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Xenotransplantation public perceptions: rather cells than organs

Omnell Persson M, Persson NH, Ranstam J, Hermerén G.
Xenotransplantation public perceptions, rather cells than organs.
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Abstract: The aim of this study was to describe some of the factors that might play a role in influencing attitude to xenotransplantation: first, the consideration of receiving cells and tissue from xenotransplants in relation to whole xeno-organs; secondly, the fact that there is greater uncertainty regarding the result and risk of infection associated with xenotransplantation than with allotransplantation. We also describe the attitude to research on xenotransplantation, and the relationship between the attitude to receiving a xenotransplant and an allotransplant. Finally, we describe the attitude to xenotransplantation in relation to treatment for renal failure and waiting-time for allotransplantation. A questionnaire was sent to randomly selected members of the public aged 18 to 75 ($n = 1000$) and to all patients in the same age range who were waiting for kidney transplants in Sweden in the spring of 1998 ($n = 460$). The response rate was 60% among the public and 87% among the patients. Both study groups were positive to a greater extent in their attitude to receiving cells and tissue than to receiving a whole organ such as a kidney. The response 'rather positive' to receiving organs was generally favored by the public, whereas the most generally favored response to receiving cells and tissue was 'very positive'. When there was suggested to be a greater uncertainty regarding the outcome with xenotransplantation compared with allotransplantation, the number of negative and uncertain respondents increased, both among the public and the patients. Eighty percent of the public and about 90% of the patients were in favor of continued research on xenotransplantation. Of those members of the public who responded, the attitude to receiving an organ from a human was positive in 86% of cases, with an emphasis on 'very positive'. There was a moderate relation between the attitude to receiving an organ from a human and to receiving a xenotransplant. Among the patients, there was no systematic or strong relation between the attitude to xenotransplantation and the kind of dialysis treatment they were on. Neither was there any systematic or strong relation to the waiting-time. The overall impression is that the attitude to xenotransplantation seems to be most influenced by whether the xenotransplant would involve whole organs or cells and uncertainty regarding the outcome.

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Key words: attitude – cells – patients – public opinion – research, risk – transplantation heterologous

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Introduction

We reported earlier on the attitudes to xenotransplantation among both patients waiting for kidney transplantation and the general public [1]. The conclusion was that the majority of the patients

and the general public would accept a transplant from an animal provided that the result and risk of infection were the same as with a transplant from a human. There was a greater proportion of patients with a positive attitude toward receiving a xenotransplant than amongst the general public.

The aim of this study was to describe:

- The attitude to cells and tissue from xeno-transplants in relation to the attitude to whole xeno-organs
- The attitude to xenotransplantation with the same predicted outcome as with allotrans-plantation in relation to the attitude to xeno-transplantation with greater uncertainty regarding the outcome
- The attitude to continued research on xeno-transplantation
- The relationship between the attitude to receiving a xenotransplant and an allotrans-plant
- The attitude to xenotransplantation in relation to treatment for renal failure and waiting-time for allotransplantation.

The attitude was measured on a level of individual acceptance. The results were previously presented in Swedish in a different form [2].

Materials and methods

The same study population and questionnaire was used as in a previous study and for all details we refer the reader to [1]. The study was approved by the regional research ethics committee at Lund University.

A questionnaire was sent both to randomly selected members of the public in the age group 18 to 75 ($n = 1000$), and also to all patients in the same age range who had end-stage renal failure and who were on a waiting list for kidney transplantation in Sweden in the spring of 1998 ($n = 460$). Among the public, 596 (60%) sent in processable questionnaires: 294 (49%) were male and 302 (51%) were female and all well representative of the general population concerning age, gender and education. Among the patients, 398 (87%) sent in processable questionnaires: 259 (65%) were male and 139 (35%) were female. This gender distribution is compared with the gender distribution among the non-respondents and among the patients on the waiting list (Table 1). The mean age among the respondents as well as among all the patients on the waiting list

was 50 yrs. Sixty percent underwent dialysis in hospital, 3% underwent home hemodialysis, and more than one-third had continuous ambulatory peritoneal dialysis (CAPD). The median waiting-time for transplantation was 5 months (1–132).

