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Experience with the Meek micrografting technique in Major Burns

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CONTENTS OF DISSERTATION

1. Part A: Plagiarism declaration                  page 3
2. Part B: Final abstract                         page 4
3. Part C: Protocol                               page 6
4. Part D: Acknowledgements                      page 11
5. Part E: List of tables                         page 12
6. Part F: Abbreviations                         page 12
7. Part G: Appendices list                        page 12
8. Part H: Structured literature review          page 13
9. Part I: Journal article                       page 34
10. Part J: Appendices                           page 47
I, Dr Dawid Jacobus Potgieter, hereby declare that the work, on which this dissertation/thesis is based, is my original work (except where acknowledgements indicate otherwise) and that neither the whole work nor any part of it has been, is being, or is to be submitted for another degree in this or any other university.

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Signed

Dr DJ Potgieter
31/01/2016
Part B: Final Abstract

Experience with the Meek micrografting technique in major burns

**Background.** Early excision of burn eschar and urgent skin cover is mandatory for survival in all major burns. The tremendous cost and time delay in cultured skin and the shortage of donor allograft can make early skin cover a life threatening problem for paediatric patients in this country. The Meek micrografting technique was introduced in 2003 as a rescue method to achieve epithelialisation in major burns.

**Objective.** To evaluate its role in the management of major burns with reference to its efficacy, technical detail and role in major burn surgery.

**Methods.** A retrospective review of 27 patients over a 12 year period who received Meek micrografting as part of their management in achieving skin cover for major burns. Baseline characteristics of the patients were collected from patient records and operative notes.

**Results.** Twenty-seven children were treated with the micrografting technique. Their ages varied from 3 months to 11 years and total body surface area (TBSA) was 49.7%. Eight children had concomitant inhalation injury. Five were late and neglected referrals of whom 2 developed the re-feeding syndrome. Length of stay was 9-262 days (mean 70 days, 1.4 days/1% burn).

Micrografting was performed on days 5-117 (mean 26 days) and a mean area of 25.6% TBSA (range 5-63%) was grafted. On average 7.8 operations were performed to complete skin cover. On average 2.7 (range 0-9) surgical procedures preceded the micrografting and a further 3.2 (range 0-10) procedures were required after micrografting to complete wound cover.

Graft take at 1 month was more than 90% in 16 children of whom 3 subsequently died. Eleven patients had less than 90% graft take, of whom 5 died.

**Discussion.** The lack of adequate donor sites therefore mandates other temporary or permanent methods to achieve wound cover as rapidly as possible. The micrografting technique allows small areas to be utilised as donor areas where otherwise they would not have been suitable as donor areas for skin procurement.

There is a steep learning curve associated with the use of the technique. Technically, we have identified aspects that would improve graft take. These include a non-infected, vascularized deep dermal, viable subcutaneous or viable fascial layer. The bed can be prepared by excision followed by allografts or biosynthetic skin. Skin loss was mainly due to wound infection. The 19 children who survived, had an average TBSA of 62.2% in comparison to the 67.15% in
those who demised. However, of the 3 out of the 8 who died, one was electively palliated, one had severe re-feeding syndrome and one had Propranolol toxicity with non-occlusive mesenteric ischaemia and infarction. In 2, skin grafting was completed, but they died from multi-organ failure.

**Conclusion.** The Meek technique is technically demanding, but provides high expansion ratios thereby facilitating wound cover in the presence of limited donor sites. With the results obtained, and the excellent skin quality and decrease in donor site, we will contemplate using the micrografting technique on smaller burns in the future.
Part C: Protocol

Experience with the Meek micrografting technique in major burns

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1. Aim of the study:

To assess the outcome of Meek micrografting in major burns.

2. Objectives of the study:

The investigators anticipate that the micrografting technique is greatly beneficial in obtaining autologous wound cover in major burns.

3. Study background:

The survival of patients with major burns is hampered by a lack of autograft and donor skin. This limiting factor is increasingly encountered as the main impediment in achieving wound cover. Mesh autografts require the presence of approximately an equal surface area to cover the excised wound. In burns exceeding 30% total body surface area (TBSA), this is not possible. To overcome this shortage in available donor skin, the use of alternative methods are required. Collectively however they are very expensive and not readily available in South Africa. Measures to overcome this shortage of donor skin include the use of allografts,
either fresh or hydrolysed. Unfortunately there is no skin bank in South Africa and allografts currently can only be procured from solid organ donors.

A second method includes cultured epithelial autografts either as spray on or as sheet grafts. Both methods are prohibitively expensive and not readily available here. They also have potential major disadvantages.

A third method involves extensive expansion of autografts from 1:3 to 1:9 ratios. This method is effective to cover large areas but needs an overlay of biological/synthetic dressings or allografts to prevent desiccation and hypergranulation of the denuded areas.

The fourth method is utilising the modified Meek technique of micrografting. This technique was introduced in 1962 and modified in 1993. The technique effectively expands procured skin surface area three to four to nine fold. It is now used extensively internationally as a rescue method for major burns in the presence of deficient donor skin area. The system was introduced into South Africa in 2003 to overcome the acute shortage of allografts and functions as a permanent autologous skin cover technique with widely expansive properties.

We have had limited exposure to this technique in our attempts to save the lives of patients with major burns. A review of its efficacy, technical problems encountered and place in major surgery has not been established in the burns unit. Retrospective review of the 27 patients to date who had received micrografting will help to define its position in the future management of major burns. This is particularly needed in view of the absence of a skin bank and the major difficulties we have in procuring suitable allografts.

4. **Significance of the study:**

The micrografting technique was introduced to achieve autologous skin cover in an attempt to improve the survival in patients with major burns.

5. **Methodology:**

Between 2003 and 2016 a total of 27 children underwent micrografting procedures involving the modified Meek technique to achieve wound cover. The parents were fully informed about the reasons for using micrografting and were all consented for the procedure. The Meek Micromesher (Humeca, Netherlands) was used.

The micrografting technique used in the study was as follow:
1. Split skin autograft was procured
2. Skin was then placed on cork squares of 42mm x 42mm
3. This cork was then placed in a carrier block of this special dermatome and the skin was cut in tiny blocks, by 13 parallel blades, 3mm apart.

4. After the first pass the cork was rotated through 90 degrees and passed again through the dermatome, which allows the cutting of 14 x 14 tiny blocks of 3mm x 3mm each.

5. The cork was then sprayed with a special glue and the blocks transferred to a pre-folded polyester gauze.

6. This gauze was then unfolded to achieve the desired expansion ratio before being applied to the burn surface and secured with skin staples.

7. The grafted sheets were then covered with a Xeroform dressing.

Base line characteristics of the patients: age, gender, cause of injury, TBSA, component partial and full thickness, inhalation injury, resuscitation, number of operations to achieve full skin cover, methods to achieve skin cover, bacteriology and wound and systemic infections, management of the wounds prior to grafting, status of the recipient bed, the preparations required to optimise graft take (in particular allograft placement at the time of sheet removal), factors influencing the take rate after transplantation, the role of wound bacteria in graft take, percentage graft take, outcome and reasons for failure of the Meek technique were collected.

The surgical procedures all followed standard procedures, of patient preparedness for the operation, standard anaesthesia, wound preparation, procurement of donor skin and meek preparation, the application of the micrografts, and standard postoperative care including the use of allografts if available post operatively. Routine post-operative care was given.

6. Preparing the burn wound for micrografting surgery:

Following the introduction of anaesthesia, completion of the WHO checklist, the dressings were removed and the burn wound washed with 1% Chlorhexidene soap followed by the topical application of 0.006% sodium hypochlorite solution for 20 minutes. The body was divided into 6 priority segments: head and neck, anterior and posterior trunk, upper and lower extremities and the gluteal and perineal areas. The surgical aim was to reduce the wound area as soon as possible to below 30% TBSA, hence the individual selection of the areas to excise and to graft. The pre-selected wound area was then excised to viable level either deep dermal or viable fat or down to the fascial layer. The donor areas were selected from unburned areas that were usually scattered throughout the surface area. The technique of harvesting, preparation and application of the micrografts is well described.

The post-operative dressings were changed on day one and there after regularly on day 3, 5 and 7 when the outer plastic sheeting was removed leaving the micrografts exposed. They were then covered with an antibacterial dressing which were
changed on alternative days until full epithelialisation had occurred. Infections were closely monitored and treated according to the sensitivity patterns and standard wound care procedure. Allograft was applied over the micrografts as soon as possible after the sheets were removed. This obviously subject to availability.

7. **Inclusion criteria:**

Major burns with a deficiency of donor sites.

8. **Exclusion criteria:**

These operations are done as the sole option to attempt to save the lives of children with major burns, hence no major burn cases were excluded.

9. **Statistical analysis:**

The data will be assessed and descriptive statistics will be applied to investigate and compare outcomes.

10. **Informed consent:**

Full consents were taken for the surgery from parents or guardians and this included the expectations and possible complications of surgery of this nature.

11. **Data safety monitoring:**

Data will be kept on spreadsheets in the Department of Paediatric Surgery and will be password protected. Only patient folder numbers will be entered.

12. **Risks and benefits:**

Due to donor site limitations, we had to use this procedure and no extra risks were incurred. Allografts were not available in all cases, neither was spray-on skin or cultured epithelial autografts. Benefits are the ability to obtain the fastest possible autologous skin graft cover and gaining experience with this technique for future improvement. It has now become standard practice in the management of massive burn injury.
13. Reimbursement:

There is no reimbursement as this is a practice review audit.

