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Medical Decision and Consent – A Review

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ABSTRACT

In medical care delivery, patient involvement, information and consent are connected with decisions to act, i.e., to examine the patient, to prescribe drugs, to undertake diagnostic or surgical intervention or to provide mechanical ventilation. However, a medical decision is not necessarily a decision to intervene. It may also imply withholding an intervention or discontinuing it. It is obvious, that such a decision may affect the interests of the patients at the beginning or during the continuation of an intervention. At the same time, this kind of decision can very easily remain hidden or be implicit. In particular it entails a complete withholdment of the treatment. This article addresses the question as to what extent the rights to information and consent should equally apply to non-treatment decisions. It encompasses all medical decisions: to initiate, not to initiate or to stop a medical intervention.

Key words: Treatment, consent

INFORMATION AND CONSENT

The rights to information and consent are considered as the patient's most important tools to participate in medical decision-making. Over the last decades, the right to informed consent has generally been accepted as a basic principle, at least at the international level, and to a large degree at the national level also. As to the international documents, reference can be made for instance to the Convention on Human Rights and Biomedicine and the WHO Declaration on the promotion of patient's rights in Europe. In the last years there have been quite a few publications based on empirical data questioning the effectiveness of informed consent. They show that "true" informed consent may sometimes be difficult to achieve. That calls for an effort to improve the communication process. It does not invalidate the principle of informed consent. The patient does not have a duty to receive information and to make his own decisions. What that principle requires is that the health care provider enables the patient to do so as to follow the four principles of medical ethics namely autonomy, justice, beneficence and non-maleficence.

The right to consent encompasses the right to refuse a medical intervention. The

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fact that a patient's previous consent must be obtained also implies that his opinion and preferences should be taken into account as to the way the intervention is to take place. Furthermore, in principle, consent may be withdrawn at any time. If a patient is incompetent, a proxy or other representative of the patient should be enabled to give or to refuse consent on behalf of the patient (1).

According to the accepted doctrine, consent is only valid if it is free and voluntary. The decision of the patient should – as far as reasonably possible given his often dependent and vulnerable position – be free from constraints.

This does not mean that there is no room for medical advice, but the physician should respect the patient as a person with his or her own values.

There seems to be a general agreement that valued informed consent presupposes adequate information. This point is further elaborated in many national and international documents, including guidelines and codes of conduct of medical associations. As an example I refer to the WHO Declaration on the promotion of patients' rights to Europe, which states that *"patients have the right to be fully informed about their health status including the medical facts about their condition; about the proposed medical procedures, together with the potential risks and benefits of each procedure; about alternatives to the proposed procedures, including the effect of non-treatment, and about the diagnosis, prognosis and progress of treatment."* The principle of informed consent may be subject to limitations. This holds not only for the right to consent but also for the right to information. A traditional, and generally accepted exception of the right to information, is the so-called therapeutic privilege. In recent documents this exception is defined narrowly, to avoid the risk that it would "swallow the rule". The WHO Declaration, for instance, states that information may only be withheld from patients exceptionally when there is good reason to believe that this information would cause them serious harm.

As far as limits to the duty of disclosure are concerned, I refer also to the right of the patient not to be informed at his explicit request, brought about by the emergence of modern genetics and other forms of predictive medicine like recently the Indian parliament passed the Prenatal Diagnostic Technique Act 1994 which prohibits disclosure of prenatal findings related with sex of the foetus to the patient. It is generally acknowledged, that this right is again absolute, and may give way to important other concerns in a situation of conflicting interests.

Summary of what can be considered the accepted rules of consent, I have drawn most of all upon international documents. If one looks at the ways the right to informed consent has been elaborated in national law, there are many, and sometimes considerable differences between countries, not only concerning the way the right to informed consent as embodied in the law (e.g., in Indian contract law or other domains of law, statute law or court decisions), but also concerning for instance the standard of disclosure, the exceptions etc.

To some extent, personal involvement of the patient in medical decision-making

can be considered a basic requirement of good medicine: apart from the fiduciary relationship between doctor and patient information and participation are likely to render the patient better motivated and cooperative. But the underlying rationale for consent goes beyond these practical considerations. Nowadays, first of all respect for human dignity and the principle of autonomy or self-determination are seen as the basis for informed consent. This is in line with what I have identified as the main function of the right to consent: to enable the patient to participate in decisions affecting him or her.

If in the law informed consent is only required before a medical intervention is carried out, in fact only one, be it important aspect of patient participation in medical decision-making (i.e., the possibility to refuse the intervention after adequate information has been provided) has the status of a legal obligation for the physician. This creates the risk that in other situations involving the patient may be left at the discretion of the health professional, or that it may be considered only a matter of good practice, and not necessarily a legal duty.

One may wonder why patient participation in medical decisions has so often been incorporated in such a limited way into the law. One explanation may be that traditionally, at least in common law jurisdictions, the unlawful performance of a medical procedure was dealt with by the law of batter, i.e., the unauthorised intentional touching of another person. In our country it is dealt under Indian Penal Code and is regarded as a criminal offence. Although nowadays the emphasis is rather placed on the broader concept of negligence, the discussion about informed consent would still see very much preoccupied with medical acts as a potential invasion of the body. Consent is then essential to justify such an invasion, necessary to uphold the patient's right to physical integrity.

More important in the context of this paper, however, is the fact that connecting informed consent primarily to bodily or physical integrity, obscures the importance of medical decisions not to carry out an intervention or to discontinue it. In such decisions, serious and sometimes even vital interests of the person concerned may be at stake. In that case, the principle of self-determination and the fiduciary relationship between doctor and patient "may be undermined more dramatically when treatment is covertly withheld than when it is administered without proper consent". While invasive acts need to be justified and require previous involvement of the patient in terms of information and consent, basically the same can be said about decisions not to intervene, at least when they affect the patient's interests. Also in case of non-treatment decisions, self-determination and shared decision-making should be taken seriously: where the consequences of such decisions make this appropriate, they should be made explicit so as to enable to patient to be involved with them (2).

Withholding consent for treatment

For this purpose, it is useful to make a distinction between two kinds of clinical reasons for these non-treatment decisions. First of all, with regard to a particular patient an intervention which in other cases may be

effective, may not be expected to have a demonstrable effect. Secondly, an intervention may be considered to be of no net benefit to the patient in question. In the latter case, it is not the lack of effectiveness, but the lack of proportionality (in terms of burden and benefit for the patient concerned) which makes the intervention futile. A decision not to resuscitate a patient in the event of a cardiac or respiratory arrest may then be taken either because such an intervention is expected to be unsuccessful, or because – taking into account the overall medical situation of the patient – it would not seem to serve a reasonable purpose.

Let me first give some facts from a study on 'do not resuscitate [DNR]' orders in Dutch hospitals (3). This study reveals that DNR decisions are made in six percent of all hospital admissions in the Netherlands, and that 61 percent of all in-hospital deaths were preceded by a DNR decision. Patient involvement with these decisions appears to be very limited. The decision was discussed with the patient in 14 percent of all cases only. Of the 86 percent cases in whom DNR was not discussed, 56 percent patients were incompetent and 30 percent were competent. As to this latter group, in more than half of these cases the physician stated in one way or another that this discussion would be too burdensome for the patient, thus invoking the therapeutic privilege. As to patients who were incompetent, the family was only consulted in 37 percent of all cases.

The authors stress the point that in cases without patient (or family) involvement, the reasons for the DNR decision quite often went beyond determining the effectiveness of resuscitation, and included value judgements on the proportionality of the intervention. They conclude that "these value judgements should not be made behind a veil of objectivity, leaving patients and families in ignorance".

There is no reason to assume, that the practice in other countries will be completely different from that in Netherlands. The question then is, to what extent the apparently prevailing practices of not involving patients or their families with non-resuscitation decisions is reflected in the ethical and legal literature. On the whole, the literature is more supportive of information, consultation and even consent.

This holds already for the question as to whether the patient should be informed about an [envisaged] DNR order, in particular if resuscitation is not likely to be effective. According to Bruce-Jones, "The right to information about treatment options surely encompasses only those relevant to the clinical situation, and consideration of cardiopulmonary resuscitation is not relevant when the chances of survival are negligible." To claim otherwise, could result in a call for universal discussion of other treatments with little chance of success.

There is no unanimity, however, as to what such a discussion with the patient includes. According to some authorities, to make a judgement about the balance of the harms and benefits of attempted resuscitation for the patient should remain with the physician. The mere fact that value judgements play a role, would not necessarily imply that the consent of the patient should be sought for the decision: if physicians

have any rightful control over the interventions they offer to patients, it is only because they have the authority to act on judgements of value (2).

Some authors even warn against an exception to informed consent based on medical futility (4). According to Miller (5), as long as physicians are still reluctant to speak with patients about resuscitation, any exception on therapeutic or futility grounds is almost certain to be the escape hatch for physicians seeking to avoid conversations they have never understood as integral to the obligation to care for dying patients. Scofield(6) puts it even stronger: "The futility exception's suggestion of presumed consent will likely swallow the rule of actual consent in decisions to limit resuscitation, thereby enabling the medical profession to rein itself unilaterally and unaccountably".

CONCLUSION

If patient involvement is necessary, it means that in general at least the minimum level of involvement, i.e., being informed about the decision, is required. This also holds if no demonstrable effect can be expected from the treatment in question. In the Dutch literature on the subject, the view is expressed that if the patient is competent, he should be informed of such a decision and supported to cope with it; the physician should explain and if necessary-justify his decision; he should enable the patient to informed resignation or acquiescence. The patient's consent is not necessary in this case. If the intervention will have no effect at all, the physician will not even be entitled to carry it out. Still the patient should be informed. In addition to the reasons mentioned before, the patient may also have a personal interest to know, for instance he may want time to arrange his affairs if death is imminent (7).

If the intervention may have an effect, the patient should at least be consulted, i.e., the decision should be discussed with him. This is in line with the guidelines developed by the Appleton International Conference: "Where a doctor considers a life prolonging treatment not to be physiologically futile, but nonetheless 'futile' in another sense of the word because of the low probability of success or because of the low quality of life that would remain, then discussions about the withholding or withdrawal of such treatments should be made in the context of full and open discussion of the nature and extent of the 'futility' of the treatment with the patient or the patient's representative" (8).

Is consent to the decision required? As set out in the preceding section, some would say yes. In our view, a distinction should be made between situations in which a universal medical opinion exists that a certain intervention, although effective in physiological terms is futile in terms of the net benefit or proportionality, and other situations in which there is no predominant medical standard and the benefit of an intervention is open to doubt. An example of the first is resuscitation of a patient in a persistent vegetative state, an example of the second is the same intervention in an elderly patient who is severely ill and disabled, but may still live for several months if the intervention is successful.

If there is wide agreement that treatment is not medically indicated, the physician should still have the discretion to honour the demand of an-insisting patient, iftaking all circumstances into account - he feels that there are particular reasons to do so (for instance, a patient may have a personal non-medical interest to live a few days longer). However, he should not be obliged to do so and be allowed - after discussing his envisaged decision with the patient - to refrain from intervening, even if the patient would request otherwise. Therefore, in the final analysis, informed consent for the [non-treatment] decision would not be required. A doctor should not be forced to embark on an intervention which, according to the professional standard, would serve no reasonable purpose. If it is a medical duty to benefit the patient and not to do harm, and if – furthermore – society expects from physicians that they provide only appropriate care (and not care which is not medically indicated), at least to some extent doctors must be allowed to make unilateral value judgements and to act upon those judgements, like certification of brain stem death as per Transplantation of Human Organs Act 1994 passed by Indian Parliament which provides the power to the treating physician to refuse the patient to be kept on a ventilator.

This situation is different if there is no prevailing body of medical opinion against a particular intervention in a specific situation. In case of doubt, unilateral decision-making is not justified. If the clinician's judgement is not backed by the profession and has more the character of a personal decision, it should not be imposed, however careful it is made, and the patient should be enabled to an informed refusal of the non treatment option, and be allowed to make another choice.

To the extent that information and consent are required with respect to non treatment decisions, the general rules concerning informed consent apply. The information provided should be adequate, i.e., the patient should not only be informed about the [envisaged] decision itself, but also about the effects of non-treatment and about alternative options. In exceptional circumstances, when there is good reason to believe that the information would cause serious harm, the therapeutic privilege may be invoked. Information may also be withheld, if the patient has expressed a clear preference not to be informed.

When the patient is incompetent, the relevant information should be offered to, and consultation should take place with his representative [appointed by the patients or designated by the law]. The same holds for obtaining consent. In giving substitute consent, the representative should take into account what is known, and to the greatest extent possible, what may be presumed about the wishes of the patient.

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A Bone Bank for the District Hospital

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ABSTRACT

Autogenous bone grafts are the ideal bone substitutes. Allogenous bone graft substitutes are needed where the autogenous bone is either not available or inadequate. The commonly employed methods of preserving allogenous bone require expensive equipment. We describe here a technique of preserving bone in a dilute solution of formaldehyde for use as an allograft. This requires minimal resources and can be practised even at the district hospital level. These *formalin preserved allografts (FPA)* have been used in 86 patients with bone cavities, non-union and comminuted fractures and have proved to be reliable and safe although we found the incorporation to be delayed as compared to autogenous bone grafts.

Key words: Formalin, allografts, bone bank, non-union, bone cavities, fracture

INTRODUCTION

Bone grafting is a common orthopaedic procedure performed for the management of cavitary lesions and non-union of bone. The bone grafts may be autogenous, that is from the same individual, or, allogenous, that is from another genetically different individual of the same species. Autogenous bone grafts are the gold standard in terms of fast incorporation and lack of immunogenic potential. However, it carries the disadvantages of pain, haematoma, infection, cosmetic problems, neurovascular damage, peritoneal perforation, sacroiliac joint instability and herniation of abdominal contents through the defect in ilium (1). Besides, autologous bone may be inadequate in children and in conditions where quantum of bone required is large. These limitations have necessitated development of suitable alternatives to autologous bone. The techniques recommended for the preservation of such allogenous bone grafts like freeze-drying and deep freezing require expensive equipment and an uninterrupted power supply. We describe a simple, inexpensive technique of preserving bone in formaldehyde, which can be practised with minimal resources and is reliable and safe.

