Adult polycystic kidney disease: knowledge, experience, and attitudes to prenatal diagnosis

Kathy A Hodgkinson, Lauren Kerzin-Storrar, E Ann Watters, Rodney Harris

Abstract
One hundred and ninety subjects from 100 adult polycystic kidney disease (APKD) families on the North Western Regional Genetic Register were interviewed to determine the likely demand for prenatal diagnosis. A detailed questionnaire was used to assess understanding and experience of clinical, therapeutic, and genetic aspects of APKD. Major features of the disease (presence of renal cysts which can lead to renal failure) and forms of therapy (dialysis and transplantation) were known; knowledge of less common features was related to experience. The cohort had had genetic counselling and the majority knew the risk to their own offspring, although the mechanics of the mode of inheritance was often misunderstood. Detection of presymptomatic ultrasound testing was high, and some implications of early diagnosis are noted. A minority changed their reproductive behaviour as a result of APKD, and although the majority felt a prenatal test should be available, only 23% at high risk of passing on the disease and contemplating children felt they would be interested, and so far only one request for prenatal diagnosis has been received. Thus, demand appears to be low and to be related to perception of the seriousness of APKD.
second bridging marker (24–1) has now been described,24 which, used together with the 3′HVR marker, gives an error rate of less than 1%. The possibility of genetic heterogeneity has been raised,25 26 but so far has not been resolved.27 28

Application of these DNA markers permits both carrier detection and prenatal diagnosis in families with suitable pedigree structures; the first prenatal diagnosis for APKD using linked probes was carried out in 1986.29 Now that prenatal diagnosis is possible, the question arises of whether it will be an acceptable option to couples, given the late onset and partially treatable nature of the condition. In the study of Macinol et al30 only 7% of those surveyed would consider termination of an affected pregnancy, but both Macinol et al30 and Sahney et al31 found that people had little knowledge of the genetic and clinical aspects on which to base their decisions. In Manchester, a register of APKD families was established in 1980, based at the Regional Genetic Centre. We carried out a questionnaire survey to assess attitudes, knowledge of the condition, and the likely demand for prenatal tests among subjects on the register. We present here the results from 190 persons interviewed between January 1987 and June 1988.

Methods
In 1980 a voluntary and confidential register of genetic diseases was set up in the North Western Regional Genetic Centre based at St Mary’s Hospital, Manchester. The purposes of the register are several, including genetic counselling for affected subjects, assessing and explaining risks to family members, annual recall for relatives at high risk, and presymptomatic ultrasound testing at the appropriate age. Annual recall and medical review in the department is continued for those shown to be affected after testing, with the aim of preventing complications. At present there are 129 registered APKD kindreds, out of which 431 persons, either affected or at high risk, are recalled annually.

APKD has a reported gene frequency of 1 in 1000.5 The population of the North Western region is just over 4 million; we would therefore expect about 4000 gene carriers, although at the moment we have only 420 affected subjects registered. Ascertainment, even allowing for late expression, is incomplete because the APKD register has concentrated on providing a joint clinical service with the renal unit at Manchester Royal Infirmary, rather than attempting to ascertain systematically every case in the region.

For this study we contacted all those aged between 18 and 45 on the register who had been previously counselled. These made up four groups of subjects according to status: (1) affected, (2) high genetic risk (at 50% risk), (3) low genetic risk (one or more negative presymptomatic tests by a consultant radiologist), and (4) spouses of any of the above. Those agreeing to participate were then interviewed in their own homes by a genetic fieldworker (KAH). Interviews were carried out using a detailed questionnaire and responses were recorded by the interviewer. In addition to direct questions, opportunity for open ended discussion was given.

The questionnaire was divided into six sections: (1) background information, (2) knowledge and understanding of clinical aspects and available therapy, (3) knowledge of the mode of inheritance, (4) information regarding affected relatives, (5) presymptomatic, and (6) prenatal testing.

For sections (2) and (3) a person’s overall knowledge was scored using lists of weighted facts which were considered necessary for the understanding of the condition (table 1a, a, b, c). Based on these scores, knowledge was classified as excellent, good, fair, poor, and absent.