14. Emergency care of patients:

Standard emergency and intensive care was provided to all patients and this is merely a retrospective review of the process.

15. What happens at the end of the study?

The investigators anticipate that they will be able to confirm that this is life saving procedure for future use and that strengths and weaknesses will be identified retrospectively. The data will be kept in the Department of Paediatric surgery and will remain password protected.

16. Literature Review:

Part D: Acknowledgements

I would sincerely like to thank the following individuals for their assistance with this project:

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3. My co-supervisor, Dr S Adams, for help and support with this project.
4. Dr R Martinez for her help with collecting data.
5. Dr C Price for his help in proofreading this thesis.
Part E: List of tables

Table 1: Patient demographics and surgical characteristics page 39-42
Table 2: Use of allografts page 42

Part F: List of abbreviations

1. ARDS: Acute Respiratory Distress syndrome
2. ARV: Anti Retroviral Medication
3. CEA: Cultured Epithelial Autografts
4. DPT: Deep Partial Thickness
5. HIV: Human Immunodeficiency Virus
6. HREC: Human Research Ethics Committee
7. ICU: Intensive Care Unit
8. LMIC: Low and Middle Income Country
9. m: age in months
10. mm: millimetres
11. MOF: Multi-organ Failure
12. RXH: Red Cross War Memorial Children’s Hospital
13. SPT: Superficial Partial Thickness
14. TBSA: Total Body Surface Area
15. UCT: University of Cape Town
16. WHO: World Health Organisation
17. y: age in years

Part G: List of appendices

1. UCT HREC approval letter page 47
2. RXH Research approval letter page 48
3. Photographs of Meek micrografting results page 49
4. SAMJ author guidelines page 51
Part H: Structured Literature Review

List Of Contents Of Literature Review:

1) Objectives page 14

2) Literature Search Methods page 14

3) Interpretation Of Literature page 15
   • Introduction page 15
   • Epidemiology of burns in South Africa page 16
   • Classification of burn wounds page 16
   • History of skin grafting page 17
   • Available methods for resurfacing major burns page 19
     1. Temporary cover page 19
        a) Allograft skin
        b) Allograft amnion
        c) Xenograft
        d) Synthetic skin
     2. Permanent cover page 22
        a) Widely meshed autografts
        b) CEA sheets
        c) Spray-on skin
        d) Cuono technique
        e) Dermal substitutes
        f) Micrografting
   • Meek surgical technique page 26
   • Conclusion page 26

4) Aims And Objectives Of Current Study page 27

5) References page 27
1. Objectives:
   - Classify burn wounds according to depth and describe how this impacts on treatment
   - Explore the history of skin grafting and the origin and evolution of different skin grafting techniques currently available
   - Describe the technique of Meek micrografting
   - Examine the modified Meek micrografting technique with respect to:
     - benefits
     - drawbacks
   - Evaluate alternative skin cover options in massive burn wounds including
     - cultured epithelial autografts
     - sheets
     - spray-on
     - widely meshed autografts
     - allografts
     - including method of action
     - other temporary skin substitutes

2. Literature Search Methods:
   - PubMed, Medline and Google Scholar search engines were used to acquire the relevant journal articles.
   - Only articles in the English language were used
   - Search words and phrases used:
     - massive burns
     - modified Meek technique
     - cultured epithelial autografts
     - spray-on skin
     - allografts
     - cadaver skin
     - Biobrane
     - Suprathel
     - xenografts
     - skin substitutes
   - Related citations suggested by the search engine were used
   - References cited in journal articles obtained were used to further broaden the search
3. Interpretation of literature:

Introduction
A major burn is classified as a burn which exceeds 30% of total body surface area (TBSA). In order for a patient to survive such an enormous physiological insult, all aspects of the treatment should be co-ordinated. Issues which need to be addressed include resuscitation, inhalation injury, infection control, early wound closure, pain control and nutrition [1].

Early excision and wound closure has become the gold standard for deep partial and full thickness burns following the work done by Zora Janzekovic [2]. When a burn injury involves more than 30% TBSA, there are no longer enough donor sites available to achieve early autologous closure of the burn wound. Fifteen percent of the surface area of the patient is unavailable for donor sites.

Intact skin has various biological functions, but it is the barrier function which is critical to the survival of the individual. Mechanisms such as temperature and fluid regulation, as well as physical defences against trauma and infection, are all lost after a major burn injury. These all lead to a patient who is profoundly immunocompromised. Fluid and electrolyte derangements are further magnified by an intense catabolic response which leads to a poor nutritional state and impaired wound healing.

As understanding of the pathology behind a severe burn has improved, strategies have been developed to try and mitigate the effects of these pathological processes on the injured patient. Advances in fluid resuscitation, wound dressing technologies and infection control, nutritional support and intensive care management have all lead to an increase in the survival of severe burn victims. However, the most important change in the management of severe burns has been the adoption of early excision and autologous wound cover. This has led to a decrease in both morbidity and mortality.

In major burn injuries there are a paucity of donor sites, hampering early coverage with meshed autologous skin. As a result, various other techniques have been developed as alternatives. These techniques vary from temporary cover for the freshly excised wounds, to permanent and definitive wound closure. Various strategies employing artificial skin substitutes, xenografts and allografts have been described in the literature [3, 4, 5, 6]. Most of these are only temporary solutions, used to tie the patient over until permanent cover can be achieved [7].

Many techniques to get permanent autologous cover have been described in the literature [4, 6, 8, 9]. These include postage stamp grafting, widely meshed skin grafting, intermingled auto- and allografts, alternating strips of auto- and allografting, microskin grafting and the Meek technique [10].
Epidemiology of Burns in South Africa

The incidence of burn injuries is increasing in Africa. Poverty, increasing urbanisation and the subsequent proliferation of informal settlements have led to this trend [11, 12, 13]. Due to the lack of space in these dwellings, there is often a shared area for both cooking and living [12]. This places infants, toddlers and young children at risk of interacting with open fires, gas stoves and kettles or pots with boiling water [11]. Studies from African countries have confirmed that burns are a major contributor to morbidity and mortality in children and infants on the continent [14,15,16]. South Africa is no exception. Figures from the South African Medical Research Council show that approximately 3.2% of the population is affected by burns annually. Fifty percent are younger than 20 years [12]. Children below the age of four are at greatest risk of sustaining a burn injury [11]. Burn wounds are also responsible for the third highest external incidence of mortality in children below the age of 18 years in South Africa [12,14]. The commonest causes of paediatric burns in Africa are flame burns (57%), hot liquids (32%), and chemical burns (7%) [12,17].

In South Africa approximately 80% of burns are from hot liquids, 12% from fire, 5% electrical burns and 3% hot coals [11, 18, 19]. Most of these are accidental and occur in or around the house, with a strong seasonal variation [12]. The Red Cross War Memorial Children’s Hospital in Cape Town, South Africa, admits approximately 1200 paediatric burns per year [12]. A 15-year analysis of the trauma registry from Child Safe South Africa’s Western Cape database, analysing 9 438 children’s burns, showed that 39% of the injuries were minor, 56% were moderate and 5% were severe, with 49% of those seen in a level one trauma unit admitted for in hospital care [11, 20]. On an annual basis 30% of admitted children present with burns exceeding 25% TBSA. As burn care in Africa is very dependent upon financial resources, equipment and expertise [12], it is imperative to develop treatment strategies that are cost- and time-effective in order to optimise the use of scarce financial resources.

Classification of burn wounds

Burn wounds are classified on the basis of depth of the burn, as well as the percentage of total body surface area involved (TBSA). Burn depth is the most widely used method of classification of a burn wound. Burn wounds may involve the epidermis, variable depths of the dermis, as well as subcutaneous tissue; thus dividing burn wounds into superficial, partial thickness and full-thickness categories. The depth of a burn has a major impact on the ultimate healing of the wound. Correctly assessing the depth of a burn is critical in the management decisions of a burn victim [21].

a. Superficial wounds have no dermal involvement and are limited to the epidermis only. They are erythematous and painful, but typically heal within 3 to 5 days [21].
b. Partial thickness wounds can be divided further into superficial (SPT) and deep (DPT) depending on the extent of dermal involvement. They differ in their clinical appearance and ability to heal, which also affects the subsequent difference in need for excision and grafting between these two types. Superficial partial thickness wounds, as often seen with hot water scalds, may form blisters and are pink, moist, and painful, with a normal capillary refill. These wounds most often heal within 2 weeks as they spontaneously re-epithelialise from retained epidermal structures in the rete ridges and stem cells in hair follicles and sweat glands\cite{4}. These wounds generally do not cause scarring, but may result in hypo- or hyper-pigmentation.

Deep partial thickness wounds affect the full thickness of epidermis and extend into the reticular portion of the dermis. Clinically, these wounds appear paler than SPT wounds, often with a mottled, dry appearance. They have decreased or no capillary refill and are less sensate than SPT burns. Due to the deeper level of dermal loss, DPT wounds take much longer to heal than SPT, as re-epithelialisation must occur from remaining adnexal structure cells in the hair follicles. If no infection sets in, these wounds may heal in 3 to 8 weeks. These wounds, if left to heal spontaneously, will more often than not lead to severe scarring and contractures. It is widely accepted that wounds which are not completely healed by 21 days, be excised and grafted \cite{21}.

c. Full-thickness wounds involve all of the epidermis and dermis and, as such, will not heal adequately without excision and grafting. Clinically these wounds are brown, leathery and insensate \cite{21}.