The questionnaire

After pilot studies, the questionnaire was sent in April 1998 by post to individuals in each study group. An enclosed letter explained the purpose of the study, promised total anonymity and voluntary participation. In the letter, brief information about xenotransplantation was given, as well as the information that many people are waiting for transplantation of vitally important organs and that because of the scarcity of organs for trans-plantation it happens that people wait in vain and die because of their disease. A reminder was sent to all, as the study was performed under full anonymity.

With the questions, information was given to the general public regarding the circumstances surrounding dialysis and allotransplantation. This included the fact that suffering from kidney disease involves either dialysis treatment three times a week, each time about 5 h, or transplantation with human organs but with the problem of the scarcity of organs. It also included the information that waiting for a human kidney transplant means uncertainty regarding waiting-time which is estimated to 2 yrs. These facts are well known to the patients waiting for a kidney transplant.

Information was also given to both study groups on xenotransplantation, including the uncertainty regarding transmission of virus when transplanting from animals to humans. Information about the ongoing research aiming to overcome the medical difficulties related to xenotransplantation was included. In the enclosed letter, pigs were mentioned as a potential source animal for xenotrans-plantation. Concerning heart valves, it was emphasized that the pig was a source animal.

The lack of alternative treatment when in need of a heart transplantation was mentioned. Diabetes and Parkinson's disease were described briefly. This description, in connection with the questions, included information on diabetes caused by defective production of insulin and the need for injections of insulin several times a day. It also included information on the common complications of diabetes. Finally some words were written about the ongoing research aiming to cure/alleviate the disease by injecting insulin producing cells from animals. Regarding Parkinson's disease it was told that some cells in the brain get destroyed and the

Table 1. Gender distribution among patients: respondents, non-respondents and waiting-list for kidney transplantation

	Respondent patients n (%)	Non-respondents n (%)	Waiting-list n (%)
Male	259 (65)	28 (45)	287 (62)
Female	139 (35)	34 (55)	173 (38)
Total	398 (100)	62 (100)	460 (100)

symptoms of the disease. Parallel to the diabetes question, information was given about the ongoing research aiming to cure/alleviate the disease by injecting brain cells from animals to the brain of the patient. Questions concerning the attitude to xenotransplantation are shown in Table 2. Questions were also asked about the attitude to continued research in the field of xenotransplantation and the attitude to allotransplantation. The respondents were asked to answer most of the questions on a five-point scale ('very negative' – 'rather negative' – 'uncertain' – 'rather positive' – 'very positive'). At the end of the questionnaire, there was a space for comments.

Analysis

The results are presented in frequency and cross tables. The percentages are based on the number of answers given. Because of rounding, the percentages do not always add up to 100 exactly.

Paired or serial data on subjects were analyzed using Wilcoxon's signed ranks test. The Mann–Whitney *U*-test was used for statistical analyses of differences between independent groups. The relation between the attitude to xenotransplantation and allotransplantation, and also research in this area, has been evaluated with Spearman rank order correlation coefficient. This also holds true for the relation between the attitude to xenotransplantation and satisfaction with treatment. The *P*-values were used more as an index than as a tool for generalization.

Results

Attitudes to cells and tissue in relation to organs

Both the public and the patients were positive to a greater extent in their attitude to receiving cells and tissue in relation to receiving a whole organ such as a kidney. The relation between receiving a kidney and cells in the case of diabetes is shown in Table 3.

The corresponding relation when in need of new heart valves is shown in Table 4. The pattern of the answers in the case of Parkinson's disease was the same. The differences were statistically significant. The response 'rather positive' to receiving organs was generally favored by the public, whereas the most generally favored response to receiving cells and tissue was 'very positive'. We chose to use kidney in the comparison rather than a heart because there is a treatment alternative in end-stage renal disease, just as there are in diseases to be treated with cells and tissues.