MATERAL AND METHODS

The requirements for setting up a bone bank of formalin preserved allogeneic [FPA]

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bone grafts are – a refrigerator, adequate supply of normal saline and formaldehyde. It can be practised at practically any centre with an operation theatre and a microbiology laboratory for culture.

Donor cancellous bone is obtained from excised femoral heads of patients undergoing hemireplacement or total replacement arthroplasty of the hip and from excised patellae. Donors are routinely screened for human immunodeficiency virus [HIV] and Hepatitis B antigen and to rule out any associated infective or neoplastic pathology. The bone is cut into thin slices, denuded of all soft tissue and articular cartilage and thoroughly washed with saline. A 0.4 percent solution of formaldehyde is prepared by diluting commercially available 40 percent formaldehyde in saline to a proportion of 1 in 100. Bone pieces are kept in sterile glass jars containing the diluted formaldehyde solution between 2 and 6 °C in a dedicated refrigerator. The solution is changed on day 1, day 3 and then two changes are done at weekly intervals. Subsequent changes are done at monthly intervals. Culture of the preserving fluid and the bone pieces is done routinely at the time of change of solution and prior to usage of graft. The graft can be used after a minimum period of one month of preservation. Unused grafts after one year of preservation should be discarded. Three days prior to usage, the bone and the preserving solution are subjected to aerobic and anaerobic culture for infective organisms. Since the temperature used for storage is 2 to 6 °C, the grafts are not adversely affected by lack of power supply for up to 6 hours as the temperature inside a refrigerator is reasonably maintained by insulation.

The cancellous bone grafts are used in the management of patients with bone cavities, non-union and communited fractures.

Patients

Formaldehyde preserved alogeneic bone grafts were used in 86 patients [49 males and 37 females], presenting with lytic lesions of bone, non-union and comminuted fractures at the Department of Orthopaedic Surgery at King George's Medical College, Lucknow. Benign bone cavities included fourteen unicameral bone cysts, six aneurysmal bone cysts, five patients with fibrous dysplasia, and two of enchondroma. Eight patients of unicameral bone cyst had a pathologic fracture through the cyst wall. Malignant bone cavities included five patients with giant cell tumour of lower end of femur and four patients with giant cell tumour of upper end of tibia. None of these had any breach of the cortex or any soft tissue extension. Patients with non-union included seven cases of non-union of tibial diaphysis, seven cases of humeral diaphysis, five cases of non-union of femoral diaphysis and four with non-union of radius and ulna. Bone gap was present in the tibial shaft in six patients and the distal end of femur in one patient. Two of these patients were lost to follow-up and were excluded. Eighteen patients with communited fractures were primarily bone grated at the time of internal fixation.

RESULTS

We have used cancellous bone graft all the cases in this study. Post-operative complications included superficial stitch line infection in 5 patients (6.1%) and a sterile serous discharge in 22 patients (26.8%). The median duration of discharge was 5 days starting on the third post-operative day. No active intervention was required in either event. There was a severe infection in one patient undergoing bone grafting for a non-union of femoral diaphysis. This required opening the wound and debridement followed by suction irrigation. Post-operative mild pyrexia was present for a median duration of six days in 26 patients (31.7%).

The time taken for obliteration of cavity and reconstitution of trabeculae was regarded as the end point for incorporation of the bone graft. The median time taken for incorporation of bone graft was 20 weeks for benign lesions and 24 weeks for malignant lesions. No recurrence of benign or malignant lesions was encountered in any patient during a minimum follow up of 18 months. Fracture union was assessed by the visibility of fracture line in the roentgenogram in either view. In the 23 patients of atrophic non-union, one patient had a partial union at the last follow-up at 24 weeks while the rest had a fully united fracture after a median duration of 27 weeks. Among patients with gap non-union, five had union at a median duration of 40 weeks and two had only partial union at the last follow-up at 24 weeks. Comminuted fractures were fully consolidated in 18 patients after 28 weeks while 4 patients had only a partial obliteration of fracture line at the last follow-up. On comparing the results of FPA bone grafts with autogenous bone grafts, we found the time taken for obliteration of cavitary lesions was comparable between the two groups in 81.4% patients with benign cavities and 55.5% patients of malignant cavities. The remaining patients of FPA bone grafts had a delayed obliteration of cavity. The union of fracture was delayed in 17.3% patients of atrophic non-union, 60% patients of gap non-union and 31.8% patients of comminuted fractures treated by FPA bone grafts. In two patients of gap non-union, the graft was absorbed with no evidence of union of fragments. So, the FPA bone grafts show a delayed incorporation as compared to autogenous bone grafts.

DISCUSSION

The best substitute for bone is bone. Fresh autologous and vascularised autologous bone grafts are the ideal and the most effective bone replacements and these are the gold standard with which any substitute should be compared. Freeze dried bone (2) and deep frozen bone (3) are the most widely used techniques in developed countries but require expensive equipment and an uninterrupted power supply. The limitations in our centres lacking expensive equipment stimulated the search for alternate methods, which could be carried out at the secondary health care level.

To prepare formalin preserved allografts, bone is kept in a low concen-

tration of formaldehyde at 2 to 4 °C (4). This is based on the concept of Lavrishcheva et al (5) that vital processes of tissues are preserved in low concentration of formaldehyde in an inhibited state for up to one year. They observed restoration of the vital processes on restoration of optimal conditions. This is believed to result from protein molecule enlargement due to reaction of formaldehyde with the reactive group of proteins (5).

We have used donor bone from excised femoral heads and patellae as the bone is cancellous, biologically normal and available in plenty at any Orthopaedic centre. The articular cartilage was removed as it cannot be preserved by this technique. Lavrishcheva et al (5) assume a loss of antigenicity after three weeks of preservation. We have used the bone graft after a minimum preservation period of 30 days. No HLA matching was done between donor and recipients. Previous reports on he use of formalin preserved allograft have demonstrated its efficacy in animal models (4,6,7) and in humans (8).

Postoperatively, no evidence of local or systemic immunological reaction was noted. The FPA is believed to be inherently resistant to infection (5) due to local action of formaldehyde. In this study, all the cultures of donor bone and the preserving solution done prior to allografting were negative for bacterial contamination. The occurrence of sterile serous discharge in patients with no preoperative infection may indicate a local reaction to formaldehyde leftover in the graft after washing.

Follow-up of patients is based upon the radiological assessment of fracture union or cavity obliteration. In this study, the healing of malignant cavities was delayed in comparison to benign cavities which could be related to the relatively larger average size of the malignant cavities or an effect of the malignant pathology.

Tuli and Gupta (9) commenting on the use of decalcified bone reported resorption of half the mineral content and removal of cellular and organic debris without affecting the biologic activity of the remaining matrix. Decalcification is believed to enlarge marrow spaces, Haversian canals, Volkmann canals and lacunar spaces. We have not employed decalcification as the cancellous bone is sufficiently porous to facilitate ingrowth of capillaries. We believe decalcification to be of greater use for cortical bone graft.

The chief limitation of this technique lies in its inability to preserve cartilage and consequently whole joints. Furthermore, the efficacy of cortical FPA remains to be demonstrated. FPA is an inexpensive, simple and reliable method of recycling bone. Further clinical trials are needed to document its efficacy in various clinical solutions.

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Functional Anatomy of the Human Foot in Relation to Dimensions of the Sesamoid Bones

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ABSTRACT

The sesamoid bones in relation to the first metatarsal are subject to directional forces exerted by surrounding muscles. Dimensions of human hallux correspond to anthropometric parameters which are determined by functional demand and laterality. The present study on 20 embalmed male human feet (10 from each side) was undertaken to determine various anthropometric parameters in relation to the first metatarsal and the sesamoid bones associated with it and correlate them with the laterality and functional demand of the foot. Linear measurements of the articular facets of the sesamoid bones and those on the first metatarsal were recorded and analysed statistically and it was observed that majority of cases showed lateral asymmetry in favour of left feet.

Key words: Human foot, sesamoid bones, functional anatomy

INTRODUCTION

Human foot is a unique endowment of the Homo sapiens. It is not shared with any other animal unlike the hand which is shared by some of the higher animals. Only human being has a bipedal orthograde gait and the credit for the same goes to high development of the foot in addition to innumerable modifications in many parts of the body. Since feet bear body weight throughout life, carry us from one place to another and maintain balance, is not it strange that the two of them do not share equal weight? According to morphometric study of medical malleolus and greater trochanter on the two sides, there is 60: 40 ratio of dominance between left and right lower limbs in right handed individuals (1).

In the foot, maximum weight is borne by first metatarsal alone followed by the fifth. In the first metatarsophalangeal joint there are two sesamoid bones which help in weight bearing. With each step of a normal gait, most of the body weight is distributed over the big toe and its sesamoid bones (2).

Sesamoid Bones

The sesamoid bones of the first metatarsophalangeal joint are constant. They are

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lenticular and elongated with a cartilaginous dorsal surface that slides in the grooves on the plantar surface of the head of the first metatarsal bone (3).

The sesamoid bones are firmly attached to each other by a stout and thick intersesamoid ligament. Proximally they are attached by the plantar portion of metatarsophalangeal capsule to the neck of the first metatarsal.

The medial sesamoid bone receives the attachments of the medial head of flexor hallucis brevis and the abductor hallucis. Medially it is attached to the medial joint capsule. Distally the combined tendons extend from the distal extremity of the medial sesamoid into a thick strong tendinous band attaching to the plantar medial aspect of the base of the proximal phalanx. The medial portion of the plantar fascia blends in to the plantar non-articular surface of the sesamoid (4).

The lateral sesamoid receives the attachments of the lateral head of the flexor hallucis brevis and the oblique and transverse heads of the abductor hallucis under cover of the intermetatarsal ligament along its margins. The lateral conjoined tendon extends from the distal extremity of the lateral sesamoid to the plantar lateral aspect of the base of the proximal phalanx. The lateral sesamoid is also attached on its plantar surface to the plantar fascia and to the medial aspect of the neck of second metatarsal by the strong deep portion of the intermetatarsal ligament (4).

First Metatarsal

This is distinctly shorter and more stocky than the second metatarsal. Its base is opposite the medial cuneiform with a marked vertical development and is more slender transversely. It is invested with cartilage, presenting a concave cupulate aspect, particularly transversely.

The head is very large and slightly flattened vertically. Its cartilagenous cover extends well beyond its plantar surface. A prominent ridge divides the head into two regions represented by two sagittal grooves in which the sesamoids slide (3).

MATERIAL AND METHODS

The first metatarsophalangeal joint from 20 embalmed male human feet [10 of left and 10 of right side] was dissected out. The sesamoid bones [SB] were carefully removed from the joint and marked medial and lateral. The first metatarsal [MT] was cleaned and then with a planimeter gauge, following dimensions, both on sesamoid bones [SB] and first metatarsal [MT] were measured and tabulated after taking each reading thrice and noting the mean [Figure 1].

dsm = diameter of medial SB in sagittal axis
dtm = diameter of medial SB in transverse axis
am = area of medial SB
Dsm = diameter of corresponding medial articular facet on 1st MT in sagittal axis
Dtm = diameter of corresponding medial articular facet on 1st MT in transverse axis
Am = area of corresponding medial articular facet on 1st MT
dsl = diameter of lateral SB in sagittal axis
dt = diameter of lateral SB in transverse axis
al = area of lateral SB
Dsl = diameter of corresponding lateral articular facet on 1st MT in sagittal axis

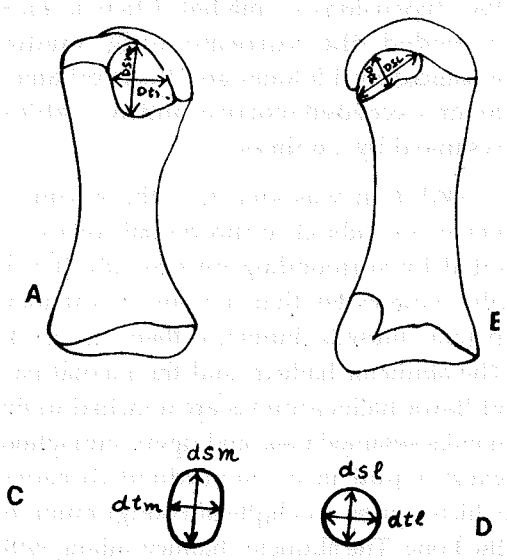

Figure 1. Medial (a) and lateral (b) aspect of first metatarsal bone. Medial (c) and lateral (d) sesamoid bones

Dtl = diameter of corresponding lateral articular facet on 1st MT in transverse axis

Al = area of corresponding lateral articular facet on 1st MT

The area of articular facets of SB [am, al] and the corresponding articular facets on head of 1st MT [Am, Al] was calculated using the formula of Pretterklieber (5) as follows:

$$\text{Area am [or Am] and al [or Al]} = \frac{\text{ds (or Ds) dt (or Dt) } \pi}{4}$$

The value of π was taken as 3.14.

RESULTS

From the analysis of the data, it has been observed that both sesamoid bones are elliptical in shape. Medial sesamoid bones [n = 20] were measured in terms of dsm, dtm and area [am]. Similar readings [dsl, dtl and al] were taken for the lateral sesamoid bones [Table 1]. It was observed that the areas of both sesamoid bones was more in the left feet, especially that of the medial sesamoids. The area of medial sesamoid in left feet was 76.150 ± 11.380 and in the right feet, it was 62.800 ± 8.400. The difference was quite significant. Similarly, values of areas of lateral sesamoids in left and right feet were also more in favour of left feet but the difference was not significant. The dsm and dtm of medial sesamoids of left feet was 10.9 ± 1.45 and 8.0 ± 0.74 respectively whereas in the right feet, the same were 10.0 ± 1.06 and 8.0 ± 0.53 respectively. These differences were significant.