Apart from the extremes of superficial and full-thickness wounds, determination of burn depth can be very difficult for the mid depth wounds. During the first few days it is often impossible to judge whether a wound will heal within 3 weeks. Many techniques have been developed to try and aid the burn surgeon in making an early decision on the depth of a burn, but none have yet been proven to be more reliable than the clinical judgement of an experienced surgeon. A discussion on these modalities is beyond the scope of this review \cite{21}.

### History of Skin Grafting

The true origin of skin grafting is lost in the mists of time \cite{22}. There is evidence of skin grafts being used for nasal reconstruction by Sushrata in India as early as 700 BC \cite{5, 22, 23}. This involved transplanting full thickness skin grafts from one individual to another. Amputation of the nose was used as punishment for adultery and theft. The Brahmin Koomes Caste, who were bricklayers, undertook the repair of these wounds \cite{22}. The first written record of burns treatment comes from the Ebers papyrus in Egypt. In this written record the different medications used to treat burn wounds are discussed, as well as the timing of their use \cite{22}.
The technique of skin grafting seems to have been lost until the European Renaissance. Various reports of surgeons performing skin grafts were noted, but it is the Swiss surgeon, JL Reverdin, who gets the most credit \([22,23]\). Working as a house physician in Paris, he published his technique of “Greffes Epidermiques” in 1869 \([22]\). Although his grafts were probably no more than 1 or 2 mm big it may have been the seminal first step popularising skin grafting \([5,24]\). Ollier, also in France, coined the term dermopidermic grafting in 1871 \([22]\).

There is some contention about who performed the first skin graft to treat a burn wound. Some authors credit Reverdin for applying small grafts to an old burn wound in 1869, although it wasn’t published until 1871 \([22]\). Others credit George David Pollock from London \([22,24]\). He published a series of articles on the subject in 1870 \([22]\). In 1886, Carl Thiersch from Germany, described his improved technique of skin grafting \([5,22]\). He used a straight razor to remove long thin strips of skin. He included some dermis in his grafts and transplanted it onto freshly excised wounds \([22]\). Many articles published in this era did not distinguish between auto and allografts, or full and partial thickness grafts. During the Boer War, Winston Churchill donated skin to help heal the open wound of a fellow officer. Years later, Churchill (1944) reported that this graft was still successful \([24]\).

During the early 20th century, the scientific understanding of the basis of skin grafting progressed slowly, together with advances in techniques and instrumentation. The first grafts were taken free hand by using a thin bladed knife, until Finochietto improved on the design in 1920, allowing the depth of the skin harvest to be better controlled \([22]\). More improvements followed, and names such as Braithwaite, Watson, Goullian, and Corbett are still today associated with burn knives \([22]\). The invention of the mechanical dermatome by Humby, from England, was a major advance in 1930 \([22]\). Nine years later Padget and Hood developed the hand-powered rotating drum dermatome \([22]\). The first powered dermatome was introduced in 1948. Dr. Brown, who invented the machine with the help of an engineer called Barron, is said to have come up with the idea while being held prisoner by the Japanese during World War II \([22]\). As techniques improved, grafting of larger wounds was attempted. It was soon realised that some form of expansion was needed for the harvested skin. The concept of “meshing” harvested skin was not new \([22]\). Lanz, a German surgeon, had already described a handheld instrument for meshing skin in 1907 \([22]\). Various refinements were made in these devices, but it is the hand cranked double roller graft mesher developed by Tanner and Vandeput in 1964 which bears a striking resemblance to the equipment used today \([22, 25]\).

Gabarro is credited with the first description of postage stamp skin grafting in 1943, and many variations on the technique was published thereafter \([26]\). Cicero Parker Meek published his article “Successful microdermagrafting using the Meek-Wall microdermatome” in the American Journal of Surgery in 1958. He was working as a general practitioner at the Aiken County Hospital in South Carolina, USA, at the
time. This was the first description of a device to produce “postage stamp-like” small skin grafts. In February 1963 together with the engineer S.P. Wall, with whom he had designed the device, he submitted the Meek-Wall Dermatome for patenting at the United States Patent Office under the name “Microdermatome” [27]. His theory was that keratinocytes would migrate from the edges of the transplanted skin to fill the areas in between, until all areas became confluent and covered. He theorised that the longer the edges of the transplanted grafts, the quicker the healing of the interstitial areas would be. Using a mathematical approach, he presented the principle that the sum of the quadratic edges of all the grafts is greater, the smaller the individual area of the transplanted rectangles is [27]. Following his second paper in 1965, in which he described his experiences with the technique, the technique was slowly forgotten.

The popularisation of meshed grafts in 1964 allowed for a faster, cheaper and technically easier method of auto-grafting split skin. It was not until the early 1990’s that the technique was re-explored. Dutch surgeons at the Red Cross Hospital in Beverwijk found that they were able to keep patients with massive burn wounds alive due to improved ICU care, but that the standard technique of meshed autografts fell short when needing large amounts of skin with limited donor sites. They modified the original Meek technique and in 1993 Kreis et al published their clinical results for the first time [27].

Available Methods for Resurfacing Major Burns

Resurfacing techniques

<table>
<thead>
<tr>
<th>Temporary Cover</th>
<th>Permanent Cover</th>
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</thead>
<tbody>
<tr>
<td>a) Allograft skin</td>
<td>a) Widely meshed autografts</td>
</tr>
<tr>
<td>b) Allograft amnion</td>
<td>b) CEA sheets</td>
</tr>
<tr>
<td>c) Xenografts</td>
<td>c) Spray on skin</td>
</tr>
<tr>
<td>d) Synthetic skin</td>
<td>d) Cuono technique</td>
</tr>
<tr>
<td>e) Dermal substitutes</td>
<td>e) Dermal substitutes</td>
</tr>
<tr>
<td>f) Micrografting</td>
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</tbody>
</table>

1) Temporary cover

a. Allograft skin

In 1881 Girdner described the use of allograft skin for the treatment of burn wounds [23, 28]. Billingham and Medawar published a paper in 1952 on the addition of
glycerol as a cryopreservant for allografts \cite{23, 29} and stated that, in order for allograft to be used as an effective cover for burn wounds, it does not have to be alive \cite{5, 23, 29}. The controversy regarding allograft viability can be better understood by explaining the processes that take place when any substance is placed on a fresh wound \cite{5, 30}. If the wound is free from necrotic tissue and micro-organisms, and the graft is left undisturbed, a thin layer of fibrin rapidly forms. This will allow the graft to adhere to the wound and then form a fibrin matrix, which produces a more durable adherence by a process called imbibition \cite{5}. The adherence of the fibrin matrix and a viable wound bed is critical for the benefits of wound cover achieved by allograft, xenograft and other materials. These benefits include reduced fluid loss via evaporation, reduced pain, reduced metabolic demands and sterilisation of the underlying wound, and is not influenced by the viability of the covering material \cite{5}. Viable allograft does however adhere quicker and easier and lasts longer than other materials.

The next step in the process involves fibroblast proliferation and collagen synthesis. This process has the ability to totally encase any foreign material and can easily be mistaken for true take. After about 48 hours, the true benefit of viable allografts versus other substances becomes apparent. At this stage autograft and viable allograft will become re-vascularised. Capillaries will grow into the graft from the wound bed and form anastomoses with graft capillaries. This revascularisation will supply the graft with all the nutrients necessary to survive and denotes true take. This final step is only possible if the graft is structurally intact \cite{5, 31}. The fresher and more viable the graft, the better the take will be. During the following days a difference in the fate between allograft dermis and epidermis might also become apparent. The epidermis, which forms the vapour barrier of the skin, has no intrinsic blood supply. It receives its oxygen and nutrients via diffusion from the underlying dermal plexus \cite{32}. During the first 48 hours after grafting, the epidermis must survive anaerobically until re-vascularisation occurs \cite{5}. If graft take is compromised for whatever reason, epidermolysis will take place and the epidermis will be lost. The epidermis also contains Langerhans cells. These cells express type II histocompatibility antigens and serve as the major stimulus to rejection \cite{5}.

Dermis, on the other hand, consists of a relatively inert extracellular matrix of proteins and glycosaminoglycans, with scattered fibroblasts that have much less antigenicity \cite{5}. This leads to dermis being better able to tolerate the metabolic demands of grafting, while also being less susceptible to rejection compared to epidermis. Allograft epidermis will start to be rejected by 1 to 2 weeks, although this process can be delayed in severe burn victims due to their underlying immunosuppression. Allograft dermis can survive and function as a scaffold for ingrowth of epidermis, but is usually turned over and replaced by autologous tissue \cite{5, 32}.

Although this sequence of events can give the initial appearance of graft take in non-viable products, there is no doubt that living allograft is far superior in function
to any other product available. Vascularised allograft will perform the functions of living skin until rejection occurs. It will reduce evaporative heat and fluid losses, reduce inflammation and metabolic demands and help to reduce infection by circulating white blood cells [5]. These benefits of allograft will last until rejection occurs. The patients with the largest burn wounds are often very immunosuppressed and therefore the allografts tend to survive longer on these patients. Fresh, living allograft remains the gold standard to which all other substances are compared [5, 33].

The benefits of allograft have been described by numerous authors. The ability of allograft and xenograft to contain and stop wound infection is particularly important in large burn wounds. By covering infected wounds on rats with fresh rat allograft and both fresh and frozen/irradiated porcine xenograft, Burleson and Eiseman showed that all these substances effectively sterilized the wound within 4 to 8 days [5, 34]. Changing the allograft every 48 hours augmented this process [5]. Allograft has also been observed to improve healing in marginal wounds beyond what can be explained simply by control of infection. This is possibly due to the provision of a moist, protected wound healing environment which is free from desiccation [5]. A further benefit of allograft is that it contains significant amounts of endogenous growth factors. The positive influence of this on wound healing was discussed by Spence and Wong, who published a series on complex wounds that healed following allograft cover [5, 35].

