38

Ultrasound-Guided Fetal Invasive Procedures: Current Status

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INTRODUCTION

Since the early eighties a varied amount of experiences and trials of fetal puncture (fine needle aspiration) have been carried out with diagnostic aims [1-5]. At the beginning, the only possible way to enter the foetal evironment was with the support of a Fetoscope but the spectacular development of the already well known Ultrasonography has permited the invasion of the intrauterine enviroment with tools that are more and more harmless in the use, especially in the gradually tighter sections and the evolution of certain characteristics of the new needles that are now being incorporated into the new biopsy techniques [3,6,7]. Fetal puncture with diagnostic aims is technically possible, provided it is done by adequatelly trained hands, but the essential problem lies in establishing the correct indications which are not yet quite defined [8].

TECHNIQUE GENERALIZATION

Whatever the location of the foetal puncture may be, a certain number of requirements are imperative.

1. The operator must have sufficient working experience in invasive echography.
2. The room should have surgical consideration or rank, it is necessary to have an aseptic room for echographic intervention. A sterile wrap is recommended for the ultrasound probe. We use a surgical glove for an airtight seal.
3. The characteristics of the surgical equipment or the obtaining of the sample.

As the tendency is to obtain samples with the maximum diagnostic guarantee and a minimal risk to the integrity of the pregnancy, it is of capital importance, with few exceptions, to use sectio needles no smaller than 18 g.

It is clear that depending on the tissue sample we are aiming to obtain, it is not always possible to use innocuos tools. A clear example are the devices used to date for skin biopsies to diagnose some types of *Genodermatosis*, which consist on clipper forceps measuring 2.5 mm.

These methods in many cases require the use of an anesthetic, including in some, General Anesthesia, previous to proceeding to the incision in the maternal abdomen, with a scalpel, and the introduction of a trocar sheath enquivalent in sectio to a Verre needle that serves as a guide vehicle for the mentioned system or method.

The complications derived from the use of 2.5mm sectio needles and the transabdomen forceps method are closer to those of the fetoscope, added to the fact that the great flexibility in many cases of the method itself, having the availability of a great variety of needles of relatively small calibre (18g standard), obteining very good biopsies, including in skin samples and visceral solid areas (Fig. 38.1) [2,7].

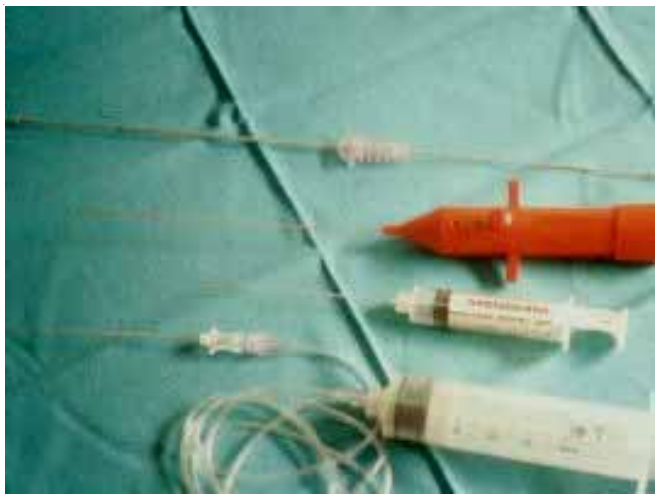

Fig. 38.1: Different types of needles and system for fetal biopsy

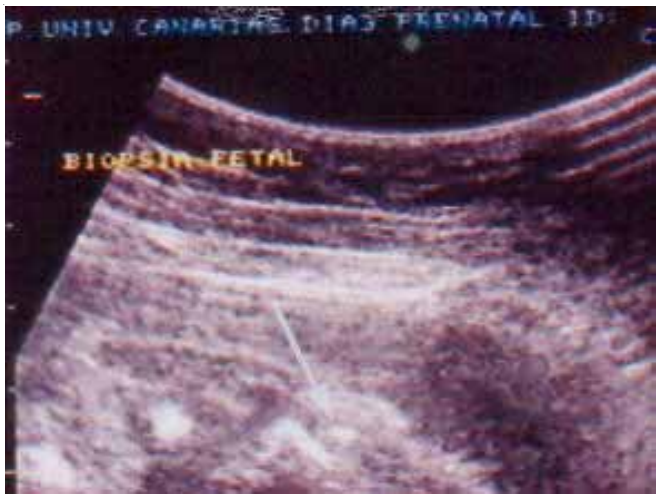

Fig. 38.2: Subtrochanteric muscle biopsy: echographic monitoring. The arrow indicates the puncture position obliquely to the fetal femur

