such as in the hand.
- A weight loss of five kilograms has been shown to be effective in reducing the risk of knee arthritis by up to 50%.
- It is important to have a structured weight loss program developed by a qualified Nutritionalist or Dietician.
- Research :

Felson, et al. Risk factors for incident radiographic knee osteoarthritis in the elderly: the Framingham Study. Arthritis Rheum 1997, 40:728-733



* "Norm - Life. Be in it." campaign.



stem cell therapy.

Advanced Medical Therapy : Adipose-derived Stem Cell Therapy

Cell based therapies (including Stem Cells) offer exciting potential in treating conditions such as osteoarthritis

Adipose (fat) tissue is a rich source of adipose-derived mesenchymal stem cells. These cells have an ability to become cartilage cells.

Adipose-derived stem cells can be taken from your own body.

Adipose-derived stem cells has been shown to improve symptomatic arthritis by :

- reducing inflammation
- assisting healing
- · replacing/regenerating damaged cartilage

Not all patients are suitable for stem cell therapy. *Further, not all 'stem cell' therapies are the same and it is important to understand the difference.* This handout explains some of the questions that you may have regarding stem cell therapy.

Further web based resources offering information regarding the development of stem cell therapies include :

- Stem Cells Australia <u>www.stemcellsaustralia.edu.au</u>
- International Society for Stem Cell Research <u>www.isscr.org</u>
- NSW Stem Cell Network <u>www.stemcellnetwork.org.au</u>
- Stem Cell Network <u>www.stemcellnetwork.ca</u>
- International Cellular Society <u>www.cellmedicinesociety.org</u>
- Kuala Lumpur Sports Medicine Centre <u>www.klsmc.com</u>

Please also review the online resources available on the Melbourne Stem Cell Centre website :

www.melbournestemcellcentre.com/resource/



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stem cell therapy.

Are stem cells safe?

Systematic review of articles on the use of mesenchymal stem cells in the treatment of various conditions has shown good evidence of safety.

A review of more than 1000 patients who had received intra-vascular injections of mesenchymal stem cells did not identify any significant adverse events other than transient fever (Lalu, et al. 2012) Further review of patients who had received intra-articular (within the joint) injections showed similar evidence of safety.

No association has been made between mesenchymal stem cell therapy and adverse events such as infection, death or malignancy.

Importantly, adipose-derived stem cells are taken from your own body.

What is the evidence?

Laboratory based trials have confirmed the ability of adipose-derived stem cells to differentiate into cartilage (Diekman, et al. 2010).

Adipose-derived stem cells have shown cartilage regrowth and functional improvement in animal studies (Dragoo, et al. 2007).

Bone marrow derived stem cell trials have shown pain and function improvement with follow-up imaging indicating improvement in cartilage volume (Wakitani, et al. 2007).

Blood derived stem cell therapy when combined with orthopaedic arthroscopy, has shown biopsy confirmed regeneration of cartilage-like tissue (Saw, et al. 2011).

Intra-articular (within the joint) injections of pure adipose derived mesenchymal stem cells has resulted in regeneration of cartilage with resultant increase in overall cartilage volume and reduction in the size or cartilage lesions (Jo, et al. 2014).

Positive results in regeneration of cartilage have been shown with injections of 50-100 million 'pure' mesenchymal stem cells

How Melbourne Stem Cell Centre is different to other clinics

Melbourne Stem Cell Centre (MSCC) is a research driven, with a focus on using evidence based techniques in stem cell therapies.

MSCC's stem cell therapies use 'pure' mesenchymal stem cell preparations that have been shown to improve pain and function and to modify the progression of arthritis.

Some other stem cell clinics commonly use techniques that result in therapies that have less than 10% stem cells. These therapies have not been associated with cartilage regeneration.

What is Involved

Adipose-derived stem cell therapy involves a harvest procedure performed under local anaesthetic and light sedation.

Adipose tissue is taken from the body (usually the abdomen) using a procedure similar to liposuction.

Harvested adipose tissue undergoes processing to extract the adipose-derived stem cell component. Stem cells undergo expansion to produce increased cell numbers and improve efficacy.

Patients will receive multiple injections of 'pure' high dose adipose-derived stem cells into their arthritic joint.

Conditions may require orthopaedic intervention prior to stem cell therapy.

All patients who undergo adipose-derived stem cell therapy will have formal follow-up with their treating physician.



stem cell therapy.

Contra-Indications

While current research indicates that adipose-derived stem cell injections are safe therapy, it is non recommended in the following conditions due to lack of data on :

- pregnancy
- current cancer
- · some bleeding disorders
- organ failure
- severe immunodeficiency
- · uncontrolled hypertension or diabetes

What are the risks?

There are risks associated with all medical procedures.

Harvest Procedure

- Infection risk is minimised through a sterile harvesting technique and also prophylactic antibiotics.
- Pain/bruising at the site of harvest.
- Abdominal asymmetry the risk of asymmetry post liposuction is limited due to the small volume (40-100mls) of adipose tissue required.