The indications for allograft use was discussed by Rogers in 2013 [36]. It can be used as biological cover to enhance re-epithelialisation in partial thickness burns and exfoliative disorders and as temporary cover for excised deep burns. It improves patient survival and subsequent autograft take by the mechanisms previously discussed. It may also be used to cover widely meshed autografts in the so-called Sandwich or Alexander technique, to protect the exposed interstitial areas while awaiting re-epithelialisation [37]. Allograft can be used to test the suitability of a wound bed for grafting. If the allograft takes well, the bed can be assumed to be ready to support autografts. Removing this allograft will then also leave a well vascularised bed on which the autografts can be placed. Should the allografts fail to take, it would be reasonable to suspect that autografts will also fail. Additional measures should then be undertaken to prepare the wound before further grafting is attempted [36]. The different techniques in preparing and preserving allograft, and their various influences on results are beyond the scope of this review and will not be discussed here. It must be noted in a recent study by Austin RE et al that the rapidity of application and cost involved in wound cover was faster and cheaper with Biobrane than with allograft [38]. However, I believe that the physiological benefits of allograft as well as the quality of wound bed that results from allograft, far outweighs the potential financial and time benefits obtained from Biobrane.
b. Allograft amnion

Human amnion allografts have also been used since 1910 as a biological dressing [39]. Although it rivals human skin allografts in its ability to preserve a healthy wound bed and deter bacterial contamination, it is more fragile and difficult to handle [3, 40]. It does not re-vascularise, and therefore has to be replaced every 2 days [40]. It can be used fresh, or refrigerated, with irradiation and glycerol preservation. As with any biological dressing, disease transmission remains a possibility [3].

c. Xenografts

Sheep skin was used for the first xenograft in the United States in 1880 [5, 41]. Since then various animals have been used as skin donors, including frog, lizard, rabbit, dog and pig [3]. Porcine xenografts from domestic pigs are currently the only commercially available products [5, 42]. Various preparation and processing techniques have reduced its antigenicity and prolonged adherence [5, 43], and allows it to be stored at room temperature [44]. Although xenografts confer much of the same benefits to burn patients as allografts, they will adhere to wounds but will not vascularise [5]. It is useful as a temporary wound cover but is inferior to allografts in this respect. Xenografts have other benefits over allografts which make them a reasonable choice if only short term cover is required and allografts are not available [5].

d. Synthetic skin

Research has focused on developing synthetic products for use as temporary wound cover. Simplistically, the aim of these products is to function as closely to normal skin as possible, while allowing wound healing to take place below [3]. Biobrane and Suprathel are two examples of products in this ever expanding category [3, 4, 5, 6]. Biobrane, a woven nylon membrane coated with silicone to which porcine collagen is chemically bonded was described by Tavis et al in 1980 [5, 45, 46]. Its structure allows adherence and the ingrowth of fibroblasts [5], which allows it to function as an artificial scab. It protects the wound while allowing epithelialisation to take place underneath. It reduces the need for regular and often painful dressing changes and, as such, is especially useful for covering superficial burns in children [4, 47]. Its main drawback is the risk of infection. As such, it should not be used on infected wounds or eschar, and any areas that do not adhere immediately should be removed to prevent fluid buildup under the product [5]. Once epithelialisation is complete, the Biobrane falls off. Suprathel is a synthetic copolymer membrane [4]. After application it adheres to the wound and peels off over the following 2 weeks as re-epithelialisation proceeds underneath [4, 48]. The main benefits of these synthetic products are their ease of availability and long shelf life.
2) Permanent cover

a. Widely meshed autologous skin graft

Meshed split thickness skin grafts are still the most widely used form of skin grafting for coverage of burn wounds as well as other wounds. It offers a quick and relatively simple method of expanding skin grafts. The equipment needed is not very expensive and requires minimal technical knowledge to operate. For all its benefits, it also has significant drawbacks. The main drawback is that the true expansion rates do not match the theoretical expansion \[49\]. In a study published by Kreis et al in 1994, the authors found that meshed skin at a ratio of 1:6 gave only the equivalent of a Meek technique expansion at 1:4 \[50\]. Another drawback is that large pieces of skin, meshed at ratios greater than 1:6 become extremely fragile and very difficult to manipulate \[51, 52, 53\]. Meshed grafts at ratios of 1:6 and greater, are also difficult to secure to the wound bed. During subsequent dressing changes small areas of meshed graft may move or shear and this may jeopardise the entire graft \[51, 54\]. The interstitial areas in widely meshed autografts (more than 1:3) can be protected from dissication by the overlay of a synthetic skin substitute (Biobrane).

b. Confluent cultured epithelial autografts (CEA sheets)

For severe burns the disparity between burn wound and donor site complicates the surgical treatment of these patients \[55\]. Widely-meshed skin grafts rely on secondary healing of the interstices \[25, 56, 57\]. Variations in dermal thickness and re-epithelialisation may limit the number of times a donor site can be harvested and the delay between re-croppings can have a significant influence on time to definitive wound closure \[3, 55, 56, 57\].

The modified Meek technique, as discussed later, is an alternative to widely meshed skin grafts. Although this technique uses much less donor site skin than conventional meshed grafts, it still relies on harvesting uninjured skin, thus enlarging the total wound area further. In light of this, cultured epithelial autografts (CEA) has been proposed as a method of achieving wound closure without the need for additional harvesting of large donor areas \[55\].

Rheinwald and Green, in 1975, were the first to generate cohesive sheets of stratified epithelium from keratinocytes grown in vitro \[55, 58, 59\]. In 1981 O'Connor et al was the first to report on the clinical application of CEA \[9, 55, 60, 61, 62\]. The process is well described\[55, 63, 64, 65\]. The cultured epithelial cells can be harvested as a confluent sheet after 3-4 weeks, or in a pre-confluent state after 1-2 weeks. The pre-confluent, or spray-on CEA, has the benefit of the cells being in a hyperproliferative state \[6\]. In 3-4 weeks the stamp-size biopsy can be expanded 5 000-10 000 times, providing enough skin to resurface the entire body of an adult \[55\]. These culture times may be significantly lengthened in the elderly \[6, 66\].
However the utilisation of CEA also has significant drawbacks. These include time delay, increased risk of infections, fragility of the grafts, blister formation, questions about long term durability, cosmetic and functional results, graft contracture, diminished pigmentation, hypertrophic scarring, increased costs and the possibility of developing squamous carcinomas [6, 9, 55, 56, 60, 67, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82].

c. Non-confluent cultured epithelial autografts (spray-on skin)
Cultured epithelial cells are transferred to the wound in a pre-confluent state. The cells are carried in a suspension instead of in sheets [83]. The benefits of this over CEA sheets is a reduced culture time, and limiting the enzymatic breakdown of cell surface proteins during the process of sheet preparation [83]. This allows the CEA cells to be more robust and actively proliferating, leading to better dermal epithelialisation [83]. This technique still remains expensive, requiring a similar level of expertise from laboratory staff and also specialist equipment compared to CEA sheet grafts [84]. In a 2013 review on the practices of United Kingdom burn surgeons by Allouni et al, it was found that the most common uses for spray-on CEA was to spray over widely meshed autografts, unhealed areas, donor sites in the elderly or where the donor sites would need to be re-harvested in a short space of time. Donor sites more than 20% TBSA were also considered an indication [84].

d. Cuono technique
A major drawback to all the techniques described is the lack of ability to replace lost dermis. Cuono et al reported on a technique aimed at replacing the lost dermis in burn wounds [85]. Cadaver skin allografts are used to cover the excised burn wound. Due to the immunosuppressant effect of the massive burn, as well as the low antigenicity of dermis [5] (as discussed under the section on allografts), the allografts can survive. At the initial surgery specimens are taken for culture to generate cultured epithelial autografts. Once the allografts are adherent, the epidermal layer of the allografts are removed and resurfaced with CEA [85]. The allogeneic dermis promotes rapid stratification, maturation, and integration of the cultures and the synthesis of anchoring fibrils [85]. No rejection has been noted. The allograft dermis is usually turned over and replaced by autologous tissue [5].

e. Dermal substitutes
The strength, elasticity and flexibility of the skin is mainly provided by the dermis. In the absence of a dermal component, Integra, which is a bovine collagen construct template for cellular and vascular reconstruction can be used. It is placed on the excised bed and rapidly vascularizes in 2 to 3 weeks, followed by split thickness autograft over the Integra. The main drawback is the cost and increased risk of infection. The use is effective and functional outcomes are better than with split skin graft alone.
f. Micrografting

Problems encountered with widely meshed autografts have led Dutch surgeons at the Red Cross Hospital in Beverwijk to modify the original Meek micrografting technique [50].

As noted before, the widely meshed autografts' true expansion is much less compared to that of micrografts [49, 50]. At wide ratios the meshed autografts also become difficult to manipulate and secure to the wound [51, 52, 53]. Because the Meek skin islands are transferred to a polyamide gauze, it is much easier to handle at large expansion ratios [52]. The polyamide mesh used in Meek grafting also provides additional support to the Meek graft skin islands. This allows greater graft take over areas of high mobility such as the shoulders and hips. It also allows the grafts to be placed over and secured to irregular surfaces [54]. The nature of the micrografts also make them more resilient to movement and dislodgement when compared to widely meshed grafts. Meshed grafts at ratios of 1:6 and greater become difficult to secure to the wound bed. During subsequent dressing changes small areas of meshed graft may move or shear and this may jeopardise the entire graft [51, 54].