As many of the subjects had not been made aware of the possibility of prenatal diagnosis, an explanation was given regarding how a prenatal test works, including discussion of the gene markers and of chorionic villus sampling. In order to facilitate this, we used linkage and recombination diagrams, designed for any autosomal dominant condition.

Results
Of the 352 subjects contacted, 190 participated (table 2). The take up rate was 54% for the group as a whole, but only 19% participated from the high risk group. Of the 190 interviewed, 43 (23%) were under the age of 25, 87 (46%) were aged between 25 and 35, and 60 (31%) were aged 36 and over. There were 114 females (60%) and 76 males (40%) (table 3).

### Table 1a Clinical features.

<table>
<thead>
<tr>
<th>Feature</th>
<th>If mentioned</th>
<th>Number (%) of subjects who mentioned each feature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct questions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple renal cysts</td>
<td>3</td>
<td>163 (86)</td>
</tr>
<tr>
<td>Renal failure</td>
<td>3</td>
<td>168 (88)</td>
</tr>
<tr>
<td>Indirect questions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain</td>
<td>2</td>
<td>85 (45)</td>
</tr>
<tr>
<td>UTIs</td>
<td>2</td>
<td>50 (26)</td>
</tr>
<tr>
<td>Haematuria</td>
<td>2</td>
<td>62 (33)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>2</td>
<td>97 (51)</td>
</tr>
<tr>
<td>Cysts elsewhere</td>
<td>1</td>
<td>21 (11)</td>
</tr>
<tr>
<td>Subarachnoid haemorrhage</td>
<td>1</td>
<td>9 (5)</td>
</tr>
<tr>
<td>Variable disease</td>
<td>1</td>
<td>30 (16)</td>
</tr>
<tr>
<td>Usual late onset</td>
<td>1</td>
<td>19 (10)</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

Overall knowledge scores were tabulated by adding the scores for each feature mentioned and then put into the following categories: 0=absent, 1-5=poor, 6-12=fair, 13-17=good, 18+=excellent.
understood that there
(table 1a).

In response to direct questions, 174 (92%) persons
correctly named the condition, 163 (86%) knew that
the kidney contained bilateral cysts, and 168 (88%)
understood that there was a possibility of renal failure
(table 1a). Asked to describe additional features of the
disease, far fewer persons knew of the increased risk
of high blood pressure, urinary tract infections (UTI),
and haematuria, and these were those who had had
experience of these, either personally or within the
family. Only nine (5%) mentioned the increased
possibility of subarachnoid haemorrhages (SAH), one
of the more severe complications of APKD. Each of
these was from a family in which SAHs had occurred.
Forty-two (22%) had a clinical knowledge score
considered good or excellent, while 26 (14%) had poor
or absent knowledge (figure). None of the 15 high risk
subjects had good or excellent knowledge and five
(33%) had poor or absent knowledge.

Table 1b Therapy.

<table>
<thead>
<tr>
<th>If mentioned score</th>
<th>Number (%) of subjects who mentioned each form of therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct questions</td>
<td></td>
</tr>
<tr>
<td>Transplantation</td>
<td>3</td>
</tr>
<tr>
<td>Haemodialysis</td>
<td>3</td>
</tr>
<tr>
<td>Indirect questions</td>
<td></td>
</tr>
<tr>
<td>Medical</td>
<td>2</td>
</tr>
<tr>
<td>CAPD</td>
<td>1</td>
</tr>
<tr>
<td>Dietary</td>
<td>1</td>
</tr>
<tr>
<td>Monitoring</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
</tr>
</tbody>
</table>

Overall knowledge scores were tabulated by adding the scores for
each form of therapy mentioned and then put into the following
categories: 0=absent, 1-3=poor, 4-6=fair, 7-9=good, 10+=
excellent.

Table 1c Genetics.

