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Views of Preimplantation Genetic Diagnosis (PGD) among Psychiatrists and Neurologists

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Abstract

Objective—As prenatal genetic testing (GT) and Preimplantation Genetic Diagnosis (PGD) use increase, providers in many specialties may play roles in patient discussions and referrals. Hence, we examined key aspects of neurologists' and psychiatrists' views and approaches.

Study Design—We surveyed attitudes and practices among 163 neurologists and 372 psychiatrists.

Results—24.9% of neurologists and 31.9% of psychiatrists had discussed prenatal GT with patients, but 95.3% didn't feel comfortable discussing PGD; only 2.9% discussed it; and only 1.8% had patients ask about PGD. Most would refer for PGD for Huntington's disease (HD) and Tay-Sachs, fewer for Cystic Fibrosis (CF), and fewer still for autism, Alzheimer's (AD), or gender selection for family balancing; in each of these cases, psychiatrists > neurologists. Providers who'd refer for PGD for HD, CF, or gender selection differed from others in proportions of patients with insurance, were more likely to have undergone a GT themselves, and be concerned about discrimination.

The authors have no conflicts of interest to report

Conclusions—These data, the first to examine how neurologists and psychiatrists view PGD, suggest they don't feel comfortable discussing PGD, but have strong views about its use. Potential PGD use is associated with concerns about discrimination, and less experience with GT. These data highlight needs for enhancing education about these technologies among various providers.

Keywords

doctor-patient communication; ethics; assisted reproductive technology; obstetrics/gynecology; eugenics

INTRODUCTION

Prenatal genetic testing (GT) and Preimplantation Genetic Diagnosis (PGD) are increasingly used in the U.S. and elsewhere. PGD consists of genetic tests carried out by performing a biopsy on polar bodies (from oocytes before fertilization), blastomeres (from 3-day-old cleavage stage embryos), or occasionally but increasingly trophoblasts (from 5-day-old blastocysts), created through in vitro fertilization (IVF), to assess whether particular genetic markers that indicate predisposition for hereditary disease are present.[1, 2] Many in vitro fertilization (IVF) centers use PGD for single gene disorders and chromosome analysis, but in the U.S. there are no guidelines on when to use PGD,[3] and its use has been controversial especially for non-medical indications, such as sex selection.[4, 5, 6] Developed for fully penetrant, monogenic, severe pediatric diseases, PGD is now used for an increasing number of heritable diseases,[4, 5, 6] including Huntington's Disease (HD), Cystic Fibrosis (CF), Rett Syndrome, Leber Congenital Amaurosis and Angelman Syndrome.[7] Ethicists and policymakers have expressed concerns regarding the use of such genetic technology for non-medical characteristics in offspring.[8]

Recently, the Ethics Committee of the American Society for Reproductive Medicine concluded that PGD for serious adult-onset conditions without available interventions or with inadequate interventions, such as HD and early onset Alzheimer's disease (AD), is ethically justifiable.[5] Both medical and non-medical indications have also received significant attention in the popular press, which has referred to it colloquially as "designing babies."

Yet, few studies have examined providers' attitudes, knowledge and practices regarding these new and often controversial procedures. We previously surveyed 220 internists about their practices and attitudes concerning PGD and found that many would recommend PGD for Cystic Fibrosis (33.7%) and Huntington's disease (32.8%), but few for social sex selection (5.2%); however, in each case, >50% were unsure. 4.9% had suggested PGD to patients, and only 7.1% felt qualified to answer patient questions about it. Internists who would refer for PGD had completed training less recently and were more likely to have privately insured patients ($p<0.033$). This study suggested that internists often feel that they have insufficient knowledge about PGD and may only refer for it based on limited understanding.[9]