Various reports in the literature also point to a shortened hospitalisation time for patients where micrografting was used compared with widely meshed skin [10, 50, 51, 54, 86, 87]. Zermani et al reported an average of 14 days shorter hospitalisation and 1 surgical procedure less in patients who received micrografting compared to patients who received widely meshed grafts [54]. This is due to quicker re-epithelialisation of the wounds and therefore earlier wound closure [53]. Re-epithelialisation times of 7-10 days for 1:4 expansions, 2-3 weeks for 1:6 expansions and 1 month for 1:9 expansions have been reported. In contrast, re-epithelialisation with 1:6 and higher meshed grafts may be delayed or even absent [53, 86].

It is also reported that micrografts seem more resilient to infection compared to meshed grafts. It would appear that the quicker re-epithelialisation times of the micrografts allow less time for microorganisms to invade the interstitial tissue. Clinical reports also suggest that where infection of micrografts does occur, the grafts are not totally lost as is the case with widely meshed grafts [10, 51, 52, 53, 54, 86, 88].

All these factors allow for a shorter hospitalisation and therefore cost savings compared with meshed grafts [52, 54, 86, 87]. This may offset the initial expense of the specialised equipment needed to perform the modified Meek micrografting [52].

Another benefit of Meek micrografting is the economy of harvested skin. Large strips of skin are not needed as with traditional meshed grafts. Even the smallest pieces of skin can be pieced together on the cork boards, similar to a puzzle, in order to produce the micrografts [52]. These small pieces may often go to waste with mesh grafts. This makes the modified Meek technique particularly suitable for use in children with limited donor sites [52].
The final aesthetic outcome of micrografting is reported to be at least equal, and in many cases superior, to widely meshed grafts (more than 1:3 ratio)\cite{8,54}. More long term comparative studies need to be done to compare the aesthetic and functional outcome between micrografts and conventional mesh grafts, but it is important to remember that micrografting is in the first place a lifesaving technique ideally suited for cases where insufficient donor sites exist for traditional mesh grafting.

Despite all the benefits of the modified Meek technique, there are some drawbacks which deserve mention. The initial setup cost is more expensive compared to standard mesh grafts. Unlike the equipment needed to perform a standard mesh skin graft, which is available in most operating theatres, the Meek cutting machine is not widely available. The equipment needed for micrografting consists of the cutting machine and the disposables. Disposable items include the micrograft gauze with various expansion rates from 1:3 to 1:9, and the Meek spray adhesive. The cost of these items is probably not justifiable outside of a dedicated burns unit.

The technique is also more labour intensive and takes longer to perform than standard mesh grafts due to the added time needed to prepare the grafts. This can be circumvented by working in two teams. The first team starts by harvesting skin. While the second team prepares the grafts from the harvested skin, the first team proceeds to excising/preparing the wound bed. Once the wound bed is ready, the first micrographs will be ready for the first team to proceed with grafting\cite{10,53}. Although this method saves valuable operating time, it also means that a larger team is needed in theatre\cite{53,54}. Although improved graft take, fewer infections, fewer returns to theatre for repeat grafting and shorter hospital stays may offset all the extra costs incurred in the modified Meek technique, more studies are needed to quantify the exact cost benefit.

**Meek Surgical Technique**

The donor site selection was pre-determined by the extent of the burn, previous donor site procurement and the state of healing thereof and the anatomical site of the residual available donor skin. Although some patients can present with ideal unburnt donor areas like the thighs, some smaller burns only have inaccessible areas over bony prominences, ribs, paraspinal areas, peri-anal and neck areas. Adequate strip procurement of this skin is almost impossible. This accounted for the cases of 6 burns less than 30% TBSA to have received micrografts.

Split skin is harvested in the usual fashion. This is then placed, dermal side down, on a 42mm x 42mm piece of cork. Smaller pieces of skin can also be utilised by putting them together on the cork in a puzzle-like manner. The cork, with skin on, is then passed through a purpose built machine with 13 parallel circular blades. This results in 14 strips of skin of 3mm width each. After the first pass the cork is rotated 90 degrees and once again passed through the machine. The blades will only cut
the skin graft, and leave the cork intact. This second pass results in a graft that is cut into 196 square pieces of 3mm x 3mm each. The epidermal surface, which is facing up on the cork, is then sprayed with a special adhesive spray and left to dry until the spray becomes sticky. The cork with the 196 square pieces of cut skin graft is then placed onto a pre-folded polyamide gauze. Due to the spray-on glue the skin and gauze then stick to each other. The gauze itself is not flat but pre-folded into 14x14 square pleats on an aluminium foil backing. These pleats correspond to the size of the cuts in the graft. As the gauze and skin graft is now adherent to one another, the cork can gently be removed. By pulling in all four directions on the foil, it expands with the gauze until all pleats are unfolded. Finally the foil is gently removed, leaving only the gauze with adherent skin graft islands ready for transfer to the wound. The gauze is then placed graft side down on the wound and secured with surgical staples. As the skin was initially placed dermal side down on the cork, the dermal side of the graft is now correctly orientated on the wound bed. After 5 to 7 days the grafts are sufficiently adherent to the wound and the glue will have loosened enough to allow the gauze to be gently pulled off the graft. The adherent skin islands can then be dressed with a wound dressing of the surgeon's choice, awaiting re-epithelialisation of the interstitial areas. [Humeca company literature]

Aesthetic aspects of micrografting
Although the aim of this thesis was to look at the technique and immediate surgical outcome of the micrografting technique as a life-saving measure, rather than a cosmetic consideration, preliminary results would indicate that the cosmetic outcome is even, if not better than 1:3 expanded autograft with Biobrane. Refer to photographs in children who had both procedures done.

Conclusion
Early tangential excision and grafting is the gold standard in treating deep burns. The dilemma in large burns in excess of 30% TBSA is the lack of adequate donor sites to allow for early wound cover. Various techniques have been proposed as a solution to this problem. The modified Meek micrografting technique is a valuable method to achieve early, permanent and long term durable cover. The 8 children with burns exceeding 50% TBSA, who survived, had an average TBSA of 62.2% in comparison to the 67.15% in the 8 children who demised. However, of the 3 out of the 8 who died, one child with stage 4 AIDS and tuberculosis was electively palliated, one referral to us at 3 months post burn, had severe re-feeding syndrome, kwashiorkor, trace elements deficiency and hypothyroidism and one had Propranolol toxicity with non-occlusive mesenteric ischaemia and infarction. In 2, skin grafting was completed, but they died from multi-organ failure.

Although the aim of this study was to look at the technique and immediate surgical outcome of the micrografting technique as a life-saving measure, rather than a cosmetic consideration, preliminary results would indicate that the cosmetic
outcome is even, if not better than 1:3 expanded autograft with Biobrane. It could therefore be considered in the future for smaller burns.

4. Aims And Objectives Of Current Study

- To evaluate the role of the modified Meek micrografting technique in the management of major burn wounds.
- Document the efficacy of micrografting in obtaining early and permanent wound cover in major burn surgery.
- Review the limitations of micrografting as burn wound cover.
- Assess possible changes in management protocols to improve outcomes in major burn wounds.

5. References

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Part I: Journal Article

Experience and outcome with micrografting for major burns

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Abstract:

Background. The Meek micrografting technique was introduced in 2003 as a rescue method to achieve epithelialisation in major burns.

Objective. To evaluate its role in the management of major burns with reference to its efficacy, technical detail and role in major burn surgery.

Methods. A retrospective review of 27 patients over a 12 year period who received Meek micrografting as part of their management in achieving skin cover for major burns. Baseline characteristics of the patients were collected from patient records and operative notes.

Results. Twenty-seven children were treated with the micrografting technique. Their ages varied from 3 months to 11 years, total body surface area (TBSA) was 49.7%. Eight children had concomitant inhalation injury. Five were late and neglected referrals of whom 2 developed the re-feeding syndrome. Length of stay was 9-262 days (mean 70 days, 1.4 days/1% burn).

Micrografting was performed on days 5-117 (mean 26 days) and a mean area of 25.6% TBSA (range 5-63%) was grafted. On average 7.8 operations were performed to complete skin cover. On average 2.7 (range 0-9) surgical procedures preceded the micrografting and a further 3.2 (range 0-10) procedures were required after micrografting to complete wound cover.

Graft take at 1 month was more than 90% in 16 children of whom 3 subsequently died. Eleven patients had less than 90% graft take, of whom 5 died.

Conclusion. The Meek technique is technically demanding, but provides high expansion ratios thereby facilitating wound cover in the presence of limited donor sites.
Introduction

The survival of patients with major burns is hampered by a lack of autograft donor skin in low and middle income countries (LMIC). This restrictive factor is increasingly encountered as the main impediment in achieving wound cover. Mesh grafts require the presence of approximately an equal surface area to cover the excised wound. In burns exceeding 30% total body surface area (TBSA) this is problematic due to the unavailability of sufficient donor skin areas [1].

To overcome this shortage in available donor skin, the use of alternative methods are required. Collectively however they are very expensive and not readily available in South Africa. Measures to overcome this shortage of donor skin include the use of allografts, either fresh or hydrolysed. Unfortunately there is not an established skin bank in South Africa and allografts, currently are often only procured from solid organ donors. A second method includes cultured epithelial autografts either as spray on or as sheet grafts. Both methods are prohibitively expensive and not readily available here. They also have potentially major disadvantages [2].

