

CLINICAL ETHICS

Informed consent should be obtained from patients to use products (skin substitutes) and dressings containing biological material

S Enoch, H Shaaban, K W Dunn



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Correspondence to:
Mr S Enoch, Wound Healing Research Unit, University Department of Surgery, Medicentre, University of Wales College of Medicine, Cardiff CF14 4UJ, UK; enochstuart@hotmail.com

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Background: Biological products (tissue engineered skin, allograft and xenograft, and biological dressings) are widely used in the treatment of burns, chronic wounds, and other forms of acute injury. However, the religious and ethical issues, including consent, arising from their use have never been addressed in the medical literature.

Aims: This study was aimed to ascertain the views of religious leaders about the acceptability of biological products and to evaluate awareness among healthcare professionals about their constituents.

Methods: The religious groups that make up about 75% of the United Kingdom population were identified and a questionnaire on 11 biological products was sent to its leaders. Another questionnaire concerning 17 products (11 biological and 6 synthetic dressings) was sent to 100 healthcare professionals working in seven specialist units in the UK.

Results: All religious leaders (100% response rate) replied, some after consultation with international bodies. Among them, 77% said that patients should be informed of the constituents of the biological products and consent obtained. Some leaders expressed concerns about particular products including the transmission of viral and prion diseases, cruelty to animals, and material derived from neonates. None of the healthcare professionals (73% response rate) surveyed knew the constituents of all the products correctly.

Conclusion: Ignoring religious sensitivities and neglecting consent in the usage of biological products could have very serious implications, including litigation. Hospitals and manufacturers should take immediate measures to enlighten healthcare professionals of the constituents of these products so that they can obtain informed consent from patients.

The substitution of animal skin for human skin was first tried by Canaday^{1,2} in 1692, who reported the use of water lizard skin for wound care. Since that time, xenografts, mainly from pigs, have been used in the treatment of burn wounds.^{3,4} It became well established by the early 1970s that biological skin substitutes in the form of allografts (cadaver skin, human amnion) and xenografts (mainly pig skin) held the greatest potential for restoring the body's altered physiology after severe injury including burns.⁵ Recent advances in molecular biology combined with increased understanding of the body's immune system and rapid strides in tissue engineering have resulted in an explosion of biological products (tissue engineered skin and biological wound dressings) containing porcine, bovine, or human derived contents; many being used to expedite the healing of patients with burns and other chronic wounds.

Though recent papers have tried to compare the clinical usefulness^{6,7} or cost effectiveness⁸ of individual products, the religious, ethical, and consent issues remain unaddressed in the medical literature. Currently, consent is not obtained when biological products (including allografts and xenografts) are applied to patients belonging to diverse religious and cultural backgrounds. Furthermore, the awareness of healthcare professionals about the constituents of biological products has never been evaluated, or whether they have the necessary knowledge to obtain informed consent from patients being treated with such material.

In the authors' hospital, there have been several instances when patients belonging to certain religious groups have

expressed reservations and refusal to use certain biological products. In addition, it was observed that many healthcare professionals were ignorant of the constituents of some commonly used biological products.

AIMS

This study aimed to: (1) ascertain the views of religious leaders in the United Kingdom (UK) about the acceptability of biological products and (2) evaluate the awareness of the constituents of biological products among healthcare professionals working in specialist units in the UK.

METHODS

Initial demographic data on all different religious denominations in the UK were obtained from the Office of National Statistics and Census 2001, UK.⁹ This information revealed that there were 173 religious groups in the UK. From these, 13 representative groups (table 1) encompassing 75% of the UK population were chosen.⁹ The national leaders or representatives of these religious groups were identified from their official websites and their head offices in the UK. A detailed covering letter explaining the reason for the survey, background information on some commonly used biological products (see <http://www.jmedethics.com/supplemental> for details), and a questionnaire (see <http://www.jmedethics.com> for details).

Abbreviations: CJD, Creutzfeldt-Jakob disease; DoH, Department of Health; GMC, General Medical Council.