In 2010, only 17% of Obstetrician/Gynecologists' (OB/GYNs) and Gynecological Oncologists' (GYN ONCs) felt knowledgeable or highly knowledgeable about PGD. When

asked which of six cancer syndromes were detectable by PGD, 78% said they did not know, or responded incorrectly. Physicians who had practiced for a shorter period of time were more likely to identify correctly the three hereditary cancers. Within their practice, 81% and 63% of OB/GYNs and GYN ONCs, respectively, had discussed PGD, while 43% and 20%, respectively, had referred patients with hereditary cancer for PGD. If patients were to inquire, 91% and 80%, respectively, said they would refer for PGD, with GYN ONCs being more uncertain ($p < 0.001$).[10]

But patients concerned about these diseases may speak to not only OB/GYNs and GYN ONCs, but to providers in other fields as well – from internal medicine and pediatrics to neurologists and psychiatrists. However, we have found no studies examining these issues among neurologists or psychiatrists who may face distinctive issues concerning uses of these technologies.

Neurologists and psychiatrists are often important gatekeepers and sources of information concerning medical technologies for their patients, and communicate with patients about a variety of disorders, including those for which PGD may be relevant. They also often treat patients confronting diseases (e.g., HD and Fragile X Syndrome) for which PGD might be considered. Psychiatrists also often discuss experiences of patients and family members confronting a wide range of medical conditions, including infertility and reproductive issues.

In upcoming years, genetic markers associated with other psychiatric and neurological conditions (e.g. bipolar disorder) may also be identified. Providers and patients may want to test for these, too. PGD is still relatively new and controversial and raises complex psychosocial issues, which patients may discuss with providers, including mental health professionals. Indeed, IVF clinics work closely with mental health professionals. Moreover, several additional factors may be involved in physicians' attitudes and approaches toward PGD that have not heretofore been examined (e.g. provider comfort discussing PGD with patients).

The goals of this study were thus to understand whether providers in neurology and psychiatry discuss prenatal testing and PGD with patients, and if so, how frequently, when, how and what factors are involved.

MATERIALS AND METHODS

We e-mailed invitations to a web-based survey to all neurologists and psychiatrists on the American Medical Association (AMA) master list who had provided e-mail addresses and opted-in to receive surveys. The invitation stated that the survey concerned "genetic testing and privacy" and aimed "to learn about physicians' views, knowledge and personal experiences with genetic testing." Among 2,167 neurologists and 5,316 psychiatrists with valid e-mail addresses, 535 responded, including 163 (7.5%) neurologists and 372 (7.0%) psychiatrists. The NY State Psychiatric Institute IRB approved the study.

The survey included an information sheet that described the study, and indicated that participants' consent would be presumed by their completing survey questions. The survey instrument was developed based on our prior study of internists' views of PGD,[7] past

published literature and clinical experience, and was implemented through the online survey system Survey Monkey (www.surveymonkey.com). The domains examined included: 1) the physician's personal and professional characteristics; 2) characteristics of their patient populations; 3) attitudes and practices concerning genetic testing and PGD; 4) views of factors that may be involved with PGD and genetic testing (e.g., concerns about cost, insurance, and discrimination). Appendix A contains questions about PGD from the survey. The survey also included questions that asked: "What effect, if any, would the following factors have on your likelihood of ordering a genetic test?" answered on a Likert Scale (strongly decrease, moderately decrease, no effect, moderately increase, strongly increase), with factors listed such as: "test could lead to genetic discrimination" and "test reduces uncertainty about diagnosis." Statistical analyses included cross tabulations, chi-square tests and binary logistic regressions to explore how attitudes regarding PGD and prenatal GT differed between psychiatrists and neurologists. Additionally, multivariate logistic regression was used to explore independent factors associated with willingness to order PGD for three specific indications (HD, CF, and gender selection), selected to represent a range of common current indications. For each of these three indications, all variables found to be significant or trends in univariate analyses were then entered into the multiple logistic regression model. P-values were considered significant if <.05 and trends if <.10.