Attitudes related to uncertainty

When faced with greater uncertainty regarding the result when transplanting a kidney or a heart from an animal, the proportion in favor of a xenotransplant decreased while the number of negative and uncertain increased, both among the public and the patients. These differences were statistically significant in both study groups (Tables 5 and 6).

Attitudes to research on xenotransplantation

Eighty percent of the public and about 90% of the patients were in favor of continued research on xenotransplantation (Table 7).

For the public, the following relations were found. If one was in favor of continued research, they were also in favor of receiving a kidney or a heart with the same result as with transplantation from a human. Many were also in favor of receiving cells, if suffering from diabetes or Parkinson's disease, and a heart valve from a pig (r_s varying between 0.616 and 0.678, $P < 0.001$). In situations where there would be larger uncertainty regarding the result and risk of infection, the relation was weaker ($r_s = 0.407$, $P < 0.001$ and $r_s = 0.452$, $P < 0.001$).

The pattern of the relation for the attitude of the patients was slightly different to that of the general public and not as strong. The strongest relation

Table 2. Questions concerning the attitude to xenotransplantation

What is your attitude toward receiving a kidney from an animal with the same result and risk of infection as with transplantation from a human? The operation can be planned and performed within 3 months.
What is your attitude toward receiving a kidney from an animal with a larger uncertainty regarding the result and risk of infection compared with transplantation from a human? The operation can be planned and performed within 3 months.
What is your attitude toward receiving a heart from an animal with the same result and risk of infection as with transplantation from a human? The operation can be planned and performed within 3 months.
What is your attitude toward receiving a heart from an animal with a larger uncertainty regarding the result and risk of infection compared with transplantation from a human? The operation can be planned and performed within 3 months.
If you had diabetes and could be cured with cells from animals, what would be your attitude to such a measure?
If you had Parkinson's disease and your condition could be improved using cells from animals, what would be your attitude to such a measure?
For a long time, heart valves from pigs have been used to replace diseased heart valves in humans. If you were suffering from a coronary disease, and could be cured using a heart valve from a pig, what would be your attitude to such a measure?

Table 3. The relation between the attitude of the public and the patients, respectively, to receiving a kidney with the same predicted outcome as with transplantation from a human and to receiving cells in the case of diabetes

Attitude	Public		Patients	
	Kidney same risk % (n = 586)	Cells in diabetes	Kidney same risk % (n = 387)	Cells in diabetes
Very negative	9	3	6	2
Rather negative	8	3	5	1
Uncertain	24	19	23	13
Rather positive	36	35	30	33
Very positive	24	41	37	51
	$P < 0.001$ Wilcoxon		$P < 0.001$ Wilcoxon	

Table 4. The relation between the attitude of the public and the patients, respectively, to receiving a kidney with the same predicted outcome as with transplantation from a human and to receiving heart valves from an animal

Attitude	Public		Patients	
	Kidney same risk % (n = 586)	Heart valves	Kidney same risk % (n = 389)	Heart valves
Very negative	9	3	6	2
Rather negative	8	4	5	2
Uncertain	24	16	22	13
Rather positive	35	33	29	31
Very positive	24	44	37	53
	$P < 0.001$ Wilcoxon		$P < 0.001$ Wilcoxon	

Table 5. The relation between the attitude of the public and the patients, respectively, to receiving a kidney with the same predicted outcome as with transplantation from a human, and a situation where a greater uncertainty regarding the outcome is predicted

Attitude	Public		Patients	
	Kidney same risk % (n = 591)	Kidney greater uncertainty	Kidney same risk % (n = 396)	Kidney greater uncertainty
Very negative	9	22	7	27
Rather negative	8	23	5	19
Uncertain	24	40	22	38
Rather positive	36	12	29	11
Very positive	24	4	37	5
	$P < 0.001$ Wilcoxon		$P < 0.001$ Wilcoxon	

Table 6. The relation between the attitude of the public and the patients, respectively, to receiving a heart with the same predicted outcome as with transplantation from a human, and a situation where a greater uncertainty regarding the outcome is predicted