Table 1 Religious groups surveyed

| Religious group | Official reply from leader/representative |
|-----------------------|--|
| Anglican | Canon of the Anglican Church, Chester, UK |
| Buddhists | Head of London Buddhist Vihara, London, UK |
| Chinese | Chairman of Chinese Multicultural Society, Birkenhead, Merseyside, UK |
| Multicultural Society | Archbishop of Thyateria and Great Britain, London, UK |
| Greek Orthodox | Chairman of the Hospital Liaison Committee for Jehovah's Witness Liverpool, UK |
| Jehovah's Witness | Rabbi of Childwall Synagogue, Liverpool, UK |
| Jews | Head of The Swaminarayan Hindu Mission, London, UK |
| Hindus | Headquarters, London, UK |
| Methodist | Official Islamic Institute of Fatwa, Cairo, Egypt |
| Muslims | Representative, Heswall, Wirral, UK |
| Quakers | Catholic Bishops Joint Bio-Ethics Committee, Glasgow, UK |
| Roman Catholic | Assistant Chief Secretary, London and Medical Consultant, International Headquarters, West Yorkshire, UK |
| Salvation Army | Guru Nanak Gurduwara, Birmingham, UK |
| Sikhs | |

com/supplemental) on their acceptability was sent to the national leaders or representatives of these religious groups.

A second questionnaire containing the names of 17 commonly used products and dressings (11 biological products and six synthetic dressings) was sent to 100 healthcare professionals working in seven specialist units in the UK to ascertain: (1) whether they were aware of the constituents of different biological products and (2) if they knew which of these 17 products were biological and which synthetic.

RESULTS

All 13 religious leaders returned the completed questionnaire (100% response rate) (see table 2). The leader of the Methodist Church (Headquarters, London, UK) stated that biological products should not be obtained by methods that involved cruelty to animals or human products from executed individuals. This view was also echoed by the head and resident monk of the London Buddhist Vihara (London, UK) who mentioned that Buddhists do not have any objection in using animal or human tissue, provided the animal has not been deliberately killed in order to obtain the product.

The leader of the Sikh religion (Guru Nanak Gurduwara, Birmingham, UK) mentioned that the use of animal tissue is not conflicting with Sikh religious beliefs, but patients should know the constituents of the biological products. Likewise, the Catholic Bishops Joint Bio-Ethics Committee of the Roman Catholic Church, Glasgow, UK stated that informed consent is necessary in the use of human skin. The Chairman of the Hospital Liaison Committee for Jehovah's Witness (Liverpool, UK) stated that each person must conscientiously make their own individual choice, made on and after full possession of the facts.

The leaders of the Muslim religion (Official Islamic Institute of Fatwa, Cairo, Egypt) agreed with the usage of all biological products except those obtained from pigs. However, they stated that products from the pig would also be acceptable if there were no other option for treatment. If there were an alternative, even if it took longer to heal or were more expensive, it would be better to use non-pig products. The leader of the Chinese Multicultural Society (Birkenhead, Merseyside, UK) mentioned that among their members, products obtained from cows are unacceptable to some Hindus and Buddhists, and products from pigs unacceptable to Muslims.

The leaders of The Salvation Army (Assistant Chief Secretary, London and Medical Consultant, International Headquarters, West Yorkshire, UK) although not raising any objection to the use of biological products, did raise concerns about transmission of AIDS, Creutzfeldt-Jakob disease (CJD), or unknown diseases by the application of products derived from biological sources. Though none of the dressings in the questionnaire contained material derived from fetus, the Canon of the Anglican Church (Chester, UK) stated that any product derived from fetal material should not be used (in future). The representative of Quakers (Wirral, Liverpool, UK) mentioned that products derived from neonatal prepuce (for example, TransCyte, OrCel, and Apligraf) would be unacceptable to them. All the leaders of the above three religious organisations also felt that consent was essential.

In summary, leaders of 10 religious groups (77%) expressed specific concerns about individual products and felt informed consent was necessary. The leaders of Hindu religion (Head, The Swaminarayan Hindu Mission, London, UK), Jewish religion (Rabbi, Childwall Synagogue, Liverpool, UK), and Greek Orthodox (Archbishop of Thyateria and Great Britain, London, UK) did not mention any objection to the use of biological products.