RESULTS

As shown on Table I, we found that 24.6% of neurologists and 31.9% of psychiatrists had discussed prenatal GT with patients. Most practitioners (95.3%) did not feel qualified to discuss PGD; and few (2.9%) had discussed it with patients, though neurologists were significantly more likely to have done so (6% *vs.* 1.5%). Few respondents had patients ask about PGD (1.8% overall).

Most respondents would (i.e., hypothetically) refer patients for PGD for HD and Tay-Sachs, with psychiatrists being significantly more likely to say they would do so. Fewer would refer for CF, with psychiatrists significantly more than neurologists (69.6% *vs.* 48.3%). Fewer still would refer for PGD for autism or AD (though again psychiatrists said they would do so significantly more than neurologists), or gender selection for family balancing.

As shown in Table II, we explored the correlates of respondents' willingness to refer for PGD for three selected disorders. Among neurologists and psychiatrists combined, the proportion who would order PGD for HD was greater among those who: had <25% of patients covered by Medicare; had not ordered a genetic test in the past six months; had personally had a genetic test; had tested a patient under a pseudonym; or stated that their decision would be affected by a test's reducing uncertainty about diagnosis. The proportion who said they would order PGD was also significantly lower (62%) among those who responded "Neither agree nor disagree" than among those who either agreed (76%) or disagreed (74%) to a question about adequacy of legal protections against genetic discrimination.

The pattern of results was generally similar with regard to testing for CF, but differed for gender selection. Respondents were more likely to say they would order PGD for gender

selection if they: had graduated from medical school in 1990 or later; had <25% of patients covered by private insurance; or said that their decision would not be affected by possible genetic discrimination. Binary logistic regressions showed that Asian (p<.024, OR: 2.71, CI: 1.14–6.45) and African American (p<.006, OR: 9.26, CI: 1.92–45.45) respondents were more likely than white respondents to refer for PGD for gender selection. Physicians' responses did not differ by gender or religion.

The independent predictors of referral for PGD for the three indications we investigated are shown in Table III. For HD, they were: being more likely to order a GT if they believed it would reduce diagnostic uncertainty; personal history of GT; and having fewer than 25% of patients covered by Medicare. The only independent predictor of referral for PGD for CF was not ordering a GT in the previous six months. Independent predictors of referral for PGD for gender selection were: Asian or African-American ethnicity; having 25% of patients covered by private insurance; disagreeing that GTs can cause psychological harm; and as trends, having treated patients under a pseudonym; and having graduated medical school after 1990.

DISCUSSION

These data, the first to examine how neurologists and psychiatrists view PGD and prenatal testing, suggest that these providers have not had much experience, and do not feel comfortable discussing PGD with patients; but usually have clear feelings about indications for its use. They also have little experience discussing prenatal testing with patients. Nonetheless, they distinguished between potential uses of PGD in ways that reflect current clinical capability and practices. Specifically, they largely favored its use for HD, Tay-Sachs and CF, and were wary about its use for autism, AD, and gender selection. The extent to which respondents from both specialties had discussed prenatal genetic testing with patients is striking, and highlights the extent to which physicians in specialties other than clinical genetics and OB/GYN may potentially become involved in discussing these issues with patients over time. We do not know with how many patients these providers discussed these issues, for what specific indications, and what they said, but future research can probe these questions.

In the survey, we asked about markers for several diseases for which we thought that patients of psychiatrists and neurologists might consider PGD. We sought to limit the overall length of the questionnaire (to increase potential respondents' willingness to complete it), and thus did not include all possible additional markers for which PGD might be used. However, future investigations can examine practices and attitudes concerning other genetic markers, such as hemoglobinopathies,[11] spinal muscular atrophy and other diseases for which the American College of Obstetricians and Gynecologists, American College of Medical Genetics, or others may suggest screening in couples with a family history.[12]

We found relatively few variables that distinguished between respondents who would and would not refer patients for PGD for particular indications. Results concerning HD and CF were somewhat similar, while those concerning gender selection differed. Respondents with

less experience (e.g., psychiatrists, and those less likely to have ordered a GT in the past six months) appeared more likely to order PGD for HD and CF. They may be less informed about the complex genetic and ethical complexities that can be involved with these disorders, raising concerns and highlighting needs for enhanced professional education.