Attitude	Public		Patients	
	Heart same risk % (n = 590)	Heart greater uncertainty	Heart same risk % (n = 385)	Heart greater uncertainty
Very negative	10	21	7	16
Rather negative	8	21	4	17
Uncertain	23	40	20	38
Rather positive	32	16	34	19
Very positive	28	3	36	9
	$P < 0.001$ Wilcoxon		$P < 0.001$ Wilcoxon	

was between the attitudes to research and getting a transplant with cells and tissue (for having Parkinson's disease $r_s = 0.539$, $P < 0.001$; when

in need of heart valves $r_s = 0.581$, $P < 0.001$; and for having diabetes $r_s = 0.548$, $P < 0.001$). The relation between the attitudes toward research and receiving a heart or kidney with the same risk as from humans was weaker ($r_s = 0.478$, $P < 0.001$, and $r_s = 0.493$, $P < 0.001$, respectively). The relation was even weaker when there was a greater risk, both for kidney ($r_s = 0.183$, $P < 0.001$) and for heart ($r_s = 0.343$, $P < 0.001$).

Attitudes to xenotransplantation in relation to allotransplantation

The public's attitude to receiving an organ from a human was positive (86%), with the emphasis on 'very positive' (Table 8). The patients were not asked this question because the inclusion criterion was that they had accepted to be on the waiting-list for kidney transplantation.

Table 7. What is your attitude towards continued research within this field?

Attitude	Patients n (%)	Public n (%)
Very negative	4 (1)	23 (4)
Rather negative	7 (2)	16 (3)
Uncertain	26 (7)	79 (14)
Rather positive	64 (17)	131 (22)
Very positive	282 (74)	338 (58)
Not answered	15	9
Total	398 (100)	596 (100)

Among the public, there was a moderate relation between the attitude to receiving an organ from a human and to receiving a xenotransplant. If one was in favor of receiving an organ from a human, they were also in favor of receiving a kidney or a heart if there was the same predicted result as with transplantation from a human, cells in the case of diabetes or Parkinson's disease and a heart valve from a pig (r_s varying between 0.415 and 0.484, $P < 0.001$). Also, in two situations, the relation was weaker here, concerning a kidney or a heart with greater uncertainty as to the result and risk of infection ($r_s = 0.285$, $P = < 0.001$ and $r_s = 0.290$, $P < 0.001$).

Attitudes in relation to treatment and waiting-time

Among the patients, there was no systematic or strong relation between the attitude to xenotransplantation and the kind of dialysis treatment they were on. The satisfaction with the treatment was analyzed in relation to the attitude and, among this group of patients, there was a very weak relation best expressed as 'the more satisfied with one's treatment the less positive to xenotransplantation'. However, this relation was not significant in any case. This was most apparent regarding the attitude to a kidney with the same predicted risk as with allotransplantation ($r_s = -0.093$, $P = 0.069$). The patients were divided into two groups in order to study the relationship between attitude and waiting-time. One group had been on the waiting-list for kidney transplantation for 6 months or less and the other had been waiting for 7 months or more. There was no systematic or strong relation between the attitude to xenotransplantation and the waiting-time.

Discussion

High acceptance for cells and tissue

In our study, it is obvious that people are positive to cells and tissue to a greater extent than to whole organs. There could be different theories about

why one is in favor of or against receiving cells and tissue as compared with one's attitude to receiving organs from animals. On the one hand, an organ from an animal is larger than separate cells or tissue and might be experienced as a greater encroachment on one's body. On the other hand, it is well defined and one knows exactly where it is located, which might create a certain sense of security. A collection of cells is more diffuse and less well identified, but is smaller. In many situations things that are larger are considered to be more important from a psychological perspective, but in this situation the smaller might be as important and could be even more threatening. These issues have been discussed with diabetic patients transplanted with porcine islets at Huddinge hospital [3]. The patients prioritized survival before possible ethical and existential risks. Schlitt et al. [4] performed a study in Germany which included patients transplanted with liver, heart, lung or kidney and patients waiting for the same type of organs. The overall response rate was 65% (1049, of which 722 patients were transplanted and 327 patients were waiting for transplantation). The authors found minor differences in the acceptability of different types of organs or cells. The most unacceptable tissues were heart (21%) and bone-marrow cells (19%).