Table 2 Survey results of religious leaders (n = 13)

| Product | Anglican | Buddhists | Chinese society | Greek Orthodox | Jehovah's witness | Jews | Hindus | Methodist | Muslims | Quakers | Roman catholic | Salvation army | Sikhs |
|---------------------------|----------|-----------|-----------------|----------------|-------------------|------|--------|-----------|---------|---------|----------------|----------------|-------|
| Human cadaveric allograft | C | A | A | A | C | A | A | A | A | A | C | C | A |
| Alloderm | C | C | A | A | C | A | A | A | A | A | C | C | A |
| TransCyte | C | C | C | A | C | A | A | A | C | C | C | C | A |
| Apligraf | C | C | C | A | C | A | A | A | A | C | C | C | C |
| Human amniotic membrane | C | A | A | A | C | A | A | A | A | A | C | C | A |
| Integra | A | C | C | A | C | A | A | A | A | A | A | A | C |
| Orcel | A | C | C | A | C | A | A | A | A | A | A | A | A |
| B.G.C. Matrix | A | C | C | A | C | A | A | A | A | A | A | A | A |
| Promogran | A | C | C | A | C | A | A | A | A | A | A | A | A |
| Oasis | A | C | C | A | C | A | A | A | C | A | A | A | A |
| E-Z Derm | A | C | C | A | C | A | A | A | C | A | A | A | A |
| Any product from pigs | A | C | C | A | C | A | A | C | C | A | A | A | A |
| Any product from cows | A | C | C | A | C | A | A | C | A | A | A | A | C |
| Any product from humans | C | A | A | A | C | A | A | C | A | C | C | C | A |

A, acceptance; C, consent necessary and/or subject to other conditions (see results section).

Among the 100 healthcare professionals surveyed, 73 returned the completed questionnaire (73% response rate) (table 3). Of the commonly used biological products, 7% and 18% respectively knew Alloderm and Apligraf contained human derived material: 16% knew Integra contained bovine derived contents: 29% and 19% respectively knew that TransCyte and Biobrane contained material of porcine origin. Although E-Z Derm is a porcine xenograft, 20% of respondents thought that it was a synthetic dressing (30% did not know at all) and a similar percentage thought Duoderm, a synthetic dressing, contained some form of biological material. None of the health professionals knew the constituents of all the biological products correctly.

DISCUSSION

Biological skin substitutes in the form of allografts and xenografts have long been used to treat burn victims. They act as a mechanical barrier to infection, decrease evaporative water loss, reduce exudation of protein and electrolytes, facilitate wound debridement, promote granulation tissue, and help to relieve pain.¹⁰⁻¹¹ Although allograft remains a standard treatment for burn wounds, problems with supply, preservation, immune rejection,¹² and potential infection transmission¹³ accompanying their use have underscored the need for effective alternative temporary treatment and there has been an ongoing quest for such products.

Tissue engineering combines the scientific disciplines of biology (life sciences), materials science, and biomedical engineering to mimic the complex structures and physiological behaviour of natural tissues that are lost or damaged after injury. Artificial "skin substitute", which consists of a microengineered biocompatible polymer matrix in combination with living cells, is a significant advance in the field of wound healing and is now well established in the treatment of burns and increasingly used in the treatment of chronic wounds such as pressure and leg ulcers. Recent advances in tissue engineering have aided the development of several such products (table 4) containing predominantly bovine, porcine, or human derived contents. However, the religious,

ethical, and consent issues arising from the use of such products have been overlooked.

In the latter part of the last century, radical changes in how we perceive personal rights and autonomy, astonishing advances in medical technology, and vibrant debates about what constitutes right and wrong have both complicated and enhanced the choices that health professionals and patients once considered self evident. Patients increasingly want to be better informed and to have a greater involvement in their own care.¹⁴ They demand the autonomy to decide for themselves what procedures they are prepared to agree to and what treatments they are willing to receive. Professional defence organisations in the UK report that the foremost cause for complaint is a failure of communication between the doctor and patient.¹⁵ With rapid therapeutic advances, changes in the social and religious structure of the Western world, and greater emphasis on patient autonomy, it becomes imperative that members of the health profession re-examine and re-apply the established medical ethos alongside keeping abreast of scientific progress.