Stem Cell Injections

- Infection to reduce the chance of infection all injections are done under sterile conditions using ultrasound guidance for accuracy.
- Pain/discomfort it is not uncommon for people to experience pain post injection of stem cells. You will be supplied with a prescription for appropriate analgesia/pain relief. Some people may need crutches initially, due to discomfort.
- Swelling it is expected that your joint may swell after the injection of stem cells. This can be controlled using ice and a compression bandage and usually improves within days.

Cost

Currently there is no Medicare or private health fund rebate for this procedure. The cost has three components :

- Stem Cell Isolation fee
- Facility fee
- Clinician fee

Cost will also be influenced by the specific treatment undertaken (see Treatment Options). Please discuss possible costs with the clinic.



stem cell therapy.

Treatment Options

The use of stem cell therapies has shown evidence of improvement in pain, functional and in modifying the progression of arthritis. Research has shown the potential of high-dose stem cell preparations to increase cartilage volume and reduce cartilage lesion size. Low-dose stem cell preparations have also been beneficial in symptomatic improvement. improved radiological assessment and delayed or prevented need for joint replacement.

The scientific observed benefits of different dosing programs has lead to the development of the following treatment options:

- Low-Dose Stem Cell Therapy
 - · Pure isolated mesenchymal stem cells suspended in a biological carrier media.
 - · Objectives :
 - · Pain and function/movement improvement
 - · Slow progression of disease

High-Dose Stem Cell Therapy

- Pure isolated mesenchymal stem cells suspended in a biological carrier media.
- · Objectives :
 - · Pain and function/movement improvement
 - Slow progression of disease
 - Regenerate cartilage

Research

- ADIPOA Report Summary. CORDIS European Commission, <u>www.cordis.europa.eu/result/rcn/</u>
 <u>156167_en.html</u>
- Diekman B, et al. Chondrogenesis of Adult Stem Cells from Adipose Tissue and Bone Marrow: Induction by Growth Factors and Cartilage Matrix. Tissue Eng. 2010; 16(2):523-533
- Dragoo J, et al. Healing full-thickness cartilage defects using adipose-derived stem cells. Tissue Eng. 2007; 13(7):1615-1621.
- Jo, CH., Lee, Y., et al. (2014). "Intra-articular injection of mesenchymal stem cells for the treatment of osteoarthritis of the knee: A proof of concept clinical trial.' Stem Cells: Doi: 10.1002/stem.1634
- Koh, JY., Jo, SB., Kwon, OR., et al. (2013). "Mesenchymal Stem Cell Injections Improve Symptoms of Knee Osteoarthritis." Arthroscopy - J Arthr Rel Surg. DOI: <u>dx.doi.org/10.1016/j.arthro.2012.11.017</u>
- Lalu, ML., McIntyre, L., et al. (2012) "Safety of cell therapy with mesenchymal stromal cells (safe cell): A systematic review and meta-analysis of clinical trials", PLOS One; 7(10), open access e47559
- Peeters, CM., Leijs, MJ., et al. (2013) "Safety of intra-articular cell-therapy with culture-expanded stem cells in humans: a systematic literature review" Osteo Cartilage; 21(10): 1465-1473.
- Saw KY, et al. Articular cartilage regeneration with autologous peripheral blood progenitor cells and hyaluronic acid after arthroscopic subchondral drilling: A report of 5 cases with histology. J Arthroscopic and Rel Surg. 2011; 27(4):493-506.
- Wakitani S, et al. Repair of articular cartilage defects in the patello-femoral joint with autologous bone marrow mesenchymal cell transplantation: three case reports involving nine defects of five knees. J Tissue Eng Regen Med. 2007; 1(1):74-79.
- Wakitani S, et al. Safety of autologous bone marrrow-derived mesenchymal stem cell transplantation for cartilage repair in 41 patients with 45 joints followed for up to 11 years and 5 months. J Tissue Eng Regen Med. 2011; 5(2):146-150.



advanced medical therapy. cytokine therapy (ACS/PRP).

Advanced Medical Therapy: Cytokine Therapy

Cytokine Therapy is a growth factor rich medium developed from your own blood. It is not synthetic. Preparations include Platelet Rich Plasma (PRP) or Autologous Conditioned Serum (ACS)

Studies have shown significant reduction in osteoarthritic knee pain within five weeks post injection and continued improvement in symptoms for up to one year or more.

There is no evidence to suggest that cytokine therapy results in regeneration of cartilage or slows progression of arthritis.

Why use Cytokine Therapy ?

Cytokine therapy is indicated in mild to moderate osteoarthritis where pain is not controlled by other conservative measures such as simple analgesics.

Cytokine therapy is an 'autologous' medium - it is developed from your own blood and does not contain any animal products and is not synthetic.

What is Involved ?

Cytokine therapy involves 4-6 injections performed at weekly intervals.

Blood is taken before injections for the generation of the Cytokine Therapy.