It is interesting that respondents were as positive to transplantation of xenogeneic cells as to pig heart valves despite the fact that transplantation with heart valves is a well-established method routinely used in thoracic surgery. Heart valves are dead material prepared in such a way that infectious agents will be destroyed. The technique of transplanting xenogeneic cells is new and the risk has not been fully evaluated. In connection with transplantation of cells, there is no alternative with 'greater uncertainty regarding the result and risk of infection', as with the questions concerning kidney and heart. On the other hand, the respondents had been confronted with uncertainty regarding the result and risk of infection, partly in an enclosed letter of information and partly in connection with

Table 8. Imagine that you have a chronic disease and could be cured by being transplanted. What would be your attitude towards receiving an organ in such a situation?

Public attitude	Allo-transplantation n (%)
Very negative	12 (2)
Rather negative	14 (2)
Uncertain	57 (10)
Rather positive	176 (30)
Very positive	333 (56)
Not answered	4
Total	596 (100)

other questions. The respondents thus had the opportunity to take this into consideration when answering the questions. Lundin and Widner found in interviews with patients suffering from Parkinson's disease that the patients defined xenotransplantation as a potential benefit and not as a threat, although they were well informed about the virus problem [5]. These patients had undergone allotransplantation with embryonic neural tissue.

Uncertainty brings forth uncertainty and a negative attitude

One could expect that the acceptance of any treatment should decrease if there is an obvious risk of infection or of a poor result. This was true to a high degree regarding our questions on xenotransplantation. When uncertainty regarding the result was elevated, the number of uncertain and negative respondents increased in both study groups. Among other questions in the study of Schlitt et al. [4], the respondents were asked about the acceptance of xenogeneic organ grafts under different conditions. Among the waiting-list patients, 26% accepted a xenograft if their clinical condition deteriorated or in the case of an emergency, even if more intensive drug treatment was required and thereby cause higher risk of side-effects. In our study, 28% of the patients were in favor of receiving a heart from an animal with greater uncertainty regarding the result and risk of infection. Schlitt et al. reported a refusal rate among the patients on the waiting-list of 42% in the situation with more intensive drug treatment and 29% if the function of the organ would last only for a few years. In our study, the proportion of negatives among the patients was 46% when asked about a kidney with greater risk and 33% when asked about a heart with greater risk. The questions were not formulated in exactly the same way but the meaning of their outcome points in the same direction as the results in our study.

Research should continue

Both study groups were in favor of continued research, especially the patients. Some people are obviously negative to or uncertain about receiving a xenograft but nevertheless positive to research on xenotransplantation. This could be expressed as a negative or uncertain attitude on an individual basis but a positive attitude to a procedure which will find out more about the possibilities of xenotransplantation. In this study, there was a stronger relation between the attitude to research and xenotransplantation among the public than among the patients. In other studies the attitude

varies between 55 and 94% in favor of some kind of continued research on xenotransplantation [6–9].

Receiving an allotransplant better accepted

There was a positive relation, albeit moderate, between the attitude to allotransplantation and the attitude to xenotransplantation. The question on allotransplantation only concerns organ, but it is set against organ- and cell xenotransplantation. On the one hand, a positive relation could be expected, because this is all concerned with transplantation, and on the other hand, being in favor of receiving an organ from a human donor does not necessarily mean that one is in favor of receiving an organ or tissue from an animal. Interestingly, the relation between the attitude to allo- and xenotransplantation with organs or cells, respectively, was similar. But the relation between the attitude to allo- and xenotransplantation when facing a greater degree of uncertainty regarding the result was weaker than compared with the situation where there was the same degree of uncertainty as with transplantation from human donors.

