

Evidence to Decision Frameworks: Growth Factors

Clinical question What growth factors are effective for supporting healing of pressure injuries?

Recommendation 16.1 Consider applying platelet-rich plasma for promoting healing in pressure injuries.

Option: Applying platelet rich plasma (PRP) to heal the pressure injury

Comparison: No topical applications to the pressure injury, or a placebo applied to the wound bed, or a comparator topical application

Background: Chronic wounds, including pressure injuries, are characterized by a deficiency of some growth factors and their receptors, which inhibit proliferation and maturation of wounds. Therefore, it is believed that the application of these deficient growth factors may promote wound healing.

	CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS										
BENEFITS & HARMS OF THE RECOMMENDED PRACTICE	What is the overall certainty of the evidence?	<table border="0"> <tr> <td>No included studies</td> <td>Very low</td> <td>Low</td> <td>Moderate</td> <td>High</td> </tr> <tr> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </table>	No included studies	Very low	Low	Moderate	High	<input type="checkbox"/>	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<p>Evidence for improvement in complete healing of pressure injuries</p> <ul style="list-style-type: none"> In Category/Stage II and III pressure injuries (n=124), significantly more reached complete healing at day 36 when PRP was applied on day 0 (8% vs 0%, p=0.023) compared to standard care, and when PRP was applied on day 0 and 15 compared to standard treatment (32% vs 0%, p=0.001).¹ (Level 1, low quality) 100% of Category/Stage III pressure injury fistulas (n=15) completely healed by 3 weeks,² (Level 4, low quality) and approximately 50% of PRP treated pressure injuries (n=320) completely healed after 7 weeks.³ (Level 1, low quality) <p>Evidence for reduction in wound surface area or improvement tissue type</p> <ul style="list-style-type: none"> Significantly greater percent reduction was associated with PRP compared to standard treatment control: Group A (PRP on day 0 only) 48.3% (95% CI 39.3 to 57.4, p=0.001); Group B (PRP on days 0, 15) 54.8% (95% CI 36.3 to 73.3, p=0.001); Group C (PRP and hyaluronic acid on days 0, 15) 80.4% (95% CI 71.8 to 89.1, p=0.001).¹ (Level 1, low quality) In individuals with spinal cord injury (n=25) with pressure injuries, after 5 weeks of treatment there was a statistical significant decrease in mean wound surface area for PRP group (p<0.001) but not for control group (p=0.924).⁴ (Level 2, low quality) 56% PRP-treated pressure injuries (n=25) showed necrosis and suppuration at baseline, by week 5 60% had well-formed granulation tissue and epithelialization⁵ (Level 2, low quality) Mean wound surface area reduction for pressure injuries (n=21) treated with PRP for approx. 2 weeks was 33.7%±38.1%.⁶ (Level 4, low quality) <p>Evidence for improvement in PUSH scores</p> <p>Statistically significant improvement was seen in mean PUSH scores of for pressures injuries treated with PRP, but pressure injuries treated with normal saline also had a significant improvement.⁵ (Level 2, low quality)</p> <p>Evidence for reduction in critical colonization</p> <p>After at least 4 weeks treatment with PRP, wound colonization was significantly reduced compared to baseline and compared to a control saline gauze dressing.⁵ (Level 2, low quality)</p>	<ul style="list-style-type: none"> Application of two doses (day 0,15) of PDGF may be more effective than one dose (day 0) (statistical comparison not presented).¹ (Level 1, low quality)
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CRITERIA	JUDGEMENTS	RESEARCH EVIDENCE	ADDITIONAL CONSIDERATIONS
		<p>Adverse outcomes</p> <ul style="list-style-type: none"> • A large trial had no adverse events or complications associated with application of PRP.³ (<i>Level 1, low quality</i>) • Relative risk of adverse event was reported as 0.44 (95% CI 0.05 to 3.85, p=0.46) in a systematic review that included studies conducted in other wound types.⁷ <p>Strength of Evidence: B1 — Level 1 studies of moderate to low quality, plus additional evidence from lower level studies</p>	