Within the organs that are intrauterinally reachable. With worthy guarantees, the one that follows in difficulties after the skin sampling, is the kidney, fundamentally due to its histological parenchimal stratum constitution [9].

We can only consider satisfactory the samples or cylinders that include corticomedular stratum. The fetal availability in respect of its intrauterine position, the distance and the interposed tissue to the kidney (skin, muscle) as well as perirenal fat and the very capsule, are the elements that obstruct the obtaining of valid samples.

The use in these cases of a catheter of 14-16g calibre with isometric aspiration techniques with constant vacuum, allow to obtain valid samples, between 69-80 %, while the use of 18-20g calibre catheter obtains the very best specimens between 25-30%. This means that isometric (fine needle) puncture-aspiration techniques do not always offer the results hoped for on solid organs, fundamentally the kidney, unless wider catheters are used, that are far from the "harmless philosophy" that should prevail in these processes.

For these cases and others that are similar that could present themselves, depending on the tissue characteristics, the use of methods such as the *Aspiration Biopsy Set* that includes an 18g bisided trocar syringe in all its circumference, acting as a circular blade, and a conical sheath with vacuum suction embolous contriving through its interior which allows to obtain cylinders of 2-5 mm in maximum length, with optimal safety conditions and histological quality, similar to those of the *Tru-Cut* method.

Of all the viscus solid organs within reach, the one that offers the least problem is the liver, its spongy tissue constitution and its great size and volume in the fetal abdomen allows optimal accessability and consequently offers samples in practically 100 % of all cases, using a conventional fine needle of 18-20 g.

The obtention of muscle tissue samples offers one of the main difficulties due to the topographic and anatomical characteristics of the skeleton, also the important motorous innervation. For this reason it is necessary to correctly select the spot and the muscular area least suspectible to provoke indelible functional lessions.

The most accessible topographic areas are the external face of either thigh, but it is technically more attainable the vastus externus muscle (Fig. 38.2); it is a zone covered by the subtrochanteric fascia-lata in an oblicular direction descending towards the fetal femur, The use of the *sure cut* systems 18g with incorporated vacuum aspiration allows a sucsesses

rate over 75%. Conventional spinal needles with complementary aspiration by 50cc syringe vacuum allows to obtain sample with great difficulties.

When the puncture area has liquid characteristics, the echographic view is wide ranged, allowing a large field of action.

4. In general, technically it is precise to choose the most direct route, avoiding any interpositing obstacles, being also of interest to avoid the placenta if at all possible.
5. Once the crucial point to puncture has been determined, the needle should be introduced within the field of view of the probe, frame by frame until reaching the fetus.
6. It is recommended to approximate the puncture point without making direct contact with it in the first instance, until quite certain of the needles angle to the chosen spot, being of capital importance to enter with only one *sudden jab* to avoid sudden fetal jolts or movements.
7. It is advisable in all *free-hand* fetal punctures carried out, that the operator should take into account the dynamic variations of fetal positions.
8. For better manipulation, an assistant should be in charge of carrying out the isometric aspiration process at a prudential distance, approximately a metre away from the surgical table, interplacing a serum of the same length between the needle and the syringe.
9. Except in exceptional circumstances such as pericardic and pleural overflow that need an operating time of about 15-30 minutes, it is absolutely feasable to carry out without any anaesthetic procedures.

Aspiration in cystic disorders will fundamentally orientate the diagnosis. Aspiration on ovarian cysts is only indicated in complex cases derived from its dynamic volume or due to rare structural types with therapeutic aims more than to diagnostic ones.

We collect suspicious chylous collections, where the presence of high lymphocyte concentrations practically give a sure diagnosis also the fact that it allows a genetic study in very few days, justifies this type of procedures (Fig. 38.3).