Corresponding dimensions of articular facets for medial sesamoid bones [Dsm, Dtm and Am] as well as lateral sesamoids [Dsl, Dtl and Al] on the first metatarsal head were also recorded [Table 2]. The ratio of the surface area on first metatarsal to the area of sesamoid bone in the left feet was 1.5:1 for both the sesamoids. On the right side, this ratio was 1.6:1 for both sesamoids.

Table 1. *Sesamoid bones*

Variable	Left		Right		
	Mean	SD	Mean	SD	t
dsm	10.900	1.450	10.000	1.060	1.503
dtm	8.90	0.740	8.000	0.530	2.966
am	76.150	11.380	62.800	8.400	2.831
dsl	10.800	1.910	10.100	1.640	0.834
dtl	7.700	0.640	7.400	1.510	0.549
al	66.100	9.020	60.88	19.400	0.732

Reference: t95% = 1.734, t99% = 2.552

Table 2. *1st Metatarsal bones*

Variable	Left		Right		
	Mean	sd	Mean	SD	t
Dsm	14.300	1.180	14.000	1.310	0.510
Dtm	10.180	2.790	9.280	3.070	0.651
Am	114.270	11.970	101.980	14.670	1.947
dsl	13.400	1.020	12.400	12.000	1.336
Dtl	9.800	0.830	9.110	1.370	1.292
Al	103.080	8.600	98.670	27.060	0.466

Reference: t95% = 1.734, t99% = 2.552

The area of articular facet for medial sesamoid on the head of first metatarsal was significantly higher on the left side while, that for lateral sesamoid, though higher on the left side, was not significantly so.

DISCUSSION

Lateral asymmetry in the anthropometric dimensions of sesamoid bones of human hallux is obvious from the present study. Lateral asymmetry in favour of left foot has also been demonstrated (6,7). Values of all dimensions are more in the left foot as compared to the right in the present study.

Both SB were larger in the right than in the left feet (5) and it was also found that SB of left foot have better arterial supply and accordingly, the left foot is dominant (5). These findings suggest that footedness determines the vascularization of the ossa sesamoidea in the adults. According to the author (5), the predominance of left foot (7) may be the explanation for better vascularization of the left sesamoid bones. It was also observed (5) that the dimensions of articular surfaces on the head of the first metatarsal exceeded the corresponding sesamoiid bone 1.4 times [medial bone] and 1.5 times [lateral bone]. In the present study, the dimensions of medial articular facet exceeded the corresponding medial sesamoid by 1.5 times and those of lateral facet exceeded corresponding lateral sesamoid by 1.6 times.

While it was seen that the sesamoid bones are subject to directional forces exerted by surrounding muscles (8), it was also suggested that actions of intrinsic plantar muscles influence their shape (9). The abductor hallucis and the medial part of flexor hallucis brevis are attached to the medial sesamod bone and upon contraction, exert a pull in a longitudinal direction which causes an elliptical configuration of the bone. The abductor hallucis, along with the lateral part of flexor hallucis brevis are attached to the lateral sesamoid and these exert their pull in a transverse direction giving the sesamoid bone a somewhat circular shape. In the present study, however, both the sesamoids were observed to be elliptical, the medial being more or so.

Studies on the walking mechanisms (4) show that in the stance phase, the weight is first transmitted along the lateral border of the foot and then to all the metatarsal heads. It has been found that the first and the fifth metarsal share maximum weight, with the first metatarsal accounting for about one third of total weight. In the swing phase, however, the weight is transmitted along the medial side of the foot and is again borne maximally by the first metatarsal. The direction of force is longitudinal and is borne maximally by the medial sesamoid bone [Figure 2). Besides this, the medial sesamoid is fractured more often than the lateral, which again suggests that it bears more weight than the lateral (4). The

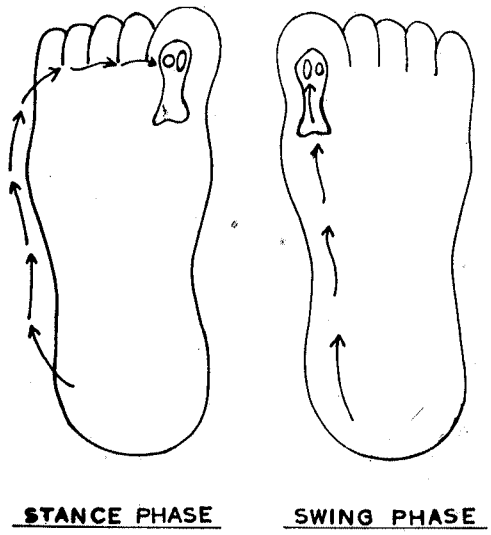

Figure 2. Direction of forces during walking

present study also shows a better developed medial sesamoid.

(1) carried out morphometric study of greater trochanter and medial malleolus of lower limb and found a 60:40 ratio in left and right limbs respectively. Present study shows a lateral asymmetry of medial sesamoid in favour of left side in a ratio of 67:33 and of lateral sesamoid in a ratio of 60:40.

The proportion, as observed by Gupta and Anand (1) shows a preference in favour of left foot.

It is is speculated that the differences in the two feet depend on the total stress imposed on a particular bone, i.e., not only quantitative but also qualitative differences have their effect on the bones (10).

It can thus be concluded that dimensions of sesamoid bones of human hallux correspond to functional demand and laterality.

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Chlamydiae as Pathogens: Newer Perspectives

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ABSTRACT

Chlamydiae are a group of intracellular organisms which have been associated with wide spectrum of clinical infections such as trachoma, pelvic inflammatory disease, infertility, psittacosis, respiratory infections, atherosclerosis, asthma and arthritis. In this review, the newer perspectives regarding the microbiology of the Chlamydiae and their association with various clinical conditions are reviewed.

Key words: Chlamydiae, microbiology, pathogenesis

INTRODUCTION

Chlamydiae are a group of intracellular organisms which have been associated with a wide spectrum of clinical infection ranging from trachoma, pelvic inflammatory disease, infertility, psittacosis, respiratory infections, atherosclerosis, asthma and arthritis [Table 1] (1). In addition to the three recognised species *Chlamydia trachomatis*, *Chlamydia penumomiae* and *Chlamydial psittaci*, a fourth species *Chlamydia pecorum*, a pathogen of ruminants has recently been proposed (2). Species were grouped according to their biologic and biochemical properties and a greater than 95% homology is their 16S ribosomal RNA sequence (3). *C. pneumoniae* is a human pathogen recognised as an important cause of respiratory illness. About 40%-60% of adult population have antibodies to *C. pneumoniae* world over, suggesting that the infection is prevalent and re-infection common. Current interest centers on the emerging role of *C. pneumoniae* infection in the pathogenesis of atherosclerosis and asthma (4). This article reviews the newer perspectives regarding the microbiology of Chlamydia and its association with various clinical conditions.

BIOLOGY OF CHLAMYDIAE: AN UPDATE

Increased awareness of the clinical significance of human Chlamydial infection in all parts of the world has been paralleled by interesting basic observations on the biology of these organism. Chlamydia have a unique biphasic life cycle with dimorphic forms that are functionally and morphologi-

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Table 1. *Spectrum of human diseases caused by Chlamydiae*

Species	Acute Diseases	Sequelae/Chronic Diseases
C. trachomatis		
Serovars A-C	conjunctivitis	trachoma
Serovars D-K	urethritis	proctitis, epididymoorchitis, Reiter's syndrome pelvic inflammatory disease, ectopic pregnancy, tubal infertility, Fitz-Hugh-Curtis syndrome
	ophthalmia neonatorum	
	neonatal pneumonia	
LGV serovars	lymphogranuloma venereum	
C. pneumoniae	pharyngitis	Cardiovascular disease
	sinusitis	pasthma
	bronchitis	
	community acquired pneumonia	
C. psittaci		
parrot	atypical pneumonia	
canaries	hepatic and renal dysfunction	
pigeons		
turkeys	endocardits	
ducks		
chickens		
cats	conjunctivitis	
ewes	abortion	

cally distinct. Life cycle is initiated when an infectious but metabolically inactive elementary body [EB] attaches to the host epithelial cell surface. The precise mechanism by which EB's attach and gain entry into the host cells is unknown (5). Recent work suggest that Chlamydia uses heparan sulfate as a bridge to attach to glycosaminoglycan [GAG] receptors on eukaryotic cell surfaces (6). Once endocytosed, the EB differentiates into a larger pleomorphic form called the reticulate body [RB], which replicates by binary fission (2). The intracellular regulatory signal that control EB to RB conversion and vice-versa are not known but the relative concentration of cAMP and cGMP appears to be important (7). Once inside the host cell, Chlamydia resides in a membrane bound vacuole that can evade phagolysosomal fusion. The endosome is transported to the distal regions of Golgi apparatus and incorporates host derived sphingolipids into the inclusion membrane (8,9). Thus it appears that Chlamydia are able to intercept host vesicular traffic bound for the plasma membrane to sequester lipids and possibly other host substances synthesized in the Golgi apparatus. Subversion of host vesicular traffic may represent a dual advantage for Chlamydia in obtaining materials form the host for its metabolism as

well as in modifying the inclusion membrane to evade lysosomal fusion and immune detection. Chlamydia lack the ability to synthesise high energy compounds such as ATP and GTP essential for replication and metabolism leading Moulder in 1974 to coin the term 'energy parasites'. Chlamydia are incapable of de-novo nucleotide biosynthesis and are dependent on host nucleotide pools (10).

ANTIGENEIC RELATIONSHIP

Chlamydia are antigenically complex organisms possessing antigens of genus, species and serotype specificity (11). The group complements fixation [CF] antigen, shared by all the members is the lipopolysaccharide [LPS], located on the outer membrane of both EB and RB (12). The major outer membrane protein [MOMP] contains both species and serotype specific antigens (13). The 15 serovars of *C. trachomatis* are best reognised by micro-immunofluorescence [micro IF] technique. MOMP is responsible for most of the reactivity seen in micro IF test. A 60 kilodalton [kDa] Cysteine rich structural protein [CHSP 60] has a highly immunogenic species - specific epitope (1). A genus specific 57 kDa protein plays an important role in immunopathology (14). Serovars of *C. psittaci* can be demonstrated by neutralisation test and by micro IF (15). Only one serovar of *C. pneumoniae* has been demonstrated.

CLINICAL SPECTRUM OF HUMAN INFECTION

C. trachomatis is almost exclusively a human pathogen known to cause trachoma, conjunctivitis, urethritis - cervicitis, proctitis, epididymoorchitis. Reiter's Syndrome, pelvic inflammatory disease, ectopic pregnancy, tubal infertility, Fitz-Hugh Curtis Syndrome (1). For Chalmydial infections, recent advances in diagnosis and screening technology and single dose antimicrobial therapy will likely have a significant impact on the efficacy of disease control programs and the opportunity for eventual disease eradication.

Human psittacosis is a zoonosis caused by exposure to infected birds or poultry and manifests as a flu-like illness or atypical pneumonia in more severe cases. Infection is characterised by multiorgan involvement often resulting in hepatic and renal dysfunction and endocarditis (16).

C. pneumoniae is a common cause of acute repiratory tract infection, accounts for 6%-10% of community acquired pneumonia (4). Infection is usually mild or asymptomatic but can be severe, especially in the elderly, probably as a result of underlying illness, impaired mucociliary clearance and immune status (17). Seroepidemiologic studies show that most primary infections occur during school age and early teenage years, among adult seroprevalence is 40%-70%. Reinfection are common, and serum antibodies do not appear to be protective.

The association of *C. pneumoniae* infection with coronary heart disease and acute myocardial infarction has been studied by many workers (18-20). The association of *C. pneumoniae* infection with coronary heart disease and acute myocardial infarction was first made on the basis of elevated IgG and IgA antibodies and LPS containing immune complexes in 50% to 60% in patients with coronary heart disease or acute myocardial

infarction compared with 7%-12% in the controls (18). Electron microscopy, polymerase chain reaction [PCR] and immunochemical evidence of *C. pneumoniae* in coronary arterial fatty streaks and atheromatous plaques have also been described (18,19).

The sustained IgA and IgG antibody levels against *C. pneumoniae* in persons with atherosclerosis suggest that chronic infection may be frequent after infection. The site of colonisation for a chronic *C. pneumoniae* infection may be in the alveolar macrophage of the lung. Thus the initial event in atherogenesis may be the formation of the fatty streak. Fatty streaks consist of lipid laden macrophages derived from blood monocytes and T-lymphocytes attracted to the arterial subintima. Conversion of the fatty streak to atheroma depends on many factors, e.g., the proliferation and differentiation of smooth muscle cells and fibroblasts. Chronic infection with *C. pneumoniae* may result form organisms harboured in macrophages trapped in the arterial wall. Growth of *C. pneumoniae* in endothelial, smooth muscle cells, and macrophages from peripheral blood monocytes has been reported (21). The idea that an infectious agent is involved in the atherogenic process is not new, but the role of *C. pneumoniae* in this process needs to be defined.

The first observations on the association of *C. pneumoniae* infection with the exacerbation of asthma were made in 1986 when wheezing was associated with acute bronchitis due to *C. pneumoniae* infection (22). Subsequent studies showed that exacerbation of asthma due to *C. pneumoniae* infection may occur in 1%-11% of respiratory infections in adults as well as children. The mechanism underlying the association is unclear. Preliminary results in animal models suggest that *C. pnemoniae* can produce persistent infection and cause pulmonary inflammation, and production of Chlamydia-specific IgE antibodies in children with reactive airway disease (23). Activated T-lymphocytes and cytokines appear to play a critical role as mediators of persistent inflammation in asthma. Interleukin-4 [IL-4] is essential for B-lymphocyte class switching form IgG to IgE. The role of persistent infection in the pathogenesis of asthma merits further study because unlike viral infections, *C. pneumoniae* infections can be eradicated through appropriate antimicrobial therapy (1). Immunopathology may also be the result of a hit-and-run mechanism in which immune response to CHSP60 breaks self-tolerance to human HSP 60 and leads to an autoimmune reaction that results in tissue damage which needs further exploration. Clinical manifestation associated with *C. pneumoniae* infection continue to emerge. Possible links to chronic conditions, such as atherosclerosis and asthma remain to be elucidated and with the recent discovery of the involvement of infectious agents in other chronic conditions, it seems reasonable to apply molecular tools for Chlamydial detection to identify their potential involvement in other aetiologically undefined chronic inflammatory conditions such as inflammatory bowel disease and rheumatoid arthritis (1).