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RESOURCE USE	How substantial are the resource requirements?	<table border="0"> <tr> <td><i>Not clear</i></td> <td><i>Not substantial</i></td> <td><i>Probably not substantial</i></td> <td><i>Probably substantial</i></td> <td><i>Substantial</i></td> <td><i>Varies</i></td> </tr> <tr> <td><input checked="" type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> <td><input type="checkbox"/></td> </tr> </table>	<i>Not clear</i>	<i>Not substantial</i>	<i>Probably not substantial</i>	<i>Probably substantial</i>	<i>Substantial</i>	<i>Varies</i>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	There is no research evidence on the cost implications of using PRP on pressure injuries.
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Balance of consequences	Undesirable consequences <i>clearly outweigh</i> desirable consequences in most settings <input type="checkbox"/>	Undesirable consequences <i>probably outweigh</i> desirable consequences in most settings <input type="checkbox"/>	The balance between desirable and undesirable consequences <i>is closely balanced or uncertain</i> <input type="checkbox"/>	Desirable consequences <i>probably outweigh</i> undesirable consequences in most settings <input checked="" type="checkbox"/>	Desirable consequences <i>clearly outweigh</i> undesirable consequences in most settings <input type="checkbox"/>
Strength of recommendation	Strong negative recommendation: Definitely don't it <input type="checkbox"/>	Weak negative recommendation: Probably don't do it <input type="checkbox"/>	No specific recommendation <input checked="" type="checkbox"/>	Weak positive recommendation: Probably do it <input type="checkbox"/>	Strong positive recommendation: Definitely do it <input type="checkbox"/>
Justification	Evidence supporting this recommendation comes from two low quality Level 1 studies ^{1,8} that indicate that application of PRP is effective in supporting healing of pressure injuries. Compared to placebo or standard care, Category/Stage II and III pressure injuries completely healed at significantly faster rates after between two and seven weeks of treatment. ^{1,8} When two applications of PRP were applied, complete healing rates were over 30% greater compared to standard care. ¹ Low quality level 1 studies ^{1,8} and lower level studies ^{4-6,9} showed that applying PRP was also associated with reductions in wound surface area, improvements in tissue type and improvement in scores on the Pressure Ulcer Scale for Healing (PUSH) after two weeks and one month. The improvements in other outcome measures were less substantial than those seen for complete pressure injury healing. Relative risk (RR) of an adverse effect occurring after application of a PRP to any type of wound has been reported as 0.44 (95% CI 0.05 to 3.85, p=0.46), ¹⁰ suggesting undesirable effects are probably not substantial. There is no information available on cost-effectiveness; however, PRPs are usually manufactured in laboratory settings and require skilled technicians and specialist resources that are likely to be limited in most clinical settings.				

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Clinical question What growth factors are effective for supporting healing of pressure injuries?

Recommendation 16.2 Consider applying platelet-derived growth factor for promoting healing in Category/Stage III and IV pressure injuries.

Option: Applying platelet-derived growth factor (PDGF) to heal the pressure injury
Comparison: No topical applications to the wound bed, or a placebo applied to the wound bed, or a comparator topical application

Background: Chronic wounds, including pressure injuries, are characterized by a deficiency of some growth factors and their receptors, which inhibit proliferation and maturation of wounds. Therefore, it is believed that the application of these deficient growth factors may promote wound healing

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<i>No</i>	<i>Probably No</i>	<i>Uncertain</i>	<i>Probably Yes</i>	<i>Yes</i>	<i>Varies</i>										
<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>										

Balance of consequences	Undesirable consequences <i>clearly outweigh</i> desirable consequences in most settings <input type="checkbox"/>	Undesirable consequences <i>probably outweigh</i> desirable consequences in most settings <input type="checkbox"/>	The balance between desirable and undesirable consequences <i>is closely balanced or uncertain</i> <input type="checkbox"/>	Desirable consequences <i>probably outweigh</i> undesirable consequences in most settings <input checked="" type="checkbox"/>	Desirable consequences <i>clearly outweigh</i> undesirable consequences in most settings <input type="checkbox"/>
Strength of recommendation	Strong negative recommendation: Definitely don't it <input type="checkbox"/>	Weak negative recommendation: Probably don't do it <input type="checkbox"/>	No specific recommendation <input checked="" type="checkbox"/>	Weak positive recommendation: Probably do it <input type="checkbox"/>	Strong positive recommendation: Definitely do it <input type="checkbox"/>

Justification A high quality Level 1 study showed 23% more Category/Stage III and IV pressure injuries reached complete healing with application of PDGF gel.¹¹ Low quality Level 1 studies provided evidence for significantly greater reduction in pressure injury depth associated with PDGF gel,^{12,13} although results were mixed for measures of wound volume.¹²⁻¹⁴ One high quality economic analysis¹⁵ based on clinical outcomes from a high quality Level 1 study estimated that treatment of one pressure injury required approximately three tubes of PDGF gel at a cost of \$920/tube. Over 12 months, individuals would need to pay \$298 USD to gain one additional pressure-injury free week with PDGF gel compared to placebo.¹⁵

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