<table>
<thead>
<tr>
<th>If mentioned score</th>
<th>Number (%) of subjects who mentioned each feature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Direct questions</td>
<td></td>
</tr>
<tr>
<td>50% risk</td>
<td>3</td>
</tr>
<tr>
<td>Doesn’t skip generations</td>
<td>3</td>
</tr>
<tr>
<td>Risk to offspring correct</td>
<td>3</td>
</tr>
<tr>
<td>Affects both sexes</td>
<td>2</td>
</tr>
<tr>
<td>Indirect questions</td>
<td></td>
</tr>
<tr>
<td>Caused by gene</td>
<td>2</td>
</tr>
<tr>
<td>Autosomal dominant</td>
<td>1</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
</tr>
</tbody>
</table>

Overall knowledge scores were tabulated by adding the scores for
each feature mentioned and then put into the following categories:
0=absent, 1-2=poor, 3-8=fair, 9-11=good, 12+=excellent.

Table 2 Study cohort.

<table>
<thead>
<tr>
<th>Affected</th>
<th>High risk</th>
<th>Low risk</th>
<th>Spouses</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Invited</td>
<td>131</td>
<td>77</td>
<td>52</td>
<td>92</td>
</tr>
<tr>
<td>No reply/refused</td>
<td>46</td>
<td>62</td>
<td>20</td>
<td>34</td>
</tr>
<tr>
<td>Interviewed</td>
<td>85</td>
<td>15</td>
<td>30</td>
<td>58</td>
</tr>
<tr>
<td>(65%)</td>
<td>(19%)</td>
<td>(58%)</td>
<td>(63%)</td>
<td>(54%)</td>
</tr>
</tbody>
</table>

Table 3 Sex of cohort.

<table>
<thead>
<tr>
<th>Status group</th>
<th>M</th>
<th>F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Affected</td>
<td>26</td>
<td>59</td>
</tr>
<tr>
<td>At high risk</td>
<td>4</td>
<td>10</td>
</tr>
<tr>
<td>At low risk</td>
<td>15</td>
<td>17</td>
</tr>
<tr>
<td>Spouses</td>
<td>30</td>
<td>28</td>
</tr>
<tr>
<td>Total</td>
<td>76</td>
<td>114</td>
</tr>
</tbody>
</table>

KNOWLEDGE OF CLINICAL ASPECTS
In response to direct questions, 174 (92%) persons
correctly named the condition, 163 (86%) knew that
the kidney contained bilateral cysts, and 168 (88%)
understood that there was a possibility of renal failure
(table 1a). Asked to describe additional features of the

KNOWLEDGE OF THERAPY
In response to direct questions, 157 (83%) subjects
knew of the availability of transplantation, and 155
(82%) of the possibility of dialysis (table 1b). When
asked what other treatment was available, 53 (28%)
knew that dietary measures could be used and 89
(47%) that medical intervention could help with
symptoms. Looking at the personal experience of the
affected subjects (n=85), 60% have required little
treatment other than monitoring at present, 30% are
on dietary control, and 10% are on dialysis or have
received a transplant. Of the whole cohort, 88 (46%)
have had relatives who have a transplant or are on
dialysis. A total of 109 (57%) had a therapy knowledge
score considered good or excellent, while 36 (19%)
had poor or absent knowledge (figure). Nearly one
half (71/15) of the high risk subjects had poor or absent
knowledge of available therapy.

KNOWLEDGE OF GENETICS
In response to direct questions, 94 (49%) subjects
knew that the disease affects males and females
equally, 76 (40%) that it does not skip a generation, 96
(50%) that the children of affected subjects are at 50%
risk, and 138 (73%) knew the risk to their offspring
(table 1c). Forty-four (23%) quoted a completely
incorrect risk to their offspring, 29 (15%) felt that it is
restricted to one sex only, whereas 38 (20%) described
its mode of inheritance as recessive. Fifty-six (29%) had a genetic knowledge score considered good or excellent, while 88 (46%) had poor or absent knowledge (figure).