The puncture of pericardic discharges has also the same diagnostic aims as well as being therapeutic.

Concerning brain punctures, the most representative, the *ventriculocentesis*, also allows us to accomplish serological marker studies in RCL, independant to any derived therapeutic attitude, although in this last case the efficiency of the derivative proceedures in hydrocefalia is uncertain (Fig. 38.4).

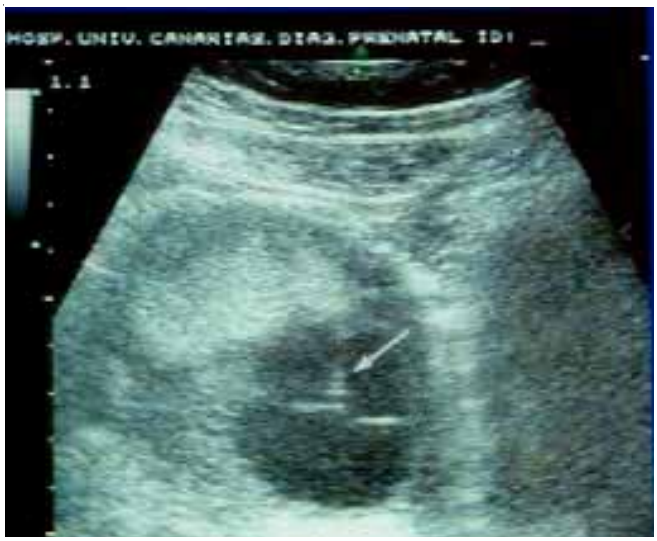

Fig. 38.3: Cystic lynphangioma: percutaneous puncture determines qualitative and genetic characteristics (lymphocytes)

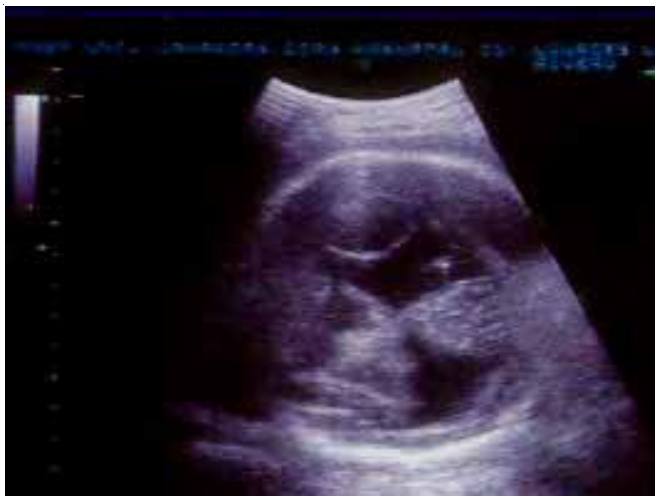

Fig. 38.4: Ventriculocentesis: obtaining cephaloraquideus liquid determines the presence of viral bodies by polymerase chain reaction

Of all the structually cystic processes, the obtention of fetal urine in dilated urological pathology represents the greatest and highest interest for diagnosis value. The biochemical analysis of the foetal urine allows us to detect irreversible tubular lessions from those which have a normal renal function.

There is no doubt that the incorporation of biological molecular techniques and DNA studies allow to establish in many of the cases, the alterations of any determined genetic locus [10-13] .

Ocassionally, we may find that we do not have enough material due to the lack of family records of desceased relations, in these cases the absence of this previous information constitutes a serious inconvenience in order to establish a prenatal diagnosis, as this is based only on a small corionic-villi, funicular or amniotic sample [11,14] .

This situation is where sampling directly from the fetal tissue is of special relevance for the diagnose of one or the other, or in order to rule out any pathological suspicion of family inheritance that are being submitted to any particular study.

"The taking of fetal samples by biopsy techniques is justified only in cases when the prenatal diagnosis of any specific pathological illness is not possible, or is frankly difficult, using any of the existing conventional techniques."

LIVER BIOPSY

Technique

Fetal transabdominal aspiration-puncture using 18g needles with conic catheter or spinal needles of the same sectio with isometric vacuum aspiration using a 50cc syringe and serum system. Once introduced into the fetal kidney, soft brief *inward outward* movements should be made in the same direction as the puncture.