Those who would refer for PGD for gender selection were more likely to be Asian or African American. This finding should be explored further in future research. We could hypothesize it may reflect a more favorable view of male than female children among certain cultural and ethnic groups,[13, 14] and more willingness to help families shape the gender distribution of their children.

We found that compared to our study of 220 internists, more psychiatrists and neurologists would refer patients for PGD for all of the conditions about which we inquired, including PGD for CF (33.7% of internists vs. 48.3% of neurologists and 69.8% of psychiatrists), HD (32.8% of internists vs. 59.3% of neurologists and 74.7% of psychiatrists) and gender selection for family balancing (5.2% of internists vs. 7.6% of neurologists and 11.5% of psychiatrists). In both studies, few respondents felt qualified to answer questions about PGD and referrals for the procedure for certain conditions were associated with discrimination concerns. In the present study, referral for certain conditions was associated, too, with having undergone a genetic test oneself, about which we did not inquire in the previous survey.

These data may have implications for future education, research, practice and policy. Given the spread of IVF[3] and the involvement we found of specialists not directly involved in prenatal care discussing prenatal genetic testing with patients, it seems clear that all physicians should receive additional training about these areas. Referrals to experts in clinical genetics or genetic counselors may not always be available, suggesting that clinicians in neurology and psychiatry (and presumably other specialties) should have enough basic familiarity with prenatal genetic testing and PGD to know that these procedures exist; to be comfortable, rather than uncomfortable discussing these procedures to a certain degree; and to know that they should refer patients, when appropriate. These data are also valuable for suggesting how physicians in specialties other than reproductive endocrinology may discuss these issues with patients in ways that can affect ‘uptake’ of these technologies, yet also how educational and attitudinal barriers may exist. Future research might consider the extents to which the experiences of other specialties are similar or different, and the degrees to which physicians’ involvement in these issues may increase over time. Broader discussions about these issues among providers and professional organizations can help in the development of improved clinical guidelines regarding education and practice as they relate to prenatal genetic testing and PGD.

This study has several limitations. We had a relatively low rate of response, but our sample nonetheless comprises the largest sample to date of both neurologists and psychiatrists exploring these domains, and is the first to examine these issues among these specialties. Moreover, response rates in studies have been declining overall,[15] particularly among doctors.[16, 17] In addition, low response rates do not necessarily result in selection bias.[17] Such bias, if it exists, may also be of less concern in surveys of physicians than in those of

the general public,[18, 19, 20, 21] as "physicians as a group are more homogeneous regarding knowledge, training, attitudes, and behavior than the general population."[21] Our sample also did not differ significantly from national samples of neurologists or psychiatrists (based on data obtained from the American Neurological Association and the American Psychiatric Association) in ethnicity (white *vs.* non-white), age, or type of practice (solo *vs.* other). Our sample of neurologists did differ from the national sample in having more women (33% *vs.* 23%, p<.012), and there was a slight trend toward younger age (p<.093). This trend for younger participants may reflect heightened comfort with the internet, which we used for recruiting and administering the survey. Women may be more likely to have undergone a genetic test as part of pregnancy, and thus may be more interested in these issues. The study also relied on self-reports, with the usual possibility of uncertain validity of responses.

In short, these data, the first to examine attitudes and practices concerning PGD and prenatal genetic testing among psychiatrists and neurologists, suggest that most have views about use of PGD for a variety of neurological and psychiatric disorders, and many have interacted with patients about prenatal genetic testing, highlighting needs for enhanced education of physicians in a variety of specialties about these realms.