**PRESYMPTOMATIC (ULTRASOUND) TESTING**

We wanted to find out what effect the availability of presymptomatic testing had. A subsidiary aim was to discover how reliable subjects believed tests to be. Of the 190 in the cohort, 132 were originally at prior risk (the remainder being spouses), and of these, 12 had alternative means of screening, leaving 120. Of these, 17 were symptomatic at the time of diagnosis. Of the remaining 103, eight have declined presymptomatic screening to date. Thus, of the 95 screened, 58 were affected, 30 were put at low risk, and seven remain at appreciable risk. Of the 58 diagnosed as affected on scanning, 99% said they felt confident in the result but only 79% viewed the scan as a ‘100% certain’ diagnosis. Of the 30 put at low risk after negative scans, 90% said they felt confident in the result while 67% viewed the negative scan as a ‘guarantee’ that they had not inherited the disease.

Of the subjects found to be affected after a positive presymptomatic test (n=58), 11 (19%) had modified their career plans, either by changing career or having employment refused. Twenty (35%) had changed their sporting activities and 19 (33%) had had insurance problems, either having a premium loaded or a policy refused. Forty-three (74%) felt that they had suffered adverse social and psychological changes after their result.

Of the high risk group, eight declined ultrasound testing. Of these, four wanted to wait until they were older, one cited logistical problems with transport, and three did not want to know their status as they felt they could not cope with being positive for a disease with no cure.

The whole cohort was asked if it saw the need to develop a new presymptomatic test to improve upon ultrasound; 137 (72%) did not. Of the 46 (24%) who did wish for a new test, 16 wanted a test at an earlier age and 20 wanted a more accurate test.

**PRENATAL TESTING**

We were interested in attitudes to childbearing, and in assessing the likely demand for prenatal diagnosis. We asked the affected group (n=85) whether the risk of the disease had influenced their childbearing. Fourteen (17%) said it had, 48 (56%) said it had not, and 23 (27%) had not yet considered their reproductive plans. Of the 14 influenced by the risk of APKD, 11 had limited their family and three had been sterilised before having children. Of the 48 (56%) who said there had been no influence, 25 felt that the disease was not serious enough to justify changing reproductive plans. Twenty-three of the 48 had in fact had their children before their diagnosis and, of these, six said that if they had known earlier they would have limited their families. Therefore, 20 (24%) of the 85 affected subjects indicated that the risk of APKD had, or would have had, an influence on reproduction.

The whole cohort was asked whether it felt the development of a prenatal test was desirable; 142 (75%) felt that it was, compared with 66 (78%) of the affected group and nine (60%) of the high risk group (table 4). A total of 78% of females and 70% of males wished to see a test developed.

Subjects were then asked whether they themselves would be interested in a prenatal test for APKD (table 5): 55 (29%) of the whole cohort said they would compared with 21 (25%) of those affected and two (13%) of those at high risk. Interestingly, of the low risk group, for whom the question was hypothetical, 47% responded in the affirmative. Of the 55 who felt that they would be interested in a prenatal test, only 23 (19 females, four males) were in fact affected or at high risk and, of these, only nine were actually planning a family at the time of the study. Of these nine, eight were female and seven had no children to date.

Looking at the relationship between perception of the severity of APKD and interest in a prenatal test, 65% of those personally interested in a test, and at high risk of passing on the gene, considered the disease to be ‘extremely serious’ compared with 34% of the affected/high risk group not interested in a test. Although the perception of the disease differs in these two groups, the objective assessment of their experience in their own relatives did not differ between the two groups. Of the whole cohort, 50% felt the disease to be ‘extremely serious’.

Subjects were asked an open ended question about

**Table 4** Q. Do you feel that the development of a prenatal test is a good thing?

<table>
<thead>
<tr>
<th>Status group</th>
<th>Affected</th>
<th>High risk</th>
<th>Low risk</th>
<th>Spouses</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>66 (78%)</td>
<td>9 (60%)</td>
<td>26 (81%)</td>
<td>41 (71%)</td>
<td>142 (75%)</td>
</tr>
<tr>
<td>No</td>
<td>16 (18%)</td>
<td>6 (40%)</td>
<td>5 (16%)</td>
<td>15 (26%)</td>
<td>42 (22%)</td>
</tr>
<tr>
<td>Don't know</td>
<td>3 (4%)</td>
<td>1 (3%)</td>
<td>2 (3%)</td>
<td>2 (3%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>85</td>
<td>15</td>
<td>32</td>
<td>58</td>
<td>190</td>
</tr>
</tbody>
</table>