LABORATORY DIAGNOSIS

Since curative antibiotic therapy for Chlamydial infections is readily available,

early diagnosis is an essential component to control these infections. The goals of early identification are to interrupt the chain of transmission in the community and prevent long-term sequelae (1). The earliest method of isolation in cell culture and embryonated hens eggs has been replaced by antigen detection methods, such as enzyme immunoassay [EIA] and direct fluorescence assay [DFA]. EIA's are suitable for public health laboratories serving large geographic areas because of simplcity in technique. However, EIA lacks the sensitivity as a screening assay because of lower detection limit of 10,000 EB's (24). Monoclonal antibodies specific for *C. pneumoniae* are now commercially available for DGA and culture confirmation (25). Nucleic acid amplification test based on PCR. Ligase chain reaction [LCR] and transcription mediated amplification technology are now commercially available. However, PCR assay have detection limit of 10-100 EBs (26,27).

The micro-IF assay the standard method used for Chlamydial serology was first developed to serotype strains of *C. trachomatis* but soon adapted for detection of antichlamydial antibody which detects type specific antibodies against individual chlamydial serotypes (28). Indian study by Rai and Mahajan (29) showed a strong correlation between micro-IF and ELISA with sensitivity of 97% and 91% respectively. However ELISA has an advantage in being simple to perform and interpret. Radioimmunoassay [RIA] has a very high sensitivity but its routine diagnotic value needs to be evaluated (30). Other tests such indirect haemagglutination [IHA] (31), neutralisation test (32) and immunoelectophoresis (33) have been used. However their sensitivity and specificity are too low and are thus unsuitable for routine diagnostic use. Availability of monoclonal antibodies and EIA for antigen and antibody detection has contributed in early and specific diagnosis of these infections.

TREATMENT

Although doxycycline and erythromycin are effective drugs used in Chlamydial infections the newer macrolides azithromycin and clarithromycin has become the drug of choice. Compared with conventional therapy, azithromycin has excellent pharmacokinetic characteristics, such as increased bio-availability, lower incidence of gastrointestinal tract side effect and increased concentration in mucus, macrophages and tissues with a half life of five to seven days (1). Although the higher cost of azithromycin may be a limiting factor the single dose regimen make it more acceptable to patients (34). Studies are needed to determine if these regimens achieved clinical and microbiological cure.

CHLAMYDIA: INDIAN SCENARIO

Indian scenario regarding the role of Chlamydia in various clinical condition is ambiguous because of limited availability of literature. Bhujwala et al (35) carried out a study on 65 patients of pelvic inflammatory disease and infertility to detect presence of antibodies against *C. trachomatis* and *N. gonorrhoea* using indirect immunoperoxidase test and ELISA. Chlamydial antibody was detected in 62.9% of cases of PID and 60% of cases infertility respectively (35-37).

In another study carried out in cases of ALRTI in children <5 years in India

Chlamydia sp was detected in 11% of cases in association with Mycoplasma or bacteria however it was a sole pathogen in 2.9% cases (38). *C. pneumoniae* infection was seen in 6.4% of cases in the first 2 years of life (39) which is contrary to the observations from previous studies, where it was observed that *C. pneumoniae* infection is uncommon in children under 5 years of age (40). A single IgG antibody titer of >1:512 is considered as diagnostic for acute *C. pneumoniae* inections. Using this criteria more number of cases were detected due to *C. pneumoniae* (38,40).

With the recent availbility of effective single dose oral antimicrobial therapy and sensitive molecular amplification tests that allow the use of non-invasive specimens for diagnosis and screening, it is expected to have a major impact in reducing the prevalence of disease in the next decade (1).

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Clinical Use of Blood, Blood Products and HIV–A Legal Review

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ABSTRACT

Human immunodeficiency virus [HIV], the cause of AIDS, was initially confined to homosexual men and needle sharing drug addicts. Later, it was diagnosed in persons who had received medication through intravenous or intramuscular injections and blood transfusions also. The danger of infection with HIV was realized and the regulation for marketing and the use of blood and blood product were introduced internationally to prevent it. This article will discuss effective monitoring of the existing procedure for marketing, supply and therapeutic use of blood and blood products and its legal implications.

Key words: Human immunodeficiency virus, acquired immunodeficiency syndrome, blood, blood products

INTRODUCTION

When a retrovirus, now known as the human immunodeficiency virus [HIV], was discovered in 1984 as the presumed cause of acquired immuno deficiency syndrome [AIDS], tests for evidence of infection were conducted in these patients and in other haemophiliac men with and without symptoms of AIDS. It was found that many of them showed serological evidence of infection with HIV, and also with hepatitis B, C and some other viruses. This had led to further developments and regulations which raise new medical, legal and economic problems in the field of medical services.

In western countries, all bloods used for transfusion and for preparation of concentrates and other products have been treated by heat and chemicals to destroy HIV and other viral contaminants. Tests have been conducted by manufacturers and regulating agencies to ensure the safety of the end products. It is now known that some of the adverse changes reported in haemophiliacs and persons receiving multiple transfusions are due to substances in or derived from the blood or blood products, independently of HIV. Governments of several countries, have agreed to various scales of compensatory payments without admitting liability

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to haemophiliacs who are presumed to have acquired infection with HIV or have developed AIDS as a result of transfusions and the use of blood products.

Regulation is generally well intentioned in democratic countries and designed to protect public and private interests. In the former case it is intended to protect the general public from exploitation by suppliers with some sort of market power or monopoly. In health care, professional qualification is a form of public regulation designed to impose minimum standards for treatment but also a form of private regulation because it enhances the economic rents of the regulated: the health care staff. The public and the private interest can easily conflict, especially where there is a market power, in the form of information asymmetries, as characterised by health care markets, between the producer [physician] and consumer. In the case of AIDS, the reliance of governments on questionable information from medical experts has been shown to be a likely explanation for resource misallocation.

MARKET FOR BLOOD

As medical technology has advanced and new treatments have become available the demand for health care services has increased in all countries. Economic growth has raised living standards and facilitated an increase in supply of health care facilities. The market for transfusable blood is no exception. Blood is a commodity similar to many others but it has come unusual supply characteristics. For example experience of countries in which a price mechanism operates suggests strongly that persons who are happy to make themselves available as blood donors no longer came forward to donate. Blood derived from donors who have every incentive to lie about their previous health record and who are encouraged to sell their very substance on more occasions than is good for them or for their eventual recipients is also less healthy. With these prophetic words Cooper and Culyer (1) reviewed the economic, as distinct from the market, approach to the allocation of the resource blood. Countries allowing blood donors to be paid, such as the United States and many third world countries, have had the worst experience with transfusion and haemophilia associated AIDS cases. Just those people who are most likely to be carrying multiple, concurrent infections are the people who have greatest incentive to donate their blood [for cash]. The "gift" of blood in this case places two people in intimate contact who otherwise would probably avoid one another at all costs. There are many critics of the ethics of paying for blood, especially when it is used by the poor as a form of income support.

In India blood is obtained by voluntary donation. It can be viewed as an act of pure philanthropy. It can also be viewed as a selfish act; part of an individual's utility function whereby the donation gives satisfaction to the donor as a 'feel good factor' or even perhaps moral superiority. It can also be viewed selfishly as a form of insurance because the donor may at some future date be a recipient. In France, the high rate of contamination was made worse by the long-term use of blood from prisoners. It has been established in the courts that there was a delay in the screening of blood in that country, following identification of HIV in

1984. Three health officials, including the former head of a state monopoly blood transfusion centre, have been given four-year custodial sentences for fraud and criminal negligence.

BLOOD PRODUCTS

The risks from transfusions are increased when blood products are used. To prepare these concentrates, large pools of blood from assorted donors are required. The numbers of persons involved may run into many thousands, from more than one pool and sometimes from more than one country. There is no regulatory requirement for manufacturers - as in other industries producing biological products for public use to advise users and recipients. Doubtless this position was facilitates by the asymmetry of information, and hence the trust relationship between patient (consumer) and physician (producer). Other aspects of corporate governance in non-market institutions in the context of AIDS have been analysed by Craven and Stewart (1995). Because of the superiority of concentrates over whole blood in controlling bleeding in haemophilia, they began to be used on a very wide scale, with few if any medical cautions, soon after they became available in the 1970s. The process of concentration did not then exclude viral contaminants, while the sources of supply and manufacture, mainly in the USA, ensured that there would be many drug addicts in the pool.

Since 1985, when the risk of AIDS was recognized and acknowledged by the manufacturers and health authorities, blood and blood products have been treated with heat or chemicals or both to exclude viral contamination. If done properly, the risk of HIV infection is removed. Yet, in 1993, despite all the information about how blood products can be treated to avoid contamination, patients in Germany were infected by products of the firm UB Plasma after quality control standards had not been adhered to. The apportionment of legal responsibility in many of these matters has been decided only in the French courts. Most governments have accepted culpability implicitly by introducing compensation schemes. Meanwhile, clearly there are enormous financial implications for providers and receivers of this aspect of medical care.

THE LEGAL OUTCOMES

Governments in most countries have recognized responsibility for those contracting antibodies to HIV following transfusions of blood and blood products, and most have introduced compensation schemes of varying magnitude and complexity. European countries such as Denmark, Switzerland, Spain, Austria, Belgium and Ireland have provided, in varying degrees, government subsidies for those developing AIDS and HIV seropositivity. Germany is the only European country where the insurance companies have paid full compensation to those developing AIDS from contaminated blood and blood products. Such a regulation is also required in Asian countries including India in addition to the Consumer Protection Act.

In the UK over 1,800 people are believed to have contracted HIV infection as a consequence of receiving transfusions of contaminated blood. Of these 592 are haemophiliacs (586 male), while 1,235 (1,224 male) are sero-positive to HIV (PHLS surveillance Protection, September 1996). The

UK Government announced in November 1989 a compensation scheme for haemophiliacs infected with HIV from contaminated blood or blood products. A further scheme, was announced in February 1992, for those infected with HIV from contaminated blood resulting from National Health Service blood transfusions (Financial Times, 1992). These schemes exclude any admission of liability on the part of the UK government. The then health secretary, William Waldgrave, admitted that whilst the government did not accept the argument for a general scheme of no fault compensation for medical accidents, HIV infection from contaminated blood and blood products is a special case. The option of litigation in the English courts, in the form of an action in negligence against either the blood transfusion service or the appropriate government department, is likely to be too expensive, time consuming and difficult for plaintiffs seeking to show either a breach of the duty of care or causation. Nevertheless, suits have been filed and support from Legal Aid funds has been granted for some test cases in recent months. The possibility of using the Consumer Protection Act 1987, with its concept of strict liability, is an alternative to exgratia compensation payments in India.

NEED FOR REGULATION

Advances in medical and surgical treatments have increased the demand for blood and blood products for necessary and life-saving purposes. This demand has been accompanied by increased supply and use. With many processes, products and services, regulation is deemed necessary. In the UK there has been little governmental action, by way of legislation, in the area of AIDS and HIV infection. To date there have been the Public Health Regulations 1988, made under the Public Health Act 1984 dealing with such issues as medical examination of AIDS patients. The AIDS Act 1987 deals with reporting of AIDS statistics, and the Health and Medicines Act 1988 prohibited the sale of do-it-yourself HIV testing equipment.

The objective of regulation is to protect public and private interests. In practice the efficacy of all regulation is likely to be compromised because of inappropriate choice of regulator, the likelihood of unnecessary or harmful regulation and probable eventual regulator capture. Regulation of blood and blood products was, prior to 1985, insufficient, ineffective and too weak to ensure uncontaminated supplies. The procedures which were technically feasible and available for testing for safety were also compromised. This was certainly the case with transfusable blood, where the required regulation should have come about before the discovery of HIV. Even without formal regulation, the need for self-regulation in the form of screening for other contaminants should have been, and probably was, recognised by medical doctors several years before it occurred. The desire to be politically correct was certainly a contributory factor in explaining why donors were not asked pertinent questions about sexual and social behaviour before 1985. In the case of blood products, it was only the recognition of the risk of hepatitis which eventually led to an exclusion by screening.

It would need to be determined that the causal agent was present in the injected

blood or concentrate given to that case. There are very few instances of this being done or even attempted. Finally, it would need to be established that diagnosis of AIDS had been confirmed. This currently depends upon seropositivity plus a variable array of secondary symptoms and signs. Many articles questioning the specificity of both the ELISA and Western Blot HIV antibody tests, especially in the presence of other infection and immunological disorders, have been published in the Lancet and elsewhere (2-4). In addition to this are the cases where signs of AIDS have developed in recipients of blood and blood products which are HIV antibody-free, but contain other organisms and contaminants which remain after heat treatment. Even if physicians knew that contaminated blood and blood products had been administered to patients, the issue becomes whether physicians believed that the possibility of recipients contracting AIDS involved an unacceptably high risk. Hence it may not be possible to demonstrate acutus reus. At the same time, a civil action in negligence is likely to founder on one of the four grounds. The first would be a failure to establish either a breach of the duty of care owned to the plaintiffs by the defendants, for example, the manufacturers of blood products, or medical personnel. The second would be a failure to establish a causal link between this breach and the resultant damage. The third would be a failure to establish that infectious HIV was transmitted. Finally a civil action would be likely to founder because of a failure to establish that AIDS would result following transmission of infectious HIV.