Informed consent is a doctrine and a practice by which patients may protect themselves from unwanted interventions and by which patients can take responsibility for shaping their lives as they see fit.¹⁶ Consent is required by law and not to get consent is to violate the patient's moral right of respect for autonomy. Healthcare professionals have a duty to explain the nature, purpose, and the risk of a proposed treatment to patients, and to obtain informed consent. This includes the application of products obtained from biological sources. The General Medical Council (GMC) has emphasised that failure to obtain consent is a breach of the professional's duty of care to the patient. According to the GMC, "When providing information you must do your best to find out about patients' individual needs and priorities. For example, patients' beliefs, culture, occupation, or other factors may have a bearing on the information they need in order to reach a decision. You should not make assumptions about patients' views, but discuss these matters with them."¹⁷ Similarly, the Department of Health (DoH) model consent policy quotes,

Table 3 Survey results of healthcare professionals (n = 100)

| Product | Biological Pig | Human | Cow | Other | Synthetic | Do not know |
|--|----------------|------------|------------|------------|------------|-------------|
| Alloderm (LifeCell Corp, USA) | 4% | 7% | | 4% | 11% | 74% |
| Tegaderm (3M Healthcare, UK) | | | | 4% | 85% | 11% |
| Apligraf (Organogenesis, USA; Navartis Pharmaceuticals Canada Inc, Canada) | 4% | 18% | 0 | 5% | 5% | 68% |
| Jelonet (Smith & Nephew, UK) | | | | 5% | 90% | 5% |
| Integra (Integra Lide Sciences Inc, USA) | 13% | 13% | 16% | 27% | 18% | 30% |
| Promogran (Johnson and Johnson Medical Ltd, UK) | | | 0 | | 5% | 95% |
| Duoderm (ConvaTec, UK) | 10% | 10% | | | 71% | 9% |
| E-Z Derm (Genetic Laboratories, USA) | 45% | 5% | | | 20% | 30% |
| Orcel (Ortec International Inc, USA) | 9% | | 0 | | 5% | 86% |
| Oasis (Cook Spencer, USA) | 0 | | | | | 100% |
| Mepitel (Molnlycke, UK) | 5% | | | | 86% | 9% |
| TransCyte (Advanced Tissue Sciences, USA) | 29% | 36% | | 14% | 5% | 16% |
| B.G.C. Matrix (Brennen Medical Inc, USA) | | 14% | 5% | 10% | 9% | 62% |
| Kaltostat (ConvaTec, UK) | | | | 57% | 38% | 5% |
| Paratulle (SSL, UK) | | | | 5% | 90% | 5% |
| Biobrane (Dow B Hickam Inc, USA) | 19% | 5% | 5% | 9% | 5% | 57% |
| Chitosan | 4% | | | 14% | 37% | 45% |

Figures in bold denote the correct constituent(s) of individual products as well as the percentage of healthcare professionals who knew it correctly (out of 100).

Table 4 Biological products: biological substitutes, tissue engineered skin substitutes, and dressings

| Biological substitutes | | Tissue engineered skin substitutes | Biological/ biosynthetic dressings |
|--------------------------------------|--|--|---|
| Allograft | Xenograft | | |
| Cadaver skin Amniotic membrane | E-Z Derm (acellular xenogenic collagen matrix) | Epicel (Genzyme Corp, USA) Alloderm Integra Dermagraft (Advanced Tissue Sciences, USA) Apligraf LaserSkin and Hyalograft 3D (Fidia Advanced Biopolymers, Italy) TransCyte OrCel | B.G.C. Matrix Promogran Oasis Biobrane |

“Patients have a fundamental legal and ethical right to determine what happens to their own bodies. Valid consent to treatment is therefore absolutely central in all forms of healthcare, from providing personal care to undertaking major surgery.”¹⁸ The DoH further states that, “different patients will make different choices in apparently similar situations.”

Although obtaining consent is widely adhered to in other aspects of healthcare, the attitude of healthcare professionals has been paternalistic when treating patients with products obtained from biological sources. This is perhaps because until recently, the majority of dressing products were synthetic and hence the issue of consent was not considered germane. Nevertheless, with the increasingly prevalent use of biological products, it becomes clear that consent for the application of these products should be dealt with the same way as for other medical or surgical procedures. This act of omission of not obtaining informed consent and failure to inform patients about the constituents of biological dressings, some of which may be religiously forbidden, is also a violation of the Human Rights Act, Article 9, which states, “Everyone has the right to manifest his religion or belief, in worship, teaching, practice and observance”.¹⁹ It, however, needs to be appreciated that in some clinical situations, as in life threatening burns, it might be impractical to obtain informed consent. The GMC guides the healthcare professionals on this issue, stating: “In an emergency, where consent cannot be obtained, you may provide medical treatment to anyone who needs it, provided the treatment is limited to what is immediately necessary to save life or avoid significant deterioration in the patient’s health. However, you must still respect the terms of any valid advance refusal you know about, or is drawn to your attention.”