**Table 5** Q. Would you be interested in a prenatal test?

<table>
<thead>
<tr>
<th>Status group</th>
<th>Affected</th>
<th>High risk</th>
<th>Low risk</th>
<th>Spouses</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>21 (25%)</td>
<td>2 (13%)</td>
<td>15 (47%)</td>
<td>17 (29%)</td>
<td>55 (29%)</td>
</tr>
<tr>
<td>No</td>
<td>55 (65%)</td>
<td>13 (87%)</td>
<td>15 (47%)</td>
<td>37 (64%)</td>
<td>120 (63%)</td>
</tr>
<tr>
<td>Don't know</td>
<td>9 (10%)</td>
<td>2 (6%)</td>
<td>4 (7%)</td>
<td>15 (15%)</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>85</td>
<td>15</td>
<td>32</td>
<td>58</td>
<td>190</td>
</tr>
</tbody>
</table>
any aspects of prenatal testing they would find difficult to accept. Of the whole cohort (n=190), 93 (49%) said that they disliked the idea of terminations being available for APKD, contrasting with 73% of the high risk group. Only 9% of the total cohort objected to termination of pregnancy in principle. Over a third of the cohort felt that the risk of the chorionic villus sampling procedure was worrying.

**Discussion**

The discovery of DNA markers linked to APKD has introduced new options with respect to presymptomatic testing and reproduction, as well as opening up future possibilities for gene therapy. Much of the decision making for individual subjects will depend upon their experience and perception of the disease and its consequences, as well as an understanding of the genetic risk.

The vast majority of the study cohort knew of the presence of renal cysts, and that these can lead to renal failure. The open ended question regarding other symptoms of the disease showed that they remembered those clinical features which either they had experienced personally or had seen in other relatives. This aspect is not so striking in terms of the therapy, where 46% of the cohort had experience of relatives either on dialysis or transplantation, but over 80% knew of the availability of both forms of treatment for patients with APKD. In qualitative terms only 16% of the cohort felt APKD was not a serious condition.

Patients with APKD are at increased risk of subarachnoid haemorrhages from rupture of intracranial aneurysms. It is usually accepted that to screen all affected subjects using cerebral arteriography is not necessary, owing to the associated risk of the technique, although newer, non-invasive measures may change this. Only nine subjects in our cohort knew of the risks of this potentially lethal complication, which underlies a reluctance to discuss this aspect with subjects from families in which SAHs have not occurred. Our nine subjects all came from two families in which more than one person has been affected by this complication.

Despite genetic counselling, and the long term follow up of a genetic register, knowledge of the genetic aspects was found to be variable, and indicated particular areas of misunderstanding. However, 73% of subjects correctly recalled the risk to their offspring, suggesting that while mechanisms of inheritance may not be recalled, the pertinent risk figure is. Furthermore, the knowledge of genetic aspects was better in APKD family members than it was in their spouses. Misinterpretation, or poor recall after genetic counselling, can result from many factors, including the emotional readiness at the time of counselling, the ability to remember the facts given, and the style and time taken by the counsellor. In particular, it may be that the use of diagrams to help with a full explanation of the mode of inheritance would decrease common misunderstandings; the linkage diagrams we have devised proved particularly useful when explaining the use of linked probes within families and the problems associated with recombination.

Of the 132 subjects from the cohort who were at prior risk of inheriting APKD, 81% had had some form of presymptomatic testing for the presence of APKD, a figure at variance with the reported uptake of genetic presymptomatic testing for Huntington’s chorea, even though both conditions are dominant and have an adult onset. This difference is probably the result in part of the well known availability of effective treatment for APKD. The availability of a non-invasive ultrasound scan for presymptomatic diagnosis will probably mean that DNA presymptomatic screening may not have the same immediate impact in APKD as it will for conditions where DNA provides the only possibility for presymptomatic tests, or where existing tests are more invasive, for example, polyposis coli. However, the impact of genetic screening for APKD will be more important for those who have negative scans in their early 20s and want to make reproductive decisions. In these cases, the results of ultrasound, and linkage can be combined. The use of linked probes for APKD will allow earlier testing, with greater accuracy (assuming the question of genetic heterogeneity is resolved). A total of 19% of this cohort felt that a test which was either more accurate, or could be done at an earlier age, would be preferable to the ultrasound test.