The circumstances which resulted in a lack of formal regulation are complex and seem to have been a combination of medical uncertainty, incompetence, negligence and capture. Governments throughout Europe have subsequently acknowledged culpability by implementing compensation schemes. Without such schemes two pressure groups would probably have been organized, one representing haemophiliacs infected by blood products, the other representing those infected by contaminated blood transfusions. Another explanation for the implementation of compensation schemes (without admitting liability) is that such schemes do not put the blame on specific individuals or organizations. Whether these outcomes were the intended objective governments' compensation schemes can only be the subject of conjecture. That the issue has been defused is the outcome, regardless of motive.

CONCLUSION

This review article has shown that medical specialists in the find practice ill-equipped to advise speculative and subject to disagreement between themselves. The full political, legal and financial implications of the medical matter relating to AIDS, blood and blood products await fuller disclosures of clinical and other outcomes of current measures of intervention. The aftermath of the accidents described above, it is not unreasonable to expect that the medical profession itself will undertake a more responsible role in monitoring and regulating procedures which they alone can authorise and assess.

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STATUTES

- Financial Services Act, 1986.
- Consumer Protection Act, 1987.
- Public Health (Infectious Disease) Regulations, 1988.
- Public Health (Control of Disease) Act, 1984,
- AIDS (Control) Act, 1987.
- Health and Medicines Act, 1988.

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True Hermaphroditism: Clinical and Cytogenetic Studies

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ABSTRACT

Clinical and cytogenetic studies of 14 patients with true hermaphroditism revealed 46, XX (5 cases); 46, XY (3 cases); 46, XX/46, XY (4 cases); 46, XX/47, XXY (1 case); 48, XXXY (1 case). Hormonal profiles of follicle stimulating hormone, luteinizing hormone and testosterone concentrations together were insignificant when compared to controls. Parental consanguinity was seen in 71.4% of the cases, supporting the role of autosomal recessive gene(s) for the cause of ambiguity in true hermaphroditism.

Key words: True hermaphroditism, ovotestes, sex determination, autosomal recessive gene

INTRODUCTION

True hermaphrodtism is defined as presence of ovarian as well as testicular tissue in either the same or opposite gonads (1,2). These patients may have a separate ovary and testis, or more often, one or more ovotestes (1,3,4). Most individuals with true hermaphroditism may have 46, XX complement (2,5), although a few individuals have 46, XY (6), 46, XX/46, XY (7), 46, XX/47, XXY (8), 46, XX/46,XY/47, XXY (9).True hermaphroditism was identified in 14 subjects out of 105 cases of sexual ambiguity attending Institute of Genetics for investigations and advice during the period January, 1993 and December, 1996. In this study, we report the clinical and cytogenetic studies conducted in these 14 patients.

METHODS

Between January 1993 and December 1996, 105 patients with ambiguous genitalia were investigated at the Institute of genetic Diseases and Hospital for Genetic Diseases, Osmania University, Begumpet, Hyderabad, India. In 14 of them, true hermaphroditism was diagnosed based on gondal histopathology. Their age, birth order, religion, maternal reproductive history, history of consanguinity and clinical

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features were recorded in a special case proforma. The external genitalia were assessed clinically according to the Prader's (10) classification. Mucosal cells obtained by buccal scrapping were stained for X-chromatin (11) and Y-chromatin (12). Chromosomal analysis was done using cultured lymphocytes from peripheral blood by arresting metaphase with colchicine according to the method of Moorhead (13) and staining for G-banding (14). Karyotypes were determined by examining 50 metaphases from each patient. Follicle stimulating hormone [FSH], luteinizing hormone [LH] and testosterone concentrations were estimated in the serum by radioimmunoassay [RIA] in patients as well as age matched control subjects.

RESULTS

The age of these patients ranged from 6 months to 18 years. The clinical manifestations encountered in these subjects included small phallus [6.7%], hypospadias [7.6%], bifid scrotum [1.9%], enlarged clitoris [4.8%]. Urethral opening was seen in 1.9% of the cases. Normal testes were found in 2.9% patients.The degree of virilization was relatively marked according to Prader's rating (10). Histopathological examination revealed: testis/ovary [21.4%], ovary/ovotestis [21.4%], testis/ovotestis [35.7%] and ovotestis/ovotestis [2.4%]. Parental consanguinity was observed in 71.4% of patients with true hermaphroditism when compared to 17.5% observed in the control group [Table 1]. The most common karyotype [Table 2] was 46, XX [5 cases] and other chromosomal constitutions were 46, XY [3 cases], chimerism 46, XX/46, XY [4 cases], 46, XX/47, XXY [1 case] and 48, XXXY [1 case].

DISCUSSION

Diagnosis of the true hermaphroditism is based mainly on the histologically verified ovarian [follicles] and testicular [seminiferous tubule] tissues and can be made irrespective of the chromosomal complement (3). The ovotestes is the most common gonadal structure observed in true

Table 1. *Parentalconsanguinity in 14 patients with true hermaphroditism and 200 controls*

Type of consanuinity	True hermaphroditism (n=14)	%	Controls (n=200)	%
First cousins	8	57.1	28	14.0
Second cousins	1	7.1	4	2.0
Uncle-niece	1	7.1	3	1.5
First cousins once removed	0	0	0	0
Uncle-niece once removed	0	0	0	0
Total	10	71.4	32	17.5
Non-consangunity	4	28.6	165	82.5

All percentage figures corrected to first decimal phase

Table 2. *Correlation between clinical, cytogenetic and hormonal findings in 14 subjects with true hermaphroditism*

Patient No.	Age	Phenotype	Karyotype	FSH	LH	Testosterone	Clinical features
1.	6 mo	Female	46, XX/47, XXY	4.20 (2.0)	7.20 (1.0)	U.D. (0.05)	Testis felt in left side labia majora, external genitalia female type, hypoplastic fallopian tube, ovotestes
2.	18 mo	Female	48, XXXY	5.80 (2.1)	4.50 (1.30)	U.D. (0.05)	Clitors enlarged, small penis, testis felt in left labial region, scrotal sacs not formed, small ovotestes in the inguinal canal, mental retardation
3.	2.5 yrs	Female	46, XX/46, XY	3.70 (3.5)	3.50 (2.20)	0.06 (0.10)	Labia majora fused, enlarged clitoris/ small penis, urethral opening at the base of the penis. Right gonad was ovary, no testicular tissue was confirmed, unicorn uterus, fallopain tube present.
4.	19 mo	Male	46, XX/46, XY	3.8 (2.1)	4.2 (1.3)	0.07 (0.05)	Simple urethral opening, no vaginal opening, clitoris enlarged or small penis, labia majora present, right testis felt in inguinal region, ovo-testes present on either side
5.	4 yrs	Male	46, XX/46, XY	4.50 (3.80)	5.20 (2.50)	0.09 (0.15)	Undescended testes on both sides, kept in scrotal sacs, dysmorphic facies, low set ears, right inguinal ovotestis, left ovary present

contd...

Patient No.	Age	Phenotype	Karyotype	FSH	LH	Testosterone	Clinical features
6.	9 mo	Female	46, XX/46, XY	3.20 (2.00)	3.90 (1.00)	0.11 (0.05)	Clitoris enlarged, labia majora and minora well developoed, palpable gonads, vagina well developed, inguinal ovotestis, left ovary present
7.	7 yrs	Male	46, XX	2.50 (4.20)	3.15 (3.50)	0.28 (0.20)	Penoscrotal hypospadias, right testis in the scrotal sac, left testis not palpable, uterus not visible but ovotestis present on left side
8.	7 mo	Male	46, XX	3.20 (2.00)	3.50 (1.00)	U.D. (0.05)	Short stature, absence of external genital organs, short penis, hypospadias, no testicular sacs, rudimentary uterus with vaginal canal, both ovary and testis present on either side
9.	12 yrs	Male	46, XX	2.10 (6.00)	3.00 (3.50)	U.D. (3.00)	Micropenis, hypospadias/chordee, testes not palpable, both ovary and testis present
10.	18 yrs	Male	46, XX	3.20 (9.10)	3.50 (12.50)	U.D. (3.00)	Penis short, urethral opening at penoscrotal junction, testes not descended both sides, rudimentary uterus present, ovotestis and testis present on both sides

contd...

Patient No.	Age	Phenotype	Karyotype	FSH	LH	Testosterone	Clinical features
11.	16 yrs	Male	46, XX	5.25 (8.90)	5.20 (12.00)	0.17 (3.00)	Thin built, breast development present, glans penis/enlarged clitoris, no scrotal sacs, labia majora present, no testis, urethral opening present below the penis, ovotestes present
12.	21 mo	Male	46,XY	2.50 (2.10)	3.15 (1.30)	U.D. (0.15)	Scrotal sacs present, vaginal opening present, small penis, both testes palpable and descended, both ovary and testis present
13.	14 yrs	Female	46, XY	7.42	12.5	1.15	Mascuine features, public hair positive, penis absent, scrotal sacs well developed, hypoplastic uterus, ovotestis was present on left side and testis present on right side
14.	14 yrs	Female	46, XY	9.25	6.35	1.23	Penis has hordee and perineal hypospadias, a blind tract about one inch long present in the location of vagina, no uterus or cervix, no breast development, scrotum developed with descended testes both sides, ovotestes present

Numbers in paranthesis are control values

Yrs = years; mo = months; U.D. = undetectable

FSH = Follicle stimulating hormone; LH = luteinizing hormone

hermaphroditism. The proportion of ovotestes observed in the present study [78.5%] is higher than that reported in earlier reports (5). Most of the cases in the present study had the chromosomal complement of 46, XX. Similar findings have been reported in other studies. Moreover, it seems likely that all the cases do not result from the same aetiology, and some could result from chimerism i.e., the presence of both XX and XY cells in a single individual (46, XX/46, XY). The aetiology of true hermaphroditism is heterogenous and varies according to chromosomal complement, mutant sex determining genes, translocation of testicular determinants from Y-chromosome to X-chromosome or an autosome. Possible explanation for the presence of testes in individuals with XX chromosomal constitution includes translocation of SRY gene from Y to X; translocation of testicular determinants from Y to an autosome; undetected mosaicism or chimerism; and sex revarsal gene(s). Presently, the key role of Y chromosome in gonadal dysgenesis is not clear (15,17). Testicular differentiation may depend not only on the absence of SRY gene but also controlled by other genes working independently of the SRY gene (18). The genetic factors, probably autosomal factors also play a role in the pathogenisis of true hermaphroditism as suggested by several familial aggregates (19,20). Perhaps different genetic factors are responsible for the occurrence of 46, XX males and true hermaphrodites in the same kindred (22,23). Eicher and Washburn (24) have suggested that autosomal genes may cause sex reversal in mice. A condition similar to that may prevail in humans. It is possible that perturbation of an ordinary autosomal gene may prelude in appropriate sex reversal in man as well. Pedigrees of these subjects with 71.4% consanguinity supports the view of autosomal recessive gene(s) responsible for the cause of ambiguity in individuals with true hermaphroditism.

The choice of sex assessment for raising the patients with true hermaphroditism depends on various age factors such as age, degree of virilization of the external genitalia, capacity of testicular tissue, presence or absence of uterus among others. The rearing of the child with sexual ambiguity may not necessarily agree with the genetic sex (25) because one must not consider not only the disorder itself but the status of the external genitalia. This decision best be made by a team consisting of pediatrician, urologist, gynecologist and geneticist.

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State of the Art Management of Burns

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INTRODUCTION

It is a great opportunity and pride for me to deliver this prestigious oration today before such an enlightened audience. Col. Lal was the Director of Medical Services in the Madras Presidency and he chose to be Surgeon in-charge of a unit at the Medical College. I had the unique privilege of being his student in Surgery, and my husband late Dr M.S. Ramakrishnan was his Surgical Registrar. His daughter Puspha was my father's student at Presidency College, Chennai. One becomes almost nostalgic, while thinking of Col. Lal and those years.

I chose the topic of burn management today, because as a Plastic Surgeon I have devoted well over 25 years in teaching and treating Burns at the Kilpauk Medical College, Chennai, where a well equipped Intensive Care Burn Unit attached to the Reconstructive Unit with 50 beds is present. This unit was established before 25 years. Though the speciality of burns is not by any means glamorous like our other counterpart, the cosmetic surgery, I chose to remain as the Professor and Head of the Department in this unit for twenty years till I superannuated.

Over the last two decades the mortality due to burns have steadily decreased all over the world, but we cannot boast of such an event in India, mainly because of lack of accurate statistical data, epidemiological surveillance and lack of implementation of good preventive programmes. The actual decline in burn mortality is essentially due to a better understanding of pathophysiology of inflammatory response in burn trauma and the availability of superior antibiotics in infection control enabling early surgery for burns. The advent of skin replacements, synthetic skin and cultured human skin has revolutionised the management of burn wounds.

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EPIDEMIOLOGY

Burns being a preventable condition, an effective preventive programme can be implemented, only after we identify the epidemiological and aetiological factors and the statistics on occurrence, mortality and survival of burns. The following charts would establish the gravity of the problem. As burn injury is not a notifiable disease, and due to the lack of National Burn Registry, our country can never talk of the actual incidence of the condition. However our statistics reveal that majority of burn injury occur in women, due to flame and there is a large proportion of paediatric burns in India. There is also a significantly high incidence of suicides (11%), mainly in women in the age group of 20 to 40 years.