Firstly the aspiration system should be extracted and last of all the needle, to avoid contaminating any other tissue. The spot to be puntured should be situated between the belly bottom and the border of the rib. This fate is helped by the physiological hepatomegalia, introducing the needle aproximately one centimetre under strict echographic monitoring. Preferably the external third of the right lobe, should be chosen, as it offers a minor principal vascularization, if not, the suprahepatic vessels should be avoided (Fig. 38.5).

If the diagnosis being sought for is histological, the cylinder should be conserved in formaldehide if on the contrary it is enzimatic, it should then be airtight sealed in carbonic snow.

The gestational age recommended should be around 20 weeks, provided that the hepatic metabolism and main enzimatic processes are well, or practically established.

Indications

Prenatal diagnosis, fundamentally of enzimatic alterations and of lethal metabolic characteristics [15,16].

Ornitil Transcarbamylase Deficiencies (OTC)

This mithocondrial enzyme of the urea cycle is synthesized in the liver or the intestines. Sex-linked disorders tied to the sex, are shown on the screening data of mothers who have urine excretion of orotic acid.

Primary Hyperoxaliuria (PH)

This is severe, charted renal insuffiency of rapid evolution, that is characterized by the presence of

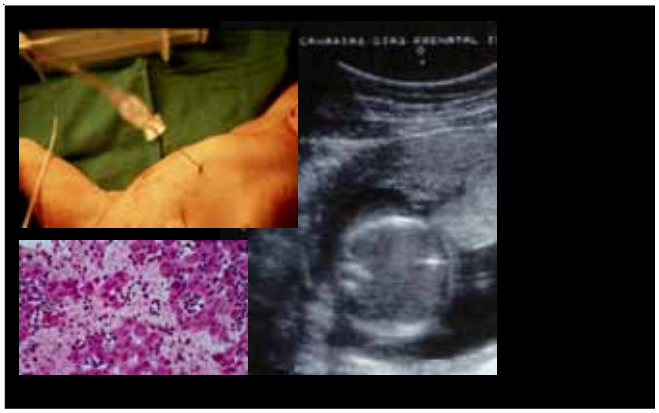

Fig. 38.5: Liver biopsy: ecographic monitoring and histological samples of fetal liver (19 weeks). Extramedullar hematopoietic foci can be detected

Calcic oxalate deposits in the renal tubule, microlithiasis and interstitial fibrosis. The hepatic level is accompanied by a total absence of alanine, inactivity of the catalitic gliosilate aminotranferase and immunoreactive proteins. This is incompatible with life.

For diagnosis it is fundamental to have the previous family clinical history available.

Carbamoyl Phosphate Synthetase Deficiency

This is an enzymatic defects of the urea cycle with recesive autosomic inheritance. Other autosomic recesive disorders may be detected by means of hepatic biopsy, including:

- Non-ketotic hyperglycinemia
- Prenatal diagnosis of infantile neuronal ceroid-lipofuscinosis.
- Biliar atresia (type I cysts).
- Long-chain 3-hydroxyacyl-CoA dehydrogenase [17-20]

Complications

The prenatal liver biopsy has few risks on a tissular level, due to its own visceral characteristics. Those risks are derived from the main vascular tears which will have great bleeding resulting in fetal death. In our experience (7 prenatal punctures), we have observed no complications (Table 38.1).

Table 38.1: Experience with seven prenatal punctures for liver biopsy

Reasons for biopsy	*Number of cases*
OTC diseases in the same family.	4
Previous affected brother.	1
Mitocondrial respiratory deficit.	1
Non-ketosic hyperglycinemia.	1
Results	
Prenatally confirmed diagnosis of OTC deficiency	2
Prenatally non-confirmed diagnosis with neonatal exitus by hyperammonemia	1
Prenatally confirmed as non-affected fetuses.	4

FETAL PUNCTURE IN THE EVALUATION OF RENAL STATUS

The correction of a theoretic renal obstruction problem is possible, in spite of the difficulties and risks that it holds, even if in the majority of cases it is not necessary. We should start by stating that an ultrasound echography diagnosis of the obstructed renal pathology does not necessarilly imply an irrevesible function alteration. In this sense the amniotic volume can be used as an indirect marker of the actual renal function, but this does have the inconvenience that it includes the possible measuring of the intrinsic clearance function.