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Appendix A: PGD Questions in Survey

Have you ever discussed the possibility of preimplantation genetic diagnosis (PGD) with a patient? (Preimplantation diagnosis is a genetic test done on an embryo produced by in vitro fertilization (IVF) at the six to eight cell stage in which one cell is analyzed to determine whether or not the embryo is likely to develop a genetic disease.) Yes or No.

If yes, for what conditions did you discuss preimplantation genetic diagnosis (PGD) with a patient?_____

Has a patient ever asked you about preimplantation genetic diagnosis (PGD)? Yes or No.

If yes, for what conditions did your patient ask you about preimplantation genetic diagnosis (PGD)? _____

Do you feel qualified to answer questions from patients about preimplantation genetic diagnosis (PGD)? Yes or No.

Would you refer patients for preimplantation genetic diagnosis (PGD) for the following:

	Yes	No	Uncertain
Autism?	❍	❍	❍
Tay-Sachs Disease?	❍	❍	❍
Huntington's Disease?	❍	❍	❍
Alzheimer's Disease?	❍	❍	❍
Cystic Fibrosis?	❍	❍	❍
Gender selection for family balancing?	❍	❍	❍

SYNOPSIS

We examined neurologists' and psychiatrists' views and practices concerning PGD, revealing strong attitudes about these technologies among broad groups of providers.

Table I

Attitudes by Specialty

	Neurologists % (N=163)	Psychiatrists % (N=372)	Neurologists *vs.* Psychiatrists (p value)
Ever discussed possibility of prenatal GT with patients? (Yes response)	24.6% (29)	31.9% (84)	NS
Feel qualified to answer questions from patients about PGD? (yes response)	5.0% (6)	4.6% (12)	NS
Ever discussed possibility of PGD with patients? (Yes response)	6.0% (7)	1.5% (4)	0.017
Patients ever asked about PGD? (Yes response)	2.5% (3)	1.5% (4)	NS
Would you refer for PGD for:			
Huntington's Disease?			0.003
Yes	59.3% (70)	74.7% (195)	
No	16.1% (19)	6.9% (18)	
Uncertain	24.6% (29)	18.4% (48)	
Tay-Sachs?			0.015
Yes	61.0% (72)	73.3% (192)	
No	12.7% (15)	5.3% (14)	
Uncertain	26.3% (31)	21.4% (56)	
Cystic Fibrosis?			<.001
Yes	48.3% (56)	69.8% (183)	
No	23.3% (27)	8.4% (22)	
Uncertain	28.4% (33)	21.8% (57)	
Autism?			<.001
Yes	16.2% (19)	42.1% (110)	
No	40.2% (47)	24.1% (63)	
Uncertain	43.6% (51)	33.7% (88)	
Alzheimer's?			<.001
Yes	16.1% (19)	37.0% (97)	
No	55.1% (65)	29.4% (77)	
Uncertain	28.8% (34)	33.6% (88)	
Gender selection for family balancing?			NS
Yes	7.6% (9)	11.5% (30)	
No	66.9% (79)	65.0% (169)	
Uncertain	25.5% (30)	23.5% (61)	