IMMUNOLOGICAL RESPONSE TO BURN INJURY

With every decade of history new insights based on technological advances change our understanding of the world around us. No where has there been more prolific change than in the field of medical research where new ways of looking at the disease have change its treatment. In the recent past relevant immunological changes were noticed to have taken plac}e over since allografts had been used to cover the burn wound. During the 1970s, our understanding of cellular and humoral immunity increased markedly. We noticed that several T-cell functions failed following burns. Burn injury also caused particular reduction in the number of helper T-cells. In 1980's the immunological alterations produced by burns were more clearly understood and every known assayable parameters were identified. It is in this era that recombinant technologies gave to the researcher unprecedented tools such as interleukins [IL], ways of assessing their function and their receptors. Consequently the examination of T-cell failure in Burn injury could be made at the molecular level. The characterization of IL-1, and IL-2 and their receptors gave us the understanding of the cell to cell interaction and broader time-course of immune events. These achievements have all been focussed on the molecular details of the immune response in burns. However as each cytokine was discovered it became evident that in burns most cytokine activities are chaotic and abnormal. Other products of immune cells like prostaglandins, oxygen free radicals and consequently lipid peroxides were also found to be involved. As this picture emerged over 1980, and more details were provided in the literature, more compound and diffuse the picture became. The newest description then, of burn immune failure has changed from simply categorising what parameters fail, to describing the condition with a unifying term 'systemic inflammatory response' (SIR), which is responsible for the eventual outcome. The concept became established because today 50% patients who die due to severe burns, do not die due to infection, as was thought previously. Today the chaotic cytokine array is deemed responsible for what ultimately kills the patient. But one has to bear in mind that assessment of cytokines is of little use as predictors of critical events because they themselves are effects rather than causes. What is needed today is an interpretation which encom-

passes most, if not all, phenomena in one hypothesis.

The first action that takes place after burn injury is macrophage activation. Then three cytokines IL-1, IL-6 and TNF-α are released. Macrophages are also responsible for producing oxidation products of lipids like prostaglandins, leukotrienes, and indirectly peroxides which are all toxic to the patient. Hence it is imperative to find out how the thermal injury activates the macrophages or neutrophils, and this would be extremely important due to a simpler treatment intending to prevent activation, rather than to arrest the consequent activity of several run away phagocyte products.

In burns, the area of burnt skin quantitatively is correlated with the mortality. Hence skin today is recognised as an immune organ and the effect of heat on the skin could well figure in the origin of the pathophysiology encountered. Area of skin burned also correlated with the degree of T-cell functional failure.

In experimental animals, a toxic material has been isolated from the burnt skin, which when infected into normal animals exhibits all the symptoms of toxic shock seen post-burn. The toxic material is a polymerized aggregate and is a lipoprotein complex [LPC]. Heat input had induced toxicity simply by polymerization. This experimental work indicates that a heat toxic polymer, from burnt skin is responsible for the death of the patient, and this mortality was linked to immune depression. The LPC acts in the following ways:

- It suppresses cell mediated immune response.
- It inhibits lymphocytes immuno globulin synthesis.
- It depresses granulocyte colony formation. LPC circulates in the serum after burns and antibodies develop. The type of dysregulation of immune function which develops post-burn seems to begin with the inability of cells to respond positively with regard to the immune response. The toxic LPC reduced the resistance of burnt mice to pseudomonas infection.

INITIAL MANAGEMENT OF SHOCK AND WHAT IS NEW IN FLUID RESUSCITATION

An accurate clinical assessment of the extent and depth of burn injury is the first step in effective resuscitation. With regard to fluid resuscitation in the early phase of burn injury, clinicians are guided by different standard management protocols. Each department over a period of years develops its own preference to formulae. In the initial examination, presence or absence of smoke inhalation and concomitant injuries must be identified, particularly because a patient with smoke inhalation may require 30% more fluid than the one without it.

Resuscitation fluids are mainly crystalloids in the form of Ringer lactate and colloids in the form of fresh frozen plasma [FFP], albumin and whole blood.

In this part of the world, Parkland formula of 4 ml/kg/% burns in the form of Ringers lactate is the most popular. Whole blood and FFP are also used. But strict vigil on viral disease transmission must be kept in mind, for human immunodeficiency virus [HIV] and hepatitis B virus. In Europe

today FFP is sterilised with a detergent so as to be completely free from virus. The goal of fluid resuscitation is to support the patient through the initial 24 to 48 hours of hypovolaemia due to sequestration of fluid into the burnt tissues. Adequate resuscitation is monitored by an urinary output of 0.5 ml to 1 ml/kg/hr. Weight based formulae overload children, hence formula based on body surface area is used in paediatric patients. However for patients with severe burns, the use of urinary output and vital signs may lead to sub-optimal resuscitation. For these patients invasive cardio-respiratory monitoring may be indicated to optimise fluid therapy.

METABOLIC RESPONSE

The degree of metabolic changes experienced by patients are directly related to the extent of injury. During the initial phase called "ebb" phase, there is lowering of cardiac output and metabolic rate. Once resuscitation takes place, cardiac output and metabolic rate may return to normal and may become elevated. This hypermetabolic phase may show a high core temperature of about 38.5 °C and remains high for 5-15 days post-burn. This is due to the direct stimulation of the hypothalamus by inflammatory mediators like cytokines that increase the thermoregulatory set point and alter the endocrine function also. Secretion of cortisol, glycogen and catecholamines are all increased. These being strongly catabolic, produces negative nitrogen balance, loss of tissue protein and bone minerals. Growth hormone [GH] and insulin like growth factor IGF-1 levels also decrease following severe burns.

If untreated, the hypermetabolic phase literally wastes the patient and he succumbs. For therapy today recombinant GH 2 mg/kg per day is given to massively burnt children. The effects of IGF-1 and GH are complementary. While GH increases the protein synthesis the IGF-1 decreases protein degradation. These have been proved by several randomized trials. But the cost of the treatment is prohibitive. Since the cardiac rate is high in burns patients, beta-blocking agents such as propranolol can reduce the rate and also the ventricular work index. Since the catecholamine levels are very high in severe burns, one can safely give propranolol.

INFECTION CONTROL

After the shock phase, prevention of infection is most important in burn patients. In developing countries the maximum mortality in burns is due to septicaemia. In infection control, prevention is accomplished by strict vigil on nursing, air sterilization, and providing isolated rooms for every patient. Prophylactic antibiotics need not be given, and a definite strategy on the administration of antibiotics is followed. Routine surface and biopsy would cultures are done and then appropriate antibiotics in the necessary dosage is given. In invasive sepsis, aggressive antibiotics and antifungal treatment are given.

Local wound is dressed every day, and each surgeon has his or her own way of taking care of the wound. In our set up:

- Superficial and superficial partial thickness wounds are treated as outpatient

cases with amniotic membrane or collagen as biological dressings. In deep partial thickness burns also, biological dressings are used to prevent infection and progress of depth of burn. However if it extends, it is treated as full thickness burn.

- Topical antimicrobials are liberally used in certain cases of circumferential burn and silver sulphadiazine invented by Fox has stood the test of time. To cover the wound with autoskin is always the primary aim of wound care.

NUTRITION

Patient with severe burns (>40%) have metabolic rates that are 100% to 150% above the basal metabolic rate. These patients need energy and proteins in order to prevent impaired wound healing, cellular dysfunction and decreased resistance to infection. Diet is provided orally, enterally or parenterally. Several formulae are available. But each physician plans a diet that would suit the patient individually. One can aim at a calorie intake anywhere between 2400 kcal to 3600 kcal and may even go up to 5000 kcal in rare occasion. Regardless of the mode administration 20% of calories must be from proteins, 30% must be fat and 50% must be carbohydrate. The role of dietary additions such as glutamine, arginine, vitamin C, vitamin E, fish oil are all under investigation. Total parenteral nutrition [TPN] in burn patients has been associated with metabolic and immunological complications and its use is limited today to supporting patients with severe gastrointestinal dysfunction.

WOUND HEÀLING

As an aggressive approach to burns wound excision is the standard of care today. All burns over 30% must be aggressively treated. However all surgical excisions must be tailored to the individual circumstance. In developing countries due to constraint on the available skin replacements and blood the management varies. The treatment of superficial and superficial partial thickness burns have already been mentioned.

- Deep burns if they are circumferential immediate escharotomy and decompression must be done to save the vascularity of the limb.
- Deep burns over 30% are tangentially excised with adequate blood support and the whole are is autografted. In the absence of sufficient autograft, homografting from the parents of the child can be contemplated. One has to be very cautious about the area to be excised, and intense planning has to be done so as to judiciously use the skin replacements. Repeated graftings are done by sequential harvesting of limited donor sites.
- In electric burns, if the area is limited, we can do primary full thickness excision and immediate flap cover. Micro surgical free flaps also can be used.
- Cadaver skin is not available in India (legislation does not permit us to use it) and what is available today to be used are [i] Biobrane which is a synthetic cover and [ii] Dermagraft JC which is essentially biobrane populated with neonatal firboblasts which secrete

structural support proteins and cytokines prior to being inactivated. Next is the cultured autologous epidermal keratinocytes. This is very expensive, and due to lack of structural integrity on a long term basis, it is becoming less popular even in the western world.

- Recently we have skin substitutes which are very useful. One is Integra which is a bilaminate of collagen with chondroitin sulphate with a silastic cover, and Alloderm which is a deepith-elialized pathogen free cadaver skin.

Ultimately the area has to be closed with patient's own skin. When none of the above is available, the patients survival gets priority and the patient is allowed to get into contractures which are later released and grafted. This extreme measure is only very rarely adopted.

RECONSTRUCTION AND REHABILITATION

Several plastic surgical procedures including flap covers, and microsurgical free flaps are used in burn reconstruction. Every reconstruction has to be followed with physical therapy and rehabilitation. Pressure bandages, garments and splints are most useful.

PSYCOTHERAPY AND OCCUPATIONAL THERAPY

Burnt victims go through a phase of depression, and disfigurement can be very traumatic. Treatment by a psychiatrist is often needed. During the phases when a person waits for staged reconstructive procedures placing them in suitable occupations will help them to rebuild the confidence.

To conclude burn management needs a multidisciplinary research and multi-professional approach. Tertiary care treatment alone will not solve this devastating problem.

RESEARCH

In burn management, research is an ongoing process. Study of the process of inflammation/immune response, its failure and the production of newer synthetic skin replacements are being conducted in many centres of the world. Every burn surgeon must be interested in research.

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Mind and Medicine

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INTRODUCTION

It is with a strange feeling of happiness and family pride that I stand before you to deliver this year's Dr. K.L. Wig Oration. Kushwant Lal Wig was my father's younger brother and hence I had known him from my childhood. A flood of memories comes back to me when I think of him today. Though I never had the privilege to be his student or work with him in the same institution, he still guided me in all important stages in my career. Few medical men in the last fifty years have attained such eminence as a clinician and teacher as Dr. K.L. Wig did. In my travels over the years, I have met his students in many parts of India, Pakistan and in many other countries. It is no exaggeration to say that no other medical teacher of that generation is so fondly remembered by his students as Dr. K.L. Wig is. Anecdotes about his perfectionist nature, legendary clinical skills, fairmindedness, his humane concern for his patients are all too well known to his students, many of whom are sitting in the audience today.

The topic of my lecture today 'Mind and Medicine' is in a way, my effort to pay my tribute to him. After I passed my M.B.B.S. from K.G. Medical College, Lucknow, in 1953, it was he who encouraged me to take up a career in psychiatry while almost everybody else, family, friends or my teachers in Lucknow - thought it to be a 'crazy' idea. Dr. K.L. Wig's further advice to me was that if I am thinking of a career in psychiatry in a teaching hospital, I must do M.D. Medicine first, before taking up psychiatry. I would always be grateful to him for his advice. The second reason for choosing this topic is even more important than reference to my career. In K.L. Wig, I found a role model of an ideal physician who always took a holistic view of the medical problem. It is from him that I had my first lessons in the role of 'Mind in Medicine' about which I am going to talk today.

MIND AND MEDICINE

The main theme of my talk is how mind and its influence on health and disease, was once considered very essential part of medi-

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cine and how in the last few hundred years mind and medicine have slowly drifted apart. Over the years, a new biomedical or biotechnical model has emerged in which mind or mental functions find very little role. This new model seemed to function very well for a while and medicine made tremendous progress. In recent years a new awareness is coming that with the present biomedical model we are running into serious difficulties in solving the current as well as the newly emerging health problems. Meanwhile, new knowledge about mind, mental functions, role of behaviour and psychosocial factors in health and disease is rapidly accumulating which is forcing us to re-examine the inadequacy of the current paradigm of biomedical model of medicine.

The term 'mind' has been used in medical literature in many different ways, in various languages and cultures in different periods of history. It will be beyond the scope of this lecture to attempt to discuss different concepts of mind. In general the term 'mind' refers to our mental faculties, our thinking, our feelings, our memory, our will, our judgement and perhaps most of all our awareness of ourselves. Before the rise of modern scientific era, any discussion of mind would also include a reference to soul or spirit. As we know, the original meaning of the world 'psyche' from which terms like psychology or psychiatry have been derived, was 'spirit' or 'soul' and not mind in the sense it is used today. In fact the separation between body and spirit was always accepted in medical history in all cultures while separation between mind and body in our thinking is a relatively recent phenomenon.