A third method involves extensive expansion of autografts from 1:3 to 1:9 ratios. This method is effective to cover large areas but needs an overlay of biological/synthetic dressings or allografts to prevent desiccation of the denuded interstitial areas.

The fourth method is utilising the modified “Meek” technique of micrografting [3-6]. This technique was introduced in 1958 and modified in 1993. The technique effectively expands the procured skin surface area three to four to nine fold in a “postage stamp” method and provide the greatest possible growing margins from the multiple small geometrically equal epithelial and dermal islands. It is now extensively used internationally as a rescue method for major burns in the presence of deficient donor skin area [4,5,8,9].

The Meek micrografting system was introduced into South Africa in 2003 to overcome the acute shortage of allografts and functions as a permanent autologous skin cover technique with widely expansive properties. We have had limited exposure to this technique in our attempts to save the lives of patients with major burns. A retrospective review of the 27 patients to date who had received micrografting will help to define its position in the future management of major burns in regards to its efficacy, technical problems encountered and place in burn major surgery. This is particularly needed in view of the absence of a skin bank and the major difficulties encountered in procuring suitable allografts [10]. This is a retrospective review of a standard surgical procedure. The investigators anticipate that the micrografting technique would be greatly beneficial in obtaining autologous wound cover in major burns.
Methodology

Between 2003 and 2016 a total of 27 children underwent micrografting procedures involving the modified Meek technique to achieve wound cover \[^4\]. The parents were fully informed about the reasons for using micrografting and were all consented for the procedure. Ethical permission was obtained from the departmental research committee, the UCT Faculty of Health Sciences Research Ethics Committee and the provincial government (HREC REF: 574/2015).

Standard emergency and intensive care was provided to all patients. Baseline characteristics of the patients were collected: age, cause of injury, TBSA, component partial and full thickness, inhalation injury, number of operations to achieve full skin cover, methods to achieve skin cover and bacteriology management of the wounds prior to grafting, status of the recipient tissue bed, the preparations required to optimise graft take in particular allograft placement), factors influencing the take rate after transplantation, the role of wound bacteria in graft take, percentage graft take, outcome and reasons for failure of the Meek technique.

Surgery followed standard procedures of preparedness for the operation, standard anaesthesia, wound preparation, procurement of donor skin and micrograft preparation, the application of the micrografts, and standard post operative care including the use of allografts if available. All children received routine post operative care.

Preparing the burn wound for micrografting surgery.

Following the induction of anaesthesia, completion of the WHO checklist, the dressings were removed and the burn wound washed with 1% chlorhexidine soap followed by the topical application of 0.006% sodium hypochlorite solution for 20 minutes\[^11\].

The body was divided into priority segments: head and neck, anterior and posterior trunk, upper and lower extremities and the gluteal and perineal areas. The surgical aim was to reduce the wound area as soon as possible to below 30% TBSA, hence the individual selection of the areas to excise and to graft. The pre-selected wound area was then excised to a viable level either deep dermal, viable fat or down to the fascial layer. The donor areas were selected from small unburned areas that were usually scattered throughout the body surface area.

Thin (0.2-0.3mm) autografts were harvested, the widely expanded micrografts (1:3, 1:4) prepared and directly transplanted onto the recipient area and covered with a topical silver antibacterial dressing. The technique of harvesting, preparation and application of the micrographs are well described \[^4,12\]. The Meek Micromesher system Humeca, Netherlands) was used. The essential component of the technique is as follows: Procurement of the skin followed by placement of the skin on cork squares, which are then cut with a special mechanical device into a 196
geometrically even square pieces of skin. These are stuck down on a pre-prepared folded plisse, which is then expanded and placed onto the wound and secured with skin staples. The transplanted sheets are then covered with an elastic silver-containing pressure bandage or negative pressure dressing, if this can be achieved. To expedite the procedure, a two teamed approach is preferred. One team procures the skin and then prepares the wound bed, while the second team processes the micrografts.

The dressings were post-operatively changed on day one and thereafter regularly on day 3, 5 and 7 when the outer gauze sheeting was removed leaving the micrografts exposed. They were then covered with an antibacterial dressing which were changed on alternative days until full epithelialisation had occurred. Alternatively the micrografts were covered with allografts if available. Infections were closely monitored and treated according to the sensitivity patterns and standard wound care procedures.

**Results**

Twenty-seven children were treated with the micrografting technique (3% of total burn operations annually). **Table 1.** The ages varied from 3 months to 11 years (mean 4.0 years) and the total body surface area (TBSA) from 15-86% (mean 49.7%). Flame burns were seen in 17 and hot liquids in 10. All had deep to full thickness burns necessitating excision and grafting. Eight children had concomitant inhalation injury, all with fire burns more than 50% TBSA. Five were late and neglected referrals of whom 2 developed the re-feeding syndrome. Frank myoglobinuria was seen in 2 children with burns >50% TBSA burns, both demised. Length of stay was 9-262 days (mean 70 days ; 1.4 days/1% burn). The length of stay for survivors were 10 days to 262 days with a mean length of stay of 75.47 days. The patients who survived had a TBSA burn ranging from 15% to 86% (mean 41.47%) This calculates to a length of stay of 1.8 days/1% burn for the survivors.

Allografts to either prepare the recipient area or post application of Meek micrografts were used in a total of 5 and 7 patients respectively.

The micrografting technique was part of additional procedures required to achieve full epithelialisation. The recipient bed consisted of viable subcutaneous tissue or fascia. Micrografting was performed on days 5-117 (mean 26 days) and a mean area of 25.6% TBSA (range 5-63%) was grafted. On average 7.8 operations (range 1-26) were performed to complete skin cover. On average 2.7 (range 0-9) surgical procedures preceded the micrografting and a further 3.2 (range 0-10) procedures were required after micrografting to complete wound cover. One child had a total repeat of micrografts. These were done on day 2 post burn and micrografts were placed on excised viable fat. She had subsequent Acinetobacter infection with 100%graft loss. This was re-grafted once adequate donor site recovery was established, the infection cleared and the debrided, well granulated bed established. Graft take the second time was 95%.
When the overlay gauze dressings were removed after 5-7 days some detachment of skin islands occurred without impairing the final outcome. Graft take on day 10-13 was satisfactory and at 1 month was more than 90% in 16 children of whom 3 subsequently died from inhalation injury (1), Propranolol toxicity (1) and 1 child palliated. Eleven patients had less than 90% graft take, with a mean of 56.16% (range 2-80%). Five of these children demised. Local infections were due to Pseudomonas (6), Klebsiella (2) and Acinetobacter (2).

Eight children (TBSA 67.8%) died. Contributing factors to mortality include: multi-organ failure in 7 and palliative care in one infant with Aids. Other factors included smoke inhalation injury (6), re-feeding syndrome (1), trace element deficiency, kwashiorkor and hypothyroidism in 1, pyroglutamic acidurea in 1, Propranolol toxicity (1). The child, with Propranolol ischaemic induced total bowel necrosis, had 97% of his skin grafting completed.

Table 2 depicts the use of allografts, which were used in 5 children before the micrografting, in 4 children following the micrografting, and in 7 children in combination before and after the micrografting procedure. The high mortality in the latter group is a reflection of the severity of the co-pathology associated with their fire burns. Inhalation injury (4), multi organ failure (5), pneumonia (1), Propranolol ischaemic bowel necrosis (1), and nutritional failure due to late referral (1) were compromising factors.

The 8 children with burns exceeding 50% TBSA, who survived, had an average TBSA of 62.2% in comparison to the 67.15% in the 8 children who demised.

The 19 surviving children had an average TBSA of 44.3%. Of this cohort, 22.1% were grafted (51% of total wound). Of the 8 children who died, with and average TBSA of 63%, 32.8% was grafted (52% of total wound). The residual areas were autografted either before or after the micrografts.

We have calculated the LD50 for burns exceeding 50% TBSA. The average TBSA was 64%. Thus, with a TBSA of 64% in this study, 50% would survive and 50% would die.
Table 1. Patient demographics and surgical characteristics