Therefore, when biological products are used on patients, their religious, cultural, and ethical beliefs should be taken into consideration and respected. This is the view shared by the majority (77%) of the contacted religious leaders. Though the opinions of the religious leaders and their committees might not reflect the views of all the people, it is however clear that the patients should be advised of the contents, their views sought, and consent obtained. In addition, one of the religious leaders raised concerns about the theoretical possibility of transmission of diseases like AIDS or CJD from biological products. This issue needs serious consideration as it has been shown that despite extensive screening and rigorous aseptic precautions, human skin equivalents (for example Apligraf) contain viable human cells and hence cannot be terminally sterilised.²⁰ Likewise, consumption of bovine meat contaminated with bovine spongiform encephalopathy agent has been implied in the causation of new variant CJD in humans.^{21 22} Prion diseases are incurable

neurodegenerative conditions affecting both animals and humans; human prion diseases include CJD, Gerstmann-Straussler-Scheiner disease, kuru, and fatal familial insomnia.²³ Therefore, despite lack of current evidence associating biological products with transmission of diseases like AIDS or pathogens including prions, patients should be clearly informed of these pertinent issues before they receive such products.

To obtain consent, however, the healthcare professionals should have a sound knowledge of the proposed treatment, as the GMC states, “it is your responsibility to discuss with the patient and obtain consent, as you will have a comprehensive understanding of the procedure or treatment”. However, as shown by this survey, many healthcare professionals are ignorant of the constituents of some commonly used biological products. With an ever increasing repertoire of such products, it becomes more difficult for healthcare professionals to be aware of the constituents of individual products. Therefore, training institutions, hospitals, and the product manufacturers should address this issue as a matter of urgency and take adequate measures to

What is already known on this subject?

- Biological products have improved the outcome of patients with burns, chronic wounds, and other forms of acute injury.
- The religious and ethical issues, including consent, arising from their use have never been addressed in the medical literature.
- At present, consent is not obtained when biological products are used.
- The awareness of the healthcare professionals about the constituents of biological products has not been evaluated previously.

What does this study add?

- Many healthcare professionals are ignorant of the constituents of the biological products they commonly use.
- Religious leaders feel that patients should be made aware of the constituents and informed consent obtained.
- Product manufacturers, regulatory authorities, and hospitals should address this issue as a matter of urgency and take adequate measures to enlighten the healthcare professionals.

enlighten healthcare professionals. Furthermore, the information provided by many manufacturers in their product literature is currently inadequate and essential information like the exact material used (cells, collagen, serum, and so on) or the country of origin is eluded. The licensing authority and other regulatory bodies should therefore ensure that the manufacturers spell out these facts unambiguously so that healthcare professionals can help patients make an informed decision. Failure to do this could deprive patients of essential information required to give informed consent. Ignoring religious sensitivities and neglecting the issue of consent in the use of biological products could have serious consequences, including litigation.

CONCLUSION

Though biological products have significantly improved the outcome of patients with burns and chronic wounds, it should be emphasised that the patients should be clearly informed of the constituents of such products. Healthcare professionals must respect the religious and cultural beliefs of patients and obtain consent. To do this, they need to be aware of the constituents of the biological products they use, so that they can help patients make an informed decision. The product manufacturers, regulatory authorities, and hospitals should address this issue as a matter of urgency and take adequate measures to enlighten healthcare professionals. Failure to do so could have potentially serious ramifications.

Authors' affiliations

S Enoch, Department of Plastic Surgery, University Hospitals of South Manchester, Manchester, UK

H Shaaban, Department of Plastic Surgery, Alder Hey Children's Hospital, Liverpool, UK

K W Dunn, University Hospitals of South Manchester, Manchester, UK

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(21–23 September 2003) and the British Association of Plastic Surgeons Winter Scientific Meeting in London, UK (3–5 December 2003).

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