Patients are required to *stop taking anti-inflammatory tablets* one week before donating blood.

Patients taking regular aspirin should continue to take aspirin as prescribed by their general practitioner.

Each procedure will take about 45 minutes.

Risks

Bleeding/Bruising

Infection

• To reduce chance of infection all injections are performed under sterile conditions using ultrasound guidance for accuracy.

Pain/discomfort

- Injections can be uncomfortable.
- A proportion of patients experience mild to moderate discomfort post injection

Contra-Indications

While very safe, use of cytokine therapy is not recommended in the following conditions -

- pregnancy
- some bleeding disorders

Cost

Cost of cytokine therapy for a single joint is up to \$1600. This includes both the preparation and the injections. Cytokine therapy is not covered by Medicare or private health insurance.





advanced medical therapy. cytokine therapy (ACS/PRP).

Evidence

Research has shown cytokine therapy to be effective in achieving pain and functional improvement in mild to moderate osteoarthritis.

Research Articles

- Spakova, et al. Treatment of Knee Joint Osteoarthritis with Autologous Platelet-Rich Plasma in Comparison with Hyaluronic Acid. Am J Phys Med & Rehab 2012;91(5):411-417
- Kon et al. Platelet-rich plasma: intra-articular knee injections produced favorable results on degenerative cartilage lesion, Knee Surg Sport Traumatol Arthrosc, 2009, Online Publication
- Baltzer, et al. Autologous conditioned serum is an effective treatment for knee osteoarthritis, Osteo and Cartilage 2009, 17:152-160
- Sanchez, et al. Intra-articular injection of autologous preparation rich in growth factors for the treatment of knee OA: a retrospective cohort study, Clin Exp Rheumatol. 2008, 26(5):910-913
- Drengk, et al. Influence of platelet-rich plasma on chondrogenic differentiation and proliferation of chondrocytes and mesenchymal stem cells. Cells Tissues Organs 2009; 189(5):317-26.
- Saito, et al. Intraarticular administration of platelet-rich plasma with biodegradable gelatin hydrogel microspheres prevents osteoarthritis progression in the rabbit knee, Clin Exp Rheumatol 2009, 27(2): 201-207.



hyaluronic acid/viscosupplement.

Advanced Medical Therapy - Hyaluronic Acid / Viscosupplements

Viscosupplements are a form of hyaluronic acid. Viscosupplements are designed to lubricate and 'cushion' the arthritic joint.

Viscosupplement injections have been shown to reduced arthritis related pain within twelve weeks.

Reduction in pain can last for up to six months

What is Involved?

Viscosupplement therapy involves 1-5 injections into the arthritic joint.

Injections are performed undert sterile conditions, with local anaesthetic and using ultrasound guidance.

It is recommended that you have someone to drive you home after an injection due to some potential residual effects of the local anaesthetic or discomfort from the procedure.

Risks/Complications

Bleeding/Bruising

Infection

• To reduce chance of infection all injections are performed under sterile conditions using ultrasound guidance for accuracy.

Pain/Discomfort post procedure

- A proportion of patients experience mild discomfort post injection
- Regular simple analgesics such as paracetamol are recommended

Post injection 'flare up'

- Up to 10% of patients may experience a post injection inflammatory `flare'.
- This may require aspiration of the joint and injection of cortisone to reduce the inflammatory response.

Contra-Indications

Use of visco-supplement is not recommended in the following conditions :

- pregnancy
- · previous 'flare up'
- allergies to bird products ie. feathers, eggs, poultry.

Cost

Cost of Viscosupplement therapy \$800. There is no Medicare rebate. This cost may be partially covered by your private health fund. It is advised that you contact your health fund to enquire about funding.

Research

Adams, et al. The role of viscosupplementation with hylan G-F 20 (Synvisc®) in the treatment of osteoarthritis of the knee: a Canadian multicenter trial comparing hylan G-F 20 alone, hylan G-F 20 with non-steroidal anti-inflammatory drugs (NSAIDs) and NSAIDs alone, OA and Cartilage 1995, Vol 3, 4:213-225.



treatment options.

Advanced Medical Therapy - Treatment Options

The choice of treatment option is determined by the chosen treatment goal/objective. These objectives are highlighted below :

Therapy	Outcome			Cost	Repeat Therapy	Repeat Therapy Cost
	Pain Relief	Slow Progression	Improve Arthritis			
Hyaluronic Acid (HA)	\checkmark			\$800	Yes (3-6months)	\$800
Cytokine Therapy (CytoT)	\checkmark			\$1600	Yes (6-12months)	\$800-\$1600
Low Dose Stem Cells - includes CytoT	\checkmark	\checkmark		\$5500	Yes (12months)	\$2200
High Dose Stem Cells - includes CytoT	1	\checkmark	1	from \$7000	Possible	from \$2400

* The results indicated in this table are what has been shown to occur in scientifically published articles which have assessed the benefits of biological therapies. These results may not always be achieved and results can be varied between patients.



treatment options.



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