<table>
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<th>Case and age</th>
<th>% TBSA</th>
<th>Meek grafting day post burn</th>
<th>Meek Grafts</th>
<th>Surface Area Covered (cm²)</th>
<th>Total number surgeries</th>
<th>Mortality</th>
<th>Comments</th>
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<td>7</td>
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<td>95 100 80 80</td>
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<td>26</td>
<td>60</td>
<td>897.6</td>
<td>5</td>
<td>Alive</td>
</tr>
<tr>
<td>6. 3y</td>
<td>28</td>
<td>14</td>
<td>18</td>
<td>80</td>
<td>1267.2</td>
<td>3</td>
<td>Alive</td>
</tr>
<tr>
<td>7. 3y</td>
<td>15</td>
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<td>15</td>
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<td>739.2</td>
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</tr>
<tr>
<td>8. 19m</td>
<td>55</td>
<td>9</td>
<td>37</td>
<td>90</td>
<td>2323.2</td>
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<td>Alive</td>
</tr>
<tr>
<td>9. 5y</td>
<td>56</td>
<td>50</td>
<td>36</td>
<td>95</td>
<td>1408</td>
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</tr>
<tr>
<td>10. 23m</td>
<td>17</td>
<td>38</td>
<td>17</td>
<td>99</td>
<td>1003.2</td>
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<td>Alive</td>
</tr>
<tr>
<td>Case and age</td>
<td>% TBSA</td>
<td>Meek grafting day post burn</td>
<td>Meek Grafts</td>
<td>Surface Area Covered (cm²)</td>
<td>Total number surgeries</td>
<td>Mortality</td>
<td>Comments</td>
</tr>
<tr>
<td>-------------</td>
<td>--------</td>
<td>----------------------------</td>
<td>-------------</td>
<td>---------------------------</td>
<td>------------------------</td>
<td>-----------</td>
<td>----------</td>
</tr>
<tr>
<td>11. 3y</td>
<td>76</td>
<td>5 6</td>
<td>41</td>
<td>3660.8</td>
<td>15</td>
<td>Alive</td>
<td>Recurrent sepsis. Pneumonia. Cardiomyopathy.</td>
</tr>
<tr>
<td>13. 7y</td>
<td>48</td>
<td>4 42</td>
<td>33</td>
<td>2006.4</td>
<td>6</td>
<td>Alive</td>
<td>Most of Meek grafts lost due to Pseudomonas infection. 2nd Meek grafting performed.</td>
</tr>
<tr>
<td>14. 18m</td>
<td>45</td>
<td>45</td>
<td>8</td>
<td>316.8</td>
<td>5</td>
<td>Alive</td>
<td>Inhalation injury. Aspiration pneumonia.</td>
</tr>
<tr>
<td>15. 8y</td>
<td>66</td>
<td>11</td>
<td>22</td>
<td>1795.2</td>
<td>7</td>
<td>Alive</td>
<td></td>
</tr>
<tr>
<td>16. 4y</td>
<td>50</td>
<td>25</td>
<td>10</td>
<td>1267.2</td>
<td>8</td>
<td>Alive</td>
<td></td>
</tr>
<tr>
<td>17. 3m</td>
<td>23</td>
<td>29</td>
<td>5</td>
<td>158.4</td>
<td>4</td>
<td>Alive</td>
<td></td>
</tr>
<tr>
<td>18. 18m</td>
<td>45</td>
<td>30</td>
<td>16</td>
<td>844.8</td>
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<tr>
<td>19. 9m</td>
<td>20</td>
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<td>6</td>
<td>316.8</td>
<td>2</td>
<td>Alive</td>
<td></td>
</tr>
<tr>
<td>20. 7y</td>
<td>80</td>
<td>15 52</td>
<td>63</td>
<td>3168</td>
<td>11</td>
<td>Died</td>
<td>Inadequate excision. Colostomy. MOF.</td>
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<tr>
<td>21. 8y</td>
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<td>17</td>
<td>28</td>
<td>1795.2</td>
<td>9</td>
<td>Died</td>
<td>Inhalation injury. Colostomy. MOF.</td>
</tr>
<tr>
<td>Case and age</td>
<td>% TBSA</td>
<td>Meek grafting day post burn</td>
<td>Meek Grafts % TBSA</td>
<td>% Graft Take</td>
<td>Surface Area Covered (cm²)</td>
<td>Total number surgeries</td>
<td>Mortality</td>
</tr>
<tr>
<td>-------------</td>
<td>--------</td>
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<td>-------------</td>
<td>-----------------------------</td>
<td>------------------------</td>
<td>---------</td>
</tr>
<tr>
<td>22.5y</td>
<td>84</td>
<td>3 4</td>
<td>46</td>
<td>90</td>
<td>2323.2</td>
<td>3</td>
<td>Died</td>
</tr>
<tr>
<td>23.6y</td>
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<td>32</td>
<td>32</td>
<td>70</td>
<td>1698.6</td>
<td>6</td>
<td>Died</td>
</tr>
<tr>
<td>24.20m</td>
<td>55</td>
<td>9 37</td>
<td>90</td>
<td>2323.2</td>
<td>13</td>
<td>Died</td>
<td>Inhalation injury. Colostomy. Propranolol toxicity. Bowel necrosis. MOF</td>
</tr>
<tr>
<td>25.11y</td>
<td>77</td>
<td>5 29</td>
<td>50</td>
<td>1760</td>
<td>8</td>
<td>Died</td>
<td>Inhalation injury. Frank myoglobinuria. Colostomy. Grafted on inadequate bed. MOF</td>
</tr>
<tr>
<td>26.5y</td>
<td>52</td>
<td>11</td>
<td>28</td>
<td>100</td>
<td>768</td>
<td>8</td>
<td>Died</td>
</tr>
</tbody>
</table>

MOF: Multiple Organ Failure
Table 2. Use of allografts

<table>
<thead>
<tr>
<th>Allograft</th>
<th>Number of Patients</th>
<th>Survivors</th>
<th>%TBSA</th>
<th>% Graft Take</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre Meek</td>
<td>5</td>
<td>5</td>
<td>50.2(40-61)</td>
<td>86(80-90)</td>
</tr>
<tr>
<td>Post Meek</td>
<td>4</td>
<td>3</td>
<td>71.25(56-86)</td>
<td>85.4(50-100)</td>
</tr>
<tr>
<td>Pre and Post Meek</td>
<td>7</td>
<td>1</td>
<td>65.28(38-86)</td>
<td>59.5(10-100)*</td>
</tr>
<tr>
<td>No Allograft</td>
<td>11</td>
<td>10</td>
<td>31.72(15-84)</td>
<td>86.2(2-100)</td>
</tr>
</tbody>
</table>

*High mortality due to propranolol ischaemic bowel necrosis(1), inhalation injury (4), MOF (5).

Discussion

With improved survival of major burns, the lack of donor sites is becoming a limiting factor in achieving wound closure expeditiously. Meshed split skin grafting has been the standard method for severely burnt patients. However the shortage of available donor sites, especially if the burn exceeds 30% TBSA has hampered early closure of the burn. This often results in wound infection, septicaemia, ongoing catabolic “burn disease” and increased mortality.

The lack of adequate donor sites therefore mandates other temporary or permanent methods to achieve wound cover as rapidly as possible. Donor sites especially in large burns often are slow to heal, may become infected or are unsuitable for skin procurement and needs to re-epithelialise (10-14 days) before it can be used again. The micrografting technique therefore allows small areas to be utilised as donor...
areas where otherwise they would not have been suitable as donor areas for skin procurement. The sequence when to do the micrografting depends on the patients’ stability, the availability of donor sites, wound preparedness and availability of allografts. The value of the micrografting technique, as a rescue method to resurface major burns, is therefore invaluable and is a viable alternative to standard techniques\[5,6\].

Our indications were specific. It was used for major burns as a rescue procedure and in small infants to obtain skin closure when there were no other options available, thereby circumventing delaying wound closures or the use of cultured epithelial autograft.

The technique differs from “spray on skin” where non-confluent cells in suspension may not always be correctly orientated (dermal side down) or CEA sheet grafting which do not expand nor having a dermal component. The technique also distributes skin elements more evenly in comparison to meshed grafts. The transplanted skin also consists of epidermis and dermis, the latter been responsible for the quality of the transplant skin. Alternatively the micrografts can also be placed on neodermis from a previously placed collagen based dermal substitute.

A true expansion ratio of 1:3, 1:4, 1:6 and 1:9 can be achieved thereby covering a wound surface of 52.8cm² to 158.4cm² from each block of 42mm² x 42 mm² used. These grafted islands are close together in a regular pattern and rapidly grow to cover the areas between the islands by creeping substitution and tissue confluence.

With meshed skin grafting there is also a significant difference between expected and actual expansion ratios with very few meshed grafts reaching their expected expansion. The expansion ratio of 1:3 meshed skin is only achieved in 53% using standard derma-carriers in comparison to 85.5-99.8% utilising the micrografting technique. This difference is particularly important when donor sites are at a premium and the need to graft large surface areas. The results obtained by us and others demonstrated that large burns can successfully be grafted with this technique\[13\].

What became apparent early on was the need to cover the micrografts on day 7-10 with allografts. This would have sealed the recipient areas and created the ideal environment for the micrografts to grow towards total surface closure. In the children were allografts were used, primary epithelialisation was satisfactory. This should be the standard procedure but in the absence of a functional skin bank alternative and inferior methods have been used. In those not covered, delayed healing was common often associated with infections. Wound infection however was not a total catastrophe and in our experience only temporarily retarded final epithelialisation except in 2 patients were major losses occurred due to an inadequately prepared recipient bed and deep seated infections. It was remarkable in the others to witness the “resurrection” of apparently lost grafts due to infection only to recover with spontaneous re-epithelialisation of the whole area. This phenomenon is not uncommon in graft losses from Pseudomonas infection. Once
the infection was brought under control, re-epithelialisation occurred spontaneously. This can only be explained by the fact that infection does not destroy all epithelial islands from which re-epithelialisation proceeded[6,12,14].

As we gained more experience it became apparent that although standard 1:3 mesh expansion skin take on fat is often successfully achieved, this may not be suitable for micrografting. To enhance "take" the future recipient area should be pre-prepared with allografts, synthetic skin, or a topical agent that stimulates granulation tissue. In addition, to stimulate rapid post graft epithelialisation, we suggest that the micrografts be covered with allografts, negative pressure dressings if achievable or CEA (non-confluent component). This will have a dual effect namely prevention of desiccation of the interstitial areas and acceleration of epithelialisation.

The 19 children who survived, had an average TBSA of 62.2% in comparison to the 67.15% in those who demised. However, of the 3 out of the 8 who died, one child with stage 4 AIDS and tuberculosis was electively palliated, one referral to us at 3 months post burn, had severe re-feeding syndrome, kwashiorkor, trace elements deficiency and hypothyroidism and one had Propranolol toxicity with non-occlusive mesenteric ischaemia and infarction. In 2, skin grafting was completed, but they died from multi-organ failure.