CONCEPTUAL MODEL OF HEALTH AND DISEASE IN EARLIER SYSTEMS OF MEDICINE

Before the arrival of modern scientific medicine in Europe around the seventeenth century, there were many other organised systems of medicine visiting in all parts of the world. Some of them like Ayurveda or Unani Tib or Chinese medicine continue to be utilized by millions of people in many countries till today. The conceptual model of health and disease in these systems of medicines is considerably different from what we now understand in modern medicine. For example if one studies some of the well known Ayurvedic texts like *Charaka Samhita, Sushruta Samhita,* one is struck by a very different approach to the subject, as compared to the modern text books of medicine. I have summed up below some of the significant points in the earlier models of health and disease.

a) Almost all the ancient texts of medicine like *Charaka Samhita* open with a reference to the place of man in the universe, aims of medical sciences, purpose of life, role of religious duties etc. All this is, in great contrast to modern text books of medicine which are presented in a very secular way without any reference to God or sprit or man's place in universe etc. Of course this approach has both, advantages and disadvantages.

b) In earlier systems like Ayurveda, the living beings are considered as made up the same five elements which constitute the universe, i.e., earth (*prithvi*), water (*apa*), fire (*tejas*), air (*vayu*) and

ether (*akasha*). The sixth controlling element is the spirit of supreme consciousness; in the universe it is the *'Brahman'* or in the living being it is the *'Atman'* (1).

c) Health is conceived essentially as a balance between different forces like, the three *Dhatus* (*kaph, pit* and *vayu)* or the three *Gunas* (*sattva, tejas* and *tamas*). Disease is regarded as an imbalance between these forces.

d) In all ancient systems of medicine, role of mind and emotions is considered very important both in health and disease. Mental processes were repeatedly invoked for healing-may it be in shamanic or spirit-possession practices in many cultures, or temple healing and dream analysis in ancient Greece, or Yoga and meditation in India. There are repeated references to the role of emotions in the writings of great physicians of Islamic medicine like Ibne Sena or Al-Rhazi. Excess of negative emotions like *kama* (lust), *krodha* (anger), *lobha* (greed), *moha* (attachment) and *ahankara* (pride) are frequently mentioned as causes of physical and mental ill health in various Indian texts.

e) Another striking thing in the earlier systems of medicine was that a treating physician or a healer used to see oneself as "working with nature" and tried to revive what Hippocrates called "nature's healing powers". In contrast a doctor of modern scientific medicine sees himself as fighting and conquering nature (2).

SEPARATION OF BODY AND MIND IN EUROPEAN THOUGHT – THE ROLE OF RENE DESCARTES

In the history of Western medicine, the separation of body and mind is generally attributed to the writings of Rene Descartes (1596-1650). Few persons have influenced the history of Western science and medicine so powerfully as Descartes. His famous statement *"Cogito, ergosum" or "I think, therefore I am"* has been quoted in innumerable books of science and medicine. But behind this seemingly simple statement lay years of rigorous introspection. The basis of Descartes' thinking is radical doubt; doubting all traditional knowledge, the impression of his senses and even the fact that he has a body-until he reaches one thing he can not doubt; the existence of himself as a thinker. For Descartes, essence of human nature lies in thought and he divided nature into two realms; that of mind *"res cogitans"* or the thinking thing and that of matter *"res extensa"* or the extended thing. This was the beginning of the separation of not only body and mind in European thought but also led to the separation of the Humanities from Natural Sciences.

Descartes influenced scientific thinking in three major ways:

1. He separated mental from material phenomenon.
2. He encouraged the attitude of doubting all traditional knowledge till clearly proven.
3. He introduced the analytical method in science i.e., breaking all problems into smaller parts and arranging them in

their logical order. This is what has been later called 'reductionism' in science.

Descartes was also a great mathematician. He saw the whole universe as a grand machine controlled by strict mathematical laws. He also visualized living organisms in terms of machines - healthy body as a perfect machine and disease as something where the machine is not functioning. It is interesting to note how this model of man as a machine, has dominated our thinking for the last three hundred years. In the seventeenth century it was the mechanical clock with which human body was repeatedly compared. In the eighteenth century came the steam engine and internal combustion engines and human body was compared with them. In the nineteenth century the favourite theme was electricity and nervous system was being compared with that. In the twentieth century, computer dominates our thinking and it has become the favourite model to explain bodily and mental functions. Three centuries after Descartes, the science of medicine is still based as George Engel has said, on "the notion of body as a machine, of disease as the consequence of breakdown of the machine, the doctor's task to repair the machine" (3).

THE BIOMEDICAL MODEL OF HEALTH AND DISEASE

The rise of modern scientific medicine began in the nineteenth century with the great advances made in biology. Progress in physics and chemistry further strengthened these developments. Following the reductionist approach, two significant trends emerged. Rudolf Virchow postulated that all illness involved structural changes at the cellular level, thus establishing cellular biology as a basis of medical sciences. The second major advancement was the study of microorganisms by Pasteur and others that has laid the foundation of modern microbiology. These developments in the nineteenth century, led to the popularity of the 'germ theory of disease'— the doctrine that specific diseases are caused by specific microbes which dominated medical thinking for the next hundred years. Further developments in medical technology, antimicrobial drugs, anaesthesia and modern surgical techniques have all contributed greatly to the current progress of modern medicine. However, it is important to note that inspite of all the recent advances in medicine, our basic understanding of the phenomenon of health and disease continues to be dominated by what is generally called the "biomedical model". I have put down the main features of this model in Table 1.

Table 1. *Main features of biomedical model of health*

- Living organism viewed as a machine. Disease viewed as malfunction of the machine
- Diseases viewed as specific entitles with specific single causes may it be microorganism or a genetic defect or a molecular change
- Medical technology viewed as the main solution to health problems
- Physical mechanisms viewed as basis of life mental events seen only as secondary phenomena

THE CURRENT DISSATISFACTION WITH MODERN MEDICINE

There is no doubt that modern medicine has made tremendous advances in the last 200 years. In our life time the life expectancy of an average Indian has nearly doubled from thirty years to sixty years Small pox has been eradicated. Polio and many other infectious diseases have been greatly brought under control. The prevalences of nutritional deficiency diseases has been greatly reduced. Modern surgery has saved the lives of many people and prolonged the lives of many others. Treatment of a large number of other medical conditions has been greatly improved.

Inspite of such spectacular progress in the medical sciences, it is surprising and a bit disturbing to note that society at large is not particularly pleased with the performance of medical profession. In fact the criticism against medical profession is mounting in the last few decades. There are largely three types of criticism which are levelled against us - all three of them are interrelated. The first and the most common criticism is that medical treatment has become very costly. Even the rich countries like USA, where health budget has reached over 10% of the national income, are finding it difficult to bear this burden. The second criticism is about the inequity and maldistribution of the benefits of modern medical service. While the rich people in big cities can have the best of medical help, the poor people especially living in the rural areas and city slums, have very little access to good quality modern health services. The third type of criticism is related to the attitude of medical professionals. People complain about too many specialists and too many investigations. They feel that doctors do not have sufficient time for patients and medical services are becoming mechanical and dehumanised. It is said that health is becoming more and more like a commodity, produced by technology and controlled by market forces. This does not mean that there are no more good and humane doctors – there are many of them and hopefully will continue to be there – but we have to take note of the increasing criticism against the current system of medicine. If we look closely at this phenomenon, we will find that essentially the present state of medical profession is directly related to the medical model which has evolved in the last three hundred years, in which diseased organs, cells and molecules have become more important than the individual human beings; where technology and machines have become more important than the doctor-patient relationship.

EMERGING HEALTH ISSUES FOR THE TWENTY FIRST CENTURY

Let us now have a look at what are the new challenges that are appearing on the medical horizon when we are approaching the twenty first century. It is true that we have partly solved the problems of common infectious diseases and nutritional deficiencies but the newer problems which are emerging appear to be even more formidable. I have put down some of these issues in the Table 2.

The main point to be noted in this table is that the pattern of serious health problems is undergoing a major change. In this list of new problems, human behaviour and

Table 2. *Emerging health issues for the twenty first century*

Rising population
Changing health dynamics
Care of the aged
Care of the chronically ill
Mental, alcohol and drug abuse disorders
Management of somatisation disorders
Violence, accidents, suicides
AIDS
Concen with quality of care (health expectancy vs life expectancy)

psychosocial factors are fast emerging as the main common theme. The conventional technology-oriented medicine as being practised today many not provide the solutions to these problems. Communicable diseases are losing their prime place as the major killers. As the life expectancy is increasing, we are now faced with increasing mortality and morbidity from non-communicable diseases like cancer, diabetes, hypertension, heart disease, strokes etc. Social pathologies like alcohol, drugs, violence, suicide are becoming new threats to health. Problems of old age like dementia are looming large as a major health concer. Long term medical care instead of cure is suddenly becoming a very important issue. There is the problem of somatisation disorders which is one of the largest groups of patients who visit primary health care services, especially in developing countries. These are the patients who have vague, ill-defined multiple somatic symptoms often expressed in colourful local cultural terms like the movement of *'ga'* or *'gole'*, displacement of viscera (called *'dharan"* in North India) or loss of important body fluids like *'dhat'* and so on. Most of these patients have dysphoric mood of anxiety and sadness and often have significant interpersonal problems in the family or at work. Our technologically oriented biomedical model of health care has very little to offer to these patients except costly irrelevant investigations and more costly medications without demonstrable benefits. The medical care of this group is a great financial drain on the limited national health resources and in the coming decades we must find some better solution to this problem.

Mental disorders of various kinds including alcohol and drug disorders are rapidly emerging as the leading causes of morbidity and disability as reported in the World Health Report 1997. Christopher Murray and Alan Lopez in their much talked about book "The Global Burden of Disease" published by Harvard University Press on behalf of World Bank and World Health Organization has projected that by the year 2020, the leading cause of disability in the world would be ischaemic heart disease while the second leading cause would be unipolar major depression.

The dramatic increase in the life expectancy is creating new problems for the health planners for the next century. Half a century ago, the great majority of the global population died before the age of 50 years. Today the average life expectancy in developing countries is 64 years and is estimated to reach 71 years by the year 2020. But while extending our life span is desirable in itself, it is much more so if it can be accompanied by freedom from additional years of suffering poverty, pain or disability. Qual-

ity of human life is at least as important as the quantity. Individuals are entitled to be concerned not so much about their life expectancy as about their health expectancy (4). In the search for quality of life indicators, one new concept which is being talked about is the 'Disability Adjusted Life Years' (DALY) which combines the years of health lost through premature death, with the years of life lived with disability. This measure was extensively used in the World Bank's 'World Development Report-1993. Investing in Health'. Percentage of DALYs lost due to mental health problems occupy an important position with 8.1% , more than heart diseases (4.4%) and cancer (5.8%). A more significant finding in this report is that 34% of disability in the world is related to behaviour related problems - in addition to the mental disorders. These include conditions such as violence, accidents, diarrhoeal diseases, malnutrition, sexually transmitted diseases etc. (5)

THE ROLE OF MIND IN HEALTH AND DISEASE – NEWER EVIDENCE

The role of mind in health and disease has been recognized from the earliest times in medical history. The powerful effect emotions have on our bodies is obvious to all of us as soon as we get angry or anxious or fearful or depressed. In the beginning of this century with the influence of psychoanalysis the term psychosomatic diseases became quite popular and referred to conditions like peptic ulcer, bronchial asthma, ulcerative colitis, urticaria etc., in which it was postulated that excessive unexpressed negative emotions produce physiological changes which in turn lead to tissue damage in the organs. A little later, attention was directed not to specific emotions but to the whole personality pattern. It was postulated for example, how 'Type A' personality traits of excessive drive, time urgency, competitiveness, need for control etc were associated with higher incidence of coronary artery disease.

In recent years a new kind of evidence has been accumulating which has led to the emergence of a new multidisciplinary speciality with the name of "psycho-neuro-immunology" or PNI (6). This term was coined by Robert Ader who was working as Clinical Psychologist in the University of Rochester School of Medicine. PNI has been defined as the study of intricate interaction of consciousness [psycho], brain and central nervous system [neuro] and the body's defence against external infection and aberrant cell division [immunology]. In a short time, researches in this field have shaken our conventional style of thinking in terms of body and mind. It seems wrong now to think that mind "located" somewhere in the brain - as we have been taught in the past. As Volhardt (8) has summed up:

"The field of psycho-neuro-immunology is in its infancy but research already make a good case for breaking down old dualistic notions that mind and body are separate systems. In fact much research indicates that the brain and immune system form a closed circuit."

Let me refer to the original experiment of Robert Ader in 1974 which led to this new direction of thinking. As we know the immune system is a surveillance system which protects the body against infection and foreign substances. There are two basic types

of immunologic reactions: humoral and cell-mediated which involved B-lymphocytes and T-lymphocytes, respectively. In this experiment, white rats had been given a medication that artificially suppressed the quantity of disease-fighting T-cells circulating in their blood. Each time they received the medication, they ate it along with saccharine-laced water. Ader accidentally discovered that giving rats only saccharine-flavoured water, without the suppressive medication, still resulted in lowering of T-cell count – to the point that some of the rats started getting sick and even died. Their immune system had learned to suppress T-cells in response to the flavoured water only. This was not expected to have happened according to the best scientific understanding at the time. Till that time all the medical scientists believed that central nervous system and immune systems were separate and neither was able to influence the operation of the other (9). As the well-known writer Francisco Varels (10) at a meeting titled 'Mind and Life', held in Dharamsala in India in 1990, beautifully put it, "the immune system is the body's brain, defining body's own sense of self, of what belongs within it and what does not". Subsequently the work of Felton and others have confirmed through electron microscopic studies that neurotransmitters and polypeptides convey the messages between autonomic nerve endings and lymph cells (11).

Through the researchers in psycho-neuro-immunology we are now increasingly aware how situations of stress, such as depression, loneliness, hopelessness lead to immunosuppression, which makes us prone to various infections, allergies and auto immune disorders. Immunosuppression also increases the risk of proliferation of cancer cells. With these new researches it suddenly makes sense why students under examination stress, develop more illnesses and why appearance of cancer is often linked with disturbing life-events. The common knowledge that when one partner of a long and happy married life dies, the health of the other partner is also likely to be seriously affected, has now acquired a new scientific validity. It is now well established after the death of a spouse, survivors are generally at greater risk of death from a variety of illnesses-including heart attack, infectious diseases, strokes, cancer as compared to other people of some age and sex (12). Life stress has also been implicated in many other disorders like tuberculosis, acute respiratory illness, the common cold, genital herpes and mononucleosis (8). It is interesting to note that just as now researches have shown that stress leads to immuno-suppression, the corollary is equally true. Behaviour interventions such as psychotherapy, relaxation techniques, family and social support leads to enhancement of optimization of immune function (13). In his popular book "Anatomy of Illness" Norman Cousins (14) has dramatically brought out the effect of affirmative emotions on disease. By watching Laurel and Hardy's comic movies and with uninhibited laughter he was above to reverse the process of a mysterious ankylosing spondylitis.