When taking into account the possibility of practising an intrauterine derived therapy, this can only be justificable in those fetus in whose kidneys there has been no irreversable damage. However, this makes it essential to establish a precise evaluation of the renal function, in order to adequately select those fetus that will benefit from prenatal therapy.

The most conflictive situation is the renal dysplasia . In the latter coexist tissular phenomena that are characterized by fibrosis, dysplasia, cartilagenosis, frequently associated to corticomedular cysts, although not always so (Fig. 38.6).

Aproximately 90% of all kidney dysplasias is associated to dilated or obstructive disorders. In these cases it can be remarked that any derived therapeutic action is unnecessary.

The high resolution echography has turned into the unquestionable kidney evaluation processes, however, it does have a few diagnostic limitations: (Table 38.2).

Table 38.2: Fetal Neuropathy. Echographic prediction

Tissue Marker	*Sensibility*	*Specificity*
Corticomedular Cysts	70%	100%
Hyperecongenity	60%	90%
Hydronefrosis	75%	70%
Hydronefrosis + Cysts	90%	100%

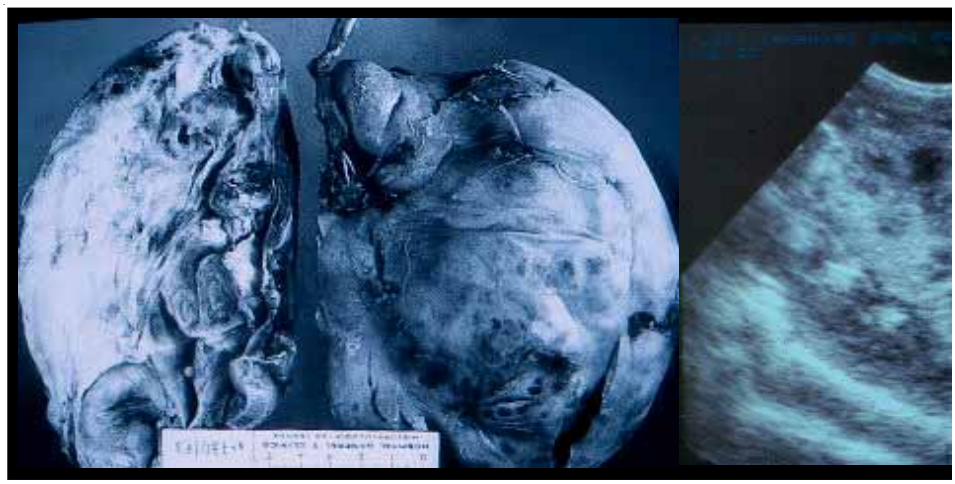

Fig. 38.6: Fibro-cortical dysplasia associated with corticomedullar cyst and renomegalia

In our experience the obstruction of a kidney without objectible cysts or hyperechos does not, however, exclude dysplasia. This quite alarming fact occurs approximately in 25-30% of all cases [8-21] .

From this we can deduce that the echography on its own does not diagnose all renal dysplasias, and for this reason fetuses with pelvic dilation are subsidiary of derived drainage.

A biochemical study of fetal urine is capital data in the managing of these fetuses. The composition of the fetal urine stays constant, practically throghout the pregnancy and with hypotonic characteristics. This fact has automatically demonstrated an optimal and reliable renal function and on the contrary and iso or hypertonic urine, a defficiency in renal function with an infastous prediction.

The biochemical markers that have close relation with a renal function are defined by the Na^+, Cl^- and osmotic urine.

Another determining factor in the normal renal clearance function derived from the near high reabsorvative tubular activity, is the establishing of specific proximal tubular lession selective markers.

These markers correspond to lisosomial proteins exclusive of the proximate tubular structure and become expressed by NAG (N-acetil D-glucosaminidase). Low molecular weight proteins filtered by the glomerular system and reabsorbed practically in their totality by the proximal tube, if it is present in fetal urine and in the amniotic