Of those subjects at prior risk of inheriting APKD, only eight declined ultrasound screening. However, among the APKD families generally, this figure is probably much higher, as 81% of the high risk subjects who were asked to participate declined. Clearly the choice not to have testing, and not to participate in the study, reflects their attitude towards the risk of the disease. It is important to remember that the very high uptake of presymptomatic testing in our cohort does partially represent a bias of subject participation very common in surveys of this sort. However, even if all of the high risk group had participated, uptake would have been at least 64% in the group as a whole.

The diagnosis of an adult onset condition many years before the onset of symptoms could potentially have major adverse consequences. These include the possibility of discrimination in employment and financial matters (for example, life insurance) as well as the psychological impact of the result, and this has been discussed in relation to presymptomatic testing for other autosomal dominant conditions, such as Huntington’s chorea. In this study 33% of those diagnosed presymptomatically had experienced
problems with insurance, and 74% described feeling depressed or having changes in behaviour after diagnosis. As one subject said: “When I was positive, the cysts were visible on the screen, I came face to face with my own mortality”. Although three-quarters felt they had experienced adverse psychosocial consequences after a presymptomatic test, we did not seek detailed information on the nature and extent of psychological sequels to a positive diagnosis.

We were interested to know what effect, if any, APKD had had on reproductive behaviour. Although the cohort considered this a serious disease, and had a good recall of the risk to their offspring, only 17% of the affected group had in fact had no children or limited their families because of the risk. This group proportionally had a greater understanding of the clinical aspects, the therapy, and the genetics than the affected group as a whole, and when asked which factors had most influenced their decision regarding children, they cited a reluctance to watch their own offspring suffer with kidney problems (“I had a vision of all my children lined up on kidney machines”), a feeling that they wouldn’t want a child to have to make the same adult decisions (both in terms of career and reproduction) as themselves, and the guilt which they would have to contend with if the condition were passed on.

A majority of the cohort felt that the development of a prenatal test was acceptable, although a minority of the cohort said they would personally be interested. Almost half of the cohort felt that APKD was not a valid reason for terminating a pregnancy, while only 9% disagreed with termination generally. Comments such as “I’m not ill. If the child turns out to be as well and fit as me then it won’t be bad” were very common. Clearly the adult onset, partially treatable nature of the condition makes termination of pregnancy a less acceptable choice than for seriously handicapping conditions apparent in newborns or children. A higher proportion of those at low genetic risk indicated that they would have had a prenatal test for APKD if they had been at high risk; it would seem that prenatal diagnosis may be more appealing in the abstract. Of those at risk of passing the APKD gene on to their offspring, and currently considering having children, nine (23%) said they would be interested in a prenatal test and only one has actively pursued the matter.

About half of those family members invited to participate in the study agreed to be interviewed; therefore study bias must be considered. However, one would imagine that persons willing to participate in a study would be more openly facing the disease and its implications than those not willing to participate, and therefore it would be difficult to imagine that those not interviewed would be more likely to want prenatal diagnosis.

Comparing the groups who would accept/not accept prenatal diagnosis, no differences in knowledge scores were noted, but those who would accept prenatal diagnosis were more likely to perceive the disease as serious, even though the objective experiences of the disease were not different.

We conclude that even for persons with a realistic perception of the disease, and a good recall of the recurrence risk, the demand for prenatal diagnosis will be low.

We are grateful to our colleagues in the Regional Genetic Centre at St Mary’s Hospital and in the Renal Unit at Manchester Royal Infirmary for their constructive comments. We also thank the APKD families who gave up their time to be interviewed; without their cooperation this study could not have taken place. This work was supported by the UK Department of Health and by the North Western Regional Health Authority.


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