A word of caution must be put in at this stage. The science of psycho-neuro-immunology is still very young. It has a long way to go. For example, at present, we are hardly familiar with half a dozen neurotransmitters but the list in this field is

going to be very long. Pert and others (15) have roughly calculated that there may be a family of 60 to 100 powerful informational biochemicals such as neurotransmitters, hormones, neuropeptides, growth factors and lymphokines which carry messages back and forth between CNS, the endocrine system and the immune system. It will also be wrong to think of one cause – one effect relationship between an emotional event and specific pathology. This would again be an old style of thinking like the germ theory of the nineteenth century. The reality is a complex interaction between body-mind and environment. As Robert Ader (6) has said, we need a multidetermined concept of health and disease rather than a linear, single cause-single effect approach. However, psycho-neuro-immunology even in a short period has made two significant contributions to medical knowledge:

- It is now possible to scientifically understand how stress and emotions affect various bodily stems.
- It is no more appropriate to talk of mind and body as two separate systems, as there is constant interaction between them.

IN SEARCH OF A NEW PARADIGM

As pointed out in the introduction of this paper, a slow awareness is coming to the medical profession that the currently popular biomedical model which some people have called Technomedicine, seems to have serious limitations in solving many of the existing and certainly the newly emerging health problems. This is even more evident when we consider the question of prevention of illness and promotion of health. This model has provided us with spectacular successes in the last two hundred years but we are now reaching a stage where more and more technology is giving us less and less good results. The nature of health problems is changing and technology alone - does not seem to be right answer. As Fritjof Capra (2) has pointed out the current biomedical model is a part of the larger western science model. The Newtonian mechanical model of science which dominated out thinking till the end of nineteenth century has outlived its utility in the twentieth century, in the light of Einstein's theory of relativity, quantum theory and Heisenberg's uncertainty principle. The existing biomedical model of medicine with its mechanical rigidity also needs to undergo change just as the scientific model is changing with the advent of sub-atomic physics.

The main direction in which this change is taking place is from reductionism to synthesis, from mechanistic to holistic model. In the paper "The need for a new medical model" published in Science in April, 1977 George Engel (3) proposed the term "biopsychosocial" which over the years has won wide acclaim. From the field of psycho-neuro-immunology, Borysenko (12) has suggested a similar tripartite model of genetic, environment and psychological factors in disease susceptibility. The important point Borysenko (12) makes is that each one of these factors can be the primary determinant of disease or can interact with other two factors in producing disease.

Thomas Kuhn in 1970 (16) introduced the concept of 'paradigm shift' in his famous book 'The structure of scientific revolution'. It refers to a profound change in the thoughts, perceptions and values that form a particular vision of reality. Such a para-

digm shift took place in Europe in 16th century when Renaissance replaced the Theological paradigm of the middle ages (15). The new scientific paradigm had dominated the life of man for the next four hundred years. This thinking included our belief in scientific method as the only valid approach to knowledge; the view of universe as a mechanical system composed of elementary material building blocks; the view of life in society as a competitive struggle for existence; and the belief in unlimited material progress to be achieved through economic and technological growth. As Capra (2) has said, it is only in recent years that all these ideas and values have been found severely limited and in need of radical revision. We are on the threshold of a paradigm shift.

How will this paradigm shift affect medical science? My submission is that the central role of mind, our thinking, our feelings, our emotions, will once again come back to medicine as an important dimension both in understanding of disease phenomenon, in the treatment of patients, in prevention of disease as well as in promotion of health. Is it not strange that as clinicians, all of us swear by the art of healing but 'healing' does not even constitute a subject in our curricula these days! Healing process is not only the eradication of disease but a coordinated response of the whole organism, body and mind to stressful environmental influences. The art of healing is our heritage for the last five thousand years, much before we learnt the modern medical technology. Hippocrates, the great Guru of modern medicine, recognised the healing forces inherent in living organisms and called them 'nature's healing powers'. The main difference which has come over is that, earlier doctors saw their role in assisting the natural forces; now we want to fight and dominate nature:

The second important shift which I foresee is the inclusion of the cultural dimension in our medical model. As Capra (2) has observed "Any system of health care including the modern Western medicine is a product of history and exists in a certain social and cultural context. As this context keeps changing, the health care system also changes. Hence the usefulness of any medical system as a model for another society is quite limited". We have worked with the borrowed model of Western medicine for the last two hundred years. Sadly it has made us aliens in our own cultures. Our ideas of health and disease as learned from Western medicine, often do not fit in with the ideas of our patients and general population. In Indian cultural tradition, mental and spiritual dimension is very much an integral part of health sciences but unfortunately this finds no place in modern medical science. While we bemoan the lack of scientific sophistication our patients, they in turn are baffled by our utter lack of cultural sensitivity. In the past, poets and philosophers, doctors and common man shared the world view about the nature of man, nature of health and is disease. Five elements - earth, fire, water, air and sky were the basis of our existence, three *Gunas* - *satva*, *rajas* and *tamas* were the basis of human personality, the imbalance of three *Doshas* – *kaph*, *pit* and *vayu* caused disease; *kama*, *krodh*, *lobh*, *moha* and *ahankar* were seen as the toxic emotions which produce psychological disturbances. All this was the shared common knowledge. Alas now, the doctors and common man speak different languages.

BRINGING MIND BACK TO MEDICINE

How to bring mind back to Medicine? How to restore the balance between currently dominant technomedicine with the desirable humanistic medicine? How to add psychosocial dimension to the biomedical model? Paradigm shift does not come easily. It takes a life time to bring attitudinal change. At present we are so deeply immersed in the biomedical tradition that we see technology as the only solution to our health problems. When technology fails we seek still more of technology as a possible way out. Medical profession changes very slowly. To change the clinical practice we must bring changes at two crucial levels, medical education and medical research. The science is dismal in both fronts currently in India. Inspite of numerous workshops, symposia, pious resolutions on the need of psychosocial component in undergraduate education, no meaningful impact has been made on our medical teaching which shapes our new doctors. Similarly there is very little money allocated for research on psychosocial factors in health and disease and whatever money Indian Council of Medical Research had been giving for this purpose has been drastically reduced in the last twenty years. Only good research can give us direction how to acquire and apply knowledge in this area.

I sometimes feel that perhaps more than medical profession, it is the general public, the society at large which is going to force us to change. Dissatisfaction with the existing techno-medicine and in fact with the whole western science, is growing. There is repeated talk of alternative to science. In the last fifty years, all around us there is rapid growth of the alternative medicine. There are large groups of new practitioners of such alternative systems of medicine. There are a number of new journals on this theme now with some highly respectable people associated with them. There have been many national and international conferences on this subject. All the talk of alternative medicine has basically one common theme, the need for a holistic approach, instead of the current reductionist approach of medical science. This does not mean to abandon technology or to give up evidence-based medicine but to restore the balance between the science of medicine and the art of healing. It is time to bring mind back to medicine.

Some times may medical colleagues have questioned the reality of mind–we can not see it, feel it or touch it. Is it really something more than the functions of the brain? I do not know the answer. I would close my talk with the following lines from the great Chinese book of wisdom. "Tao Te Ching" compiled somewhere between three to four thousand years ago. The English translation is by Stephen Mitchell (17).

> We join spokes together in a wheel,
> but it is the center hole
> that makes the wagon move
>
> We shape clay into a pot,
> but is the emptiness inside
> that holds whatever we want
>
> We hammer wood for a house
> but it is the inner space
> that makes it livable
>
> We work with being
> but non-being is what we use.

Thank you.

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BOOK REVIEW

Role of Micronutrients in AIDS: New Concepts

Varuna Kochar

This book on AIDS does not create a very good impression at first sight. Written by a biochemist with an award to her credit from the Indian Board of Alternative Medicine, it looks like an over-blown version of an intuitive flash which the author is very keen to share lest the benefits of her revelation are lost to mankind. But a perusal of the preface dispels any such notions. It is neither a revelation nor a revolution but a sensible deduction based on the well-established interaction of nutrition and infections with special reference to AIDS. The credibility of the contents is further enhanced by knowing that the manuscript was reviewed by three eminent medical scientists: Dr. C. Gopalan, Dr. S.P. Tripathy and Dr. S. Sriramachari.

The work is a remarkably lucid synthesis of knowledge culled from more than 300 references, which occupy 40 pages of the 94-page booklet. The fact that the entry of the causative virus into the body is an essential factor in the aetiology of AIDS has been duly acknowledged by the author. But what has been emphasized is the fact that the further course of the disease is profoundly influenced by the nutritional status of the host. A poorly nourished host, because of already weakened immune mechanisms, gets full-blown AIDS soon after the entry of the virus. But in a well-nourished host the gap between turning HIV-positive and getting full-blown AIDS can be several years. By the same token, the author has emphasized, a patient having clinical manifestations of AIDS may be helped by due attention to his nutritional status. The relationship between nutrition and infections has been known for very long. The vicious cycle of malnutrition predisposing to infections, and infections worsening the malnutrition was formally proposed more than 30 years ago by Nevin Scrimshaw, Carl Taylor and John Gordon on the basis of their observations in Latin American countries. Subsequent advances in immunology have only provided a firm basis for the initial epidemiological observations. Extrapolating the relationship between nutrition and infection to AIDS is also not original as acknowledged by the author through several references cited in the book. But the book does emphasize an important but frequently overlooked factor in the pathogenesis and treatment of AIDS.

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The body of the book consists of three chapters followed by an appendix and an alphabetically arranged list of all the references cited. The first chapter establishes the background for the subject of the book. The second chapter provides a well organized account of the subject in five parts. The first part emphasizes the commonality of circumstances which might predispose to malnutrition as well as AIDS. The circumstances comprise frequent ejaculation in men, frequent blood transfusions (as in haemophilia), homosexuality, alchohol and drug addiction, use of oral contraceptives, and pregnancy. Part II lists the various abnormalities of immune mechanisms resulting from micronutrient deficiency. The impairment of complement system may particularly explain why in malnourished HIV -positive patients the neutralization of the virus by HIV antibodies is poor, thereby shortening the gap between seropositivity and clinical manifestations. Part III discusses the higher prevalence of infections such as tuberculosis and candidiasis among HIV-positive patients due to their immunocompromised status. The opportunistic infections, in turn, accelerate the development of AIDS in these patients. Part IV discusses the higher susceptibility of males having AIDS to Kaposi's sarcoma and brings out the relationship of this malignancy to selenium deficiency on one hand, and the great likelihood of this deficiency in male patients due to the role of selenium in spermatogenesis. Finally, Part V builds up a good case for studies on the efficacy of flavonoids in the treatment of AIDS. The third and last chapter discusses the nutritional aspects of treatment of AIDS and gives elaborate Tables listing the dietary sources of micronutrients and flavonoids. The appendix, 14-page long, describes the role of zinc, selenium, iron, vitamin B12 and folic acid in metabolism, cell division and reproduction. This is very relevant to the theme of the book because immune mechanisms as well as reproduction require a high level of cell proliferation. When the nutritional status with respect to micronutrients required for cell division is marginal, it is quite likely that use of these nutrients for one function may be at the expense of another. In promiscuous males, excessive use of nutrients for spermatogenesis and seminal secretion may be at the expense of immunocompetence. If such a person contracts HIV, the possibility of the clinical manifestations of AIDS multiplies due to his immunocompromised status.

The writer has worked hard to provide a complete book on the subject. Although the theme is restricted, no aspect of the theme - physiological, biochemical or clinical, has been left out. However, if the reader still wants more details on any aspect, an exhaustive list of references is also available within the book. The book has a stamp of authority because several eminent experts have been consulted while preparing it. Mr. S.B. Ghosh, an expert in editing, has ensured that the language is also precise and readable. Printing errors have also been limited to the bare minimum. In short, the book is a labour of love in which no effort has been spared to make the undertaking worth-while.

No human creation is perfect, however, and I have been able to spot a few points which merit criticism. The role of nutrient losses in semen seems to have been exaggerated, keeping in view the extremely minute quantities lost in each ejaculate (page 11). In most cases, the quantity lost is

not even 10% of the daily metabolic requirement, and not even 1% of the recommended dietary allowance (RDA). It might be argued that promiscuity may lead to several ejaculations per day. But it is known that if the frequency of ejaculation increases the quantity of semen per ejaculate is reduced markedly. This criticism is by no means meant to condone promiscuity, which has undesirable implications going far beyond nutrient losses, but merely to put a scientific point in its proper perspective. Then, on page 14 drugs such as morphine and cocaine have been grouped under 'recreational drugs'. Although technically correct, the adjective `recreational' is misleading. The expression `drugs of addiction' might have been a better choice. Finally, the book gives an impression of elaborating excessively and needlessly on every single point of the central theme. For example, the seven `hypotheses' (pages 3-4) linking malnutrition, immunodeficiency and AIDS are essentially an elaboration of the well established relationship between malnutrition and impaired immunity. The seven `hypotheses' are merely seven groups of studies by different authors pointing to this single fact. In took William Harvey 60 pages of *De Motu Cordis* to describe his discovery of circulation, which may today be stated in less than a page. He had to do it because he anticipated scepticism, criticism, and even ostracism. Probably Varuna Kochar expected a similar reaction to her thesis. But today the environment is more open to new ideas, and secondly, her thesis does not have the novelty of Harvey's discovery. In fact, while her extensive bibliography is impressive, it is also a confession of lack of novelty. I claim no originality in admitting, however, that originality is nothing but judicious imitation, and would hasten to add that Kochar's book has the merit of attracting attention to a rather neglected aspect of AIDS.

The author deserves compliments for acquiring mastery over a subject which goes beyond her qualifactions as a biochemist. Her book also points out possibly fruitful lines for future research on the subject. The book would be useful for medical libraries as well as all those interested in AIDS as clinicians or for research.

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