We have learnt the following lessons from our experience. The recipient bed must be viable and vascularised and can be prepared by the application of allografts, a synthetic skin substitute or negative pressure wound dressing. Fat constitutes an unstable bed. Elastic silver nylon dressings, when applied under moderate tension, ensures constant apposition of the micrograft to the bed. Negative pressure dressings could also be applied if the site is suitable. Final epithelialisation can be enhanced by the application of allograft once the Meek sheets have been removed, or alternatively, by the use of CEA. Bio-synthetic dressings should be avoided as the infection risk is too high. Pseudomonas wound infection was a contributing factor in graft loss. Spontaneous re-epithelialisation following infection, was often seen.

**Weaknesses of the study**

This was a retrospective study of a limited number of children with very complex management problems. Although this is regarded as a rescue operation in very large burns, 6 smaller burns were included, because of the unsuitability of available donor sites to do standard strip grafts. We are unable to comment on the long term aesthetic outcome of many of the children, as they are commonly lost to follow-up in a setting of poverty and informal settlements.
Conclusion

The micrografting technique is ideally suited for major burns requiring skin cover in the presence of limited donor areas or in smaller burns where inadequate skin procurement sites are available. Large expansion ratios are possible, graft take is good with satisfactory epithelialisation and the cosmetic appearance is comparable to meshed grafting. The recipient bed must be well prepared and graft infection does not necessary lead to overall graft failure. The best method possible for major burns would be adequate preparation of the recipient bed followed by micrografting with “spray on skin” (CEA) to immediately cover the interstitial areas and finally covered with allografts\textsuperscript{[15]}. The LD50 of 64\%TBSA in this study, is acceptable taking into account the adverse co-morbidities of the study population.

Conflict of Interest

Nil

References


26 November 2015

HREC REF: 574/2015

Prof H Rode
Paediatric Surgery
Red Cross War Memorial Children's Hospital

Dear Prof Rode,

PROJECT TITLE: THE WEEK MICROGRAPH TECHNIQUE IN MAJOR PAEDIATRIC BURNS (MMed Candidate - Dr D Potgieter)

Thank you for submitting your request to the Faculty of Health Sciences Human Research Ethics Committee.

The HREC acknowledge that the MMed Student, Dr Dawid Potgieter will also be involved in this study.

The study was formally approved on 11 August 2015 and the approval is valid for one year until 30 August 2016.

Please quote the HREC REF in all your correspondence.

Yours sincerely,

[Signature]

PROFESSOR M BLOCKMAN
CHAIRPERSON, FHS HUMAN RESEARCH ETHICS COMMITTEE
Appendix 2: RXH research approval

Dr Potgieter
Red Cross War Memorial Children’s Hospital

Dear Dr Potgieter,

APPROVAL OF RESEARCH
PROJECT TITLE: EXPERIENCE WITH MEEK MICROGRAFTINGTECHNIQUE IN MAJOR BURNS

It is a pleasure to inform you that approval is hereby granted to conduct the above-mentioned study at Red Cross War Memorial Children’s Hospital.

Yours sincerely,

Dr AS Booysen
Manager: Medical Services
Date: 27.11.15

www.westerncape.gov.za
Appendix 3: Photographs of Meek micrografting results

Figure 1

Early result of micrografting showing excellent skin pliability.

Figure 2

Micrografting showing acceptable cosmetic outcome and good pliability.
Figure 3

Good cosmetic result of micrografting compared to meshed grafting
Appendix 3: SAMJ author guidelines

Author Guidelines

Accepted manuscripts that are not in the correct format specified in these guidelines will be returned to the author(s) for correction, and will delay publication.

AUTHORSHIP
Named authors must consent to publication. Authorship should be based on: (i) substantial contribution to conception, design, analysis and interpretation of data; (ii) drafting or critical revision for important intellectual content; or (iii) approval of the version to be published. These conditions must all be met (uniform requirements for manuscripts submitted to biomedical journals; refer to www.icmje.org).

CONFLICT OF INTEREST
Authors must declare all sources of support for the research and any association with a product or subject that may constitute conflict of interest.

RESEARCH ETHICS COMMITTEE APPROVAL
Provide evidence of Research Ethics Committee approval of the research where relevant.

PROTECTION OF PATIENT’S RIGHTS TO PRIVACY
Identifying information should not be published in written descriptions, photographs, and pedigrees unless the information is essential for scientific purposes and the patient (or parent or guardian) gives informed written consent for publication. The patient should be shown the manuscript to be published. Refer to www.icmje.org.

ETHNIC CLASSIFICATION
References to ethnic classification must indicate the rationale for this.

MANUSCRIPTS
Shorter items are more likely to be accepted for publication, owing to space constraints and reader preferences. Research articles (previously 'Original articles') not exceeding 3 000 words, with up to 6 tables or illustrations, are usually observations or research of relevance to clinical medicine and related fields. References should be limited to no more than 15. Please provide a structured abstract not exceeding 250 words, with the following recommended headings: Background, Objectives, Methods, Results, and Conclusion. Scientific letters will be considered for publication as shorter Research articles.
Editorials, Opinions, etc. should be about 1000 words and are welcome, but unless invited, will be subjected to the SAMJ peer review process. Review articles are rarely accepted unless invited.

Letters to the editor, for publication, should be about 400 words with only one illustration or table, and must include a correspondence address.

Forum articles must be accompanied by a short description (50 words) of the affiliation details/interests of the author(s). Refer to recent forum articles for guidance. Please provide an accompanying abstract not exceeding 150 words.

Book reviews should be about 400 words and must be accompanied by the publication details of the book.

Obituaries should be about 400 words and may be accompanied by a photograph.

Guidelines must be endorsed by an appropriate body prior to consideration and all conflicts of interest expressed. A structured abstract not exceeding 250 words (recommended sub-headings: Background, Recommendations, Conclusion) is required. Sections and sub-sections must be numbered consecutively (e.g. 1. Introduction; 1.1 Definitions; 2. etc.) and summarised in a Table of Contents. References, appendices, figures and tables must be kept to a minimum.

Guidelines exceeding 8 000 words will only be considered for publication as a supplement to the SAMJ; the costs of which must be covered by sponsorship or advertising. The Editor reserves the right to determine the scheduling of supplements. Understandably, a delay in publication must be anticipated dependent upon editorial workflow.

MANUSCRIPT PREPARATION

Refer to articles in recent issues for the presentation of headings and subheadings. If in doubt, refer to 'uniform requirements' - www.icmje.org. Manuscripts must be provided in UK English.

Qualification, affiliation and contact details of ALL authors must be provided in the manuscript and in the online submission process.

Abbreviations should be spelt out when first used and thereafter used consistently, e.g. 'intravenous (IV)' or 'Department of Health (DoH)'.

Scientific measurements must be expressed in SI units except: blood pressure (mmHg) and haemoglobin (g/dl). Litres is denoted with a lowercase 'l' e.g. 'ml' for millilitres. Units should be preceded by a space (except for %), e.g. '40 kg' and '20 cm' but '50%'. Greater/smaller than signs (> and 40 years of age'. The same applies to ± and °, i.e. '35±6' and '19°C'.

Numbers should be written as grouped per thousand-units, i.e. 4 000, 22 160...

Quotes should be placed in single quotation marks: i.e. The respondent stated: '...'. Round brackets (parentheses) should be used, as opposed to square brackets, which are reserved for denoting concentrations or insertions in direct quotes.
General formatting The manuscript must be in Microsoft Word or RTF document format. Text must be single-spaced, in 12-point Times New Roman font, and contain no unnecessary formatting (such as text in boxes, with the exception of Tables).

ILLUSTRATIONS AND TABLES
If tables or illustrations submitted have been published elsewhere, the author(s) should provide consent to republication obtained from the copyright holder.

Tables may be embedded in the manuscript file or provided as 'supplementary files'. They must be numbered in Arabic numerals (1,2,3...) and referred to consecutively in the text (e.g. 'Table 1'). Tables should be constructed carefully and simply for intelligible data representation. Unnecessarily complicated tables are strongly discouraged. Tables must be cell-based (i.e. not constructed with text boxes or tabs), and accompanied by a concise title and column headings. Footnotes must be indicated with consecutive use of the following symbols: * † ‡ § ¶ || then ** †† ‡‡ etc.

Figures must be numbered in Arabic numerals and referred to in the text e.g. '(Fig. 1)'. Figure legends: Fig. 1. 'Title...' All illustrations/figures/graphs must be of high resolution/quality: 300 dpi or more is preferable, but images must not be resized to increase resolution. Unformatted and uncompressed images must be attached individually as 'supplementary files' upon submission (not solely embedded in the accompanying manuscript). TIFF and PNG formats are preferable; JPEG and PDF formats are accepted, but authors must be wary of image compression. Illustrations and graphs prepared in Microsoft Powerpoint or Excel must be accompanied by the original workbook.

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References must be kept to a maximum of 15. Authors must verify references from original sources. Only complete, correctly formatted reference lists will be accepted. Reference lists must be generated manually and not with the use of reference manager software. Citations should be inserted in the text as superscript numbers between square brackets, e.g. These regulations are endorsed by the World Health Organization,[2] and others.[3,4-6] All references should be listed at the end of the article in numerical order of appearance in the Vancouver style (not alphabetical order). Approved abbreviations of journal titles must be used; see the List of Journals in Index Medicus. Names and initials of all authors should be given; if there are more than six authors, the first three names should be given followed by et al. First and last page, volume and issue numbers should be given.
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