Treatment and waiting-time

Patients who are responsible for their CAPD treatment or home hemodialysis are required to have greater control over their situation than patients who receive dialysis treatment in hospital. It is possible that they would thereby be less positive to xenotransplantation. No such pattern was expressed in our study, however. Mohacsi et al. performed a study on the acceptance of xenotransplantation among patients treated by hemodialysis ($n = 58$), peritoneal dialysis ($n = 31$) and transplantation ($n = 24$) [10]. According to the authors, there were no significant differences in the responses of the three patient groups. Arundell and McKenzie reported that patients with chronic peritoneal dialysis ($n = 38$) were slightly less interested (42 vs. 55%) in a xenograft than those on hemodialysis ($n = 75$) [11].

As many patients have to wait a long time for transplantation, they might be positive to a xenotransplant to a greater extent than patients who wait for a shorter time. However, there was no systematic or strong relation between the attitude to xenotransplantation and the waiting-time where the break-point was 6 months. Arundell et al. indicated that the frequency of acceptance was not higher among those patients who had waited for a long time than among those who had waited

for a short time [11]. This is also in line with the results of Schlitt et al. [4].

Are the results trustworthy?

In this article, the main purpose was not to generalize our findings but to survey some of the factors that might play a role in the complicated concept of 'attitude to xenotransplantation'. We were looking for patterns or tendencies. Therefore, the *P*-values used should be looked upon as an index.

In the random sample of the public, the proportion of non-respondents was 40%. Regarding the variables that we are able to control, i.e. gender, age and education, we found that among the respondents in the random sample, the gender proportion, the mean age and the level of education were similar to those of the general public. Among the patients the proportion of non-respondents was 13%, which suggests that the group was very motivated. The mean age among the respondents corresponded to the mean age of the waiting-list patients. The proportion of women was higher among the non-respondents than among the patients on the waiting-list. However, the distribution of women, 35%, among the respondents corresponds to 38% on the waiting list. Thus, we consider the respondents from each study group to be representative of the populations studied. A more detailed discussion has been presented previously [1].

The overall response to xenotransplantation in our study might have been influenced by the information given in the letter and the questionnaire. It is one thing to be informed when being healthy and filling in a questionnaire and another situation when ill and in the need of a transplant. In reality, if transplantations from animals to humans would be performed, the potential patients would surely be informed several times before making a decision.

Daar presented in his paper 'Analysis of factors for the prediction of the response to xenotransplantation' predictable positive public-response variables. He included perceptions of adequacy of scientific base, adherence to globally agreed-upon guidelines, legitimacy/competence of regulatory bodies and adequate infectious risk assessment and management. A likely negative predictor is the role of animal rights activists [12]. Another important factor is that of who gives the information. The Eurobarometer study carried out in 1996, included 16 246 interviews of the public aged 15 and older [13]. In this study the medical profession was the source of knowledge in which people had

most confidence (45%) regarding information about 'introducing human genes into animals to produce organs for human organ transplants', as well as in the National Kidney Foundation (NKF) study [7,14], where the doctors were seen as 'the most credible source for answering questions about this procedure'.

Conclusions

The overall impression is that the attitude to xenotransplantation seems to be most influenced by whether the xenotransplant involves whole organs or cells and uncertainty regarding the result.

Both the public and the patients seem to be positive to a greater extent in their attitude to receiving cells and tissue in relation to their attitude to whole organs such as a kidney. The proportion of individuals in favor of xenogeneic cells was as large as that to heart valves. If there is a greater uncertainty regarding the outcome with xenotransplantation than with allotransplantation, there is a change of attitude both among the public and among the patients. The positive attitude becomes reduced and, in particular the number of negative responses and also the number of uncertain responses increases. The majority of the public and patients appear to have a positive attitude to continued research, and for the public, there seems to be a rather strong relation between the attitude to xenotransplantation and to research. Also among the public, there seems to be a moderate relation between the attitude to receiving an organ from a human and to receiving a xenotransplant.

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