* Ns for different analyses vary because of missing data

Table II

Sociodemographics, Behavior and Attitudes by Type of PGD*

			HD		CF		Gender selection	
		N	Would order test	p value	Would Order Test	p value	Would Order Test	p value
PHYSICIAN SOCIODEMOGRAPHICS								
Gender	Male	239	68.6%	NS	61.1%	NS	11.7%	NS
	Female	139	71.9%		67.4%		8.0%	
Race/ethnicity	White	241	69.7%	NS	64.2%	NS	7.5%	0.003
	Asian	50	78.0%		64.7%		18.0%	
	Hispanic or Latino	23	69.6%		65.2%		17.4%	
	Black or African American	7	71.4%		57.1%		42.9%	
	Other	50	60.0%		55.1%		6.0%	
Religion	Protestant	69	19.7%	NS	18.4%	NS	20.5%	NS
	Catholic	56	15.5%		13.8%		12.8%	
	Jewish	65	17.8%		18.0%		10.3%	
	Other/Prefer not to answer	188	47.0%		49.8%		56.4%	
Year of medical school graduation	Before 1990	240	68.3%	NS	62.2%	NS	7.9%	0.096
	1990 or later	128	73.4%		66.4%		13.4%	
PATIENT CHARACTERISTICS								
Covered by private insurance	<25%	97	75.3%	NS	65.6%	NS	17.5%	0.014
	≥25%	253	68.8%		63.4%		8.3%	
Covered by Medicare	<25%	134	77.6%	0.009	69.4%	0.056	11.3%	NS
	≥25%	216	64.4%		59.3%		10.6%	
PHYSICIAN BEHAVIOR								
In the past six months have you ordered a GT?	Yes	119	63.0%	0.042	52.5%	0.003	7.7%	NS
	No	259	73.4%		68.3%		11.5%	
Have you ever personally had a GT?	Yes	83	81.9%	0.007	67.5%	NS	7.3%	NS

			HD		CF		Gender selection	
		N	Would order test	p value	Would Order Test	p value	Would Order Test	p value
Patients had GT under a pseudonym	No	294	66.7%		62.1%		11.2%	
	Yes	11	100.0%	0.027	81.8%	NS	27.3%	0.061
	No	367	68.9%		62.6%		9.8%	
PHYSICIAN ATTITUDES								
Legal protections against genetic discrimination are adequate	Disagree/Strongly Disagree	181	74.0%	0.038	69.1%	0.05	7.1%	NS
	Neither Agree nor Disagree	134	61.9%		55.6%		14.3%	
	Agree/Strongly Agree	62	75.8%		64.5%		11.5%	
GTs can psychologically harm patients	Disagree/Strongly Disagree	95	77.9%	NS	68.8%	NS	13.8%	0.065
	Neither Agree nor Disagree	110	65.5%		61.5%		13.6%	
	Agree/Strongly Agree	173	68.2%		61.6%		6.4%	
What effect would each have on your likelihood to order GT:								
Reduces uncertainty about diagnosis	Would affect	346	72.0%	0.005	64.2%	0.097	9.5%	NS
	Would not affect	28	46.4%		48.1%		14.3%	
Could lead to discrimination	Would affect	307	68.7%	NS	62.7%	NS	7.8%	0.001
	Would not affect	59	76.9%		66.2%		21.5%	

* Ns for different analyses vary because of missing data

Table III

Factors associated with willingness to order PGD

Multivariate analyses of	OR	95% CI	p value
Huntington's[a]			
If GT would reduce diagnosis uncertainty	3.75	1.50–9.35	0.005
Have personally had a genetic test	2.20	1.15–4.20	0.017
<25% of patients covered by Medicare	1.80	1.07–3.01	0.026
For Cystic Fibrosis[b]			
Did not order genetic test in past 6 months	1.75	1.11–2.63	0.016
For Gender Selection[c]			
Race (Asian *vs.* White)	3.11	1.19–8.06	0.020
Race (African American *vs.* White)	6.85	1.25–37.04	0.027
<25% of patients covered by private insurance	2.40	11.09–5.30	0.030
Disagree genetic tests can cause psychological harm	1.65	1.04–2.63	0.035
Graduated medical school after 1990	2.06	0.94–4.50	0.071
Patients had genetic test under pseudonym	3.92	0.79–19.5	0.096

[a] Other variables included in model: ordered a GT the past six months, tested patients under a pseudonym, and belief that legal protections against genetic discrimination were adequate.

[b] Other variables included in model: belief that legal protections against genetic discrimination were adequate, <25% of patients covered by Medicare, and being more likely to order a GT if it reduced uncertainty about diagnosis.

[c] Other variable included in model: belief that GTs could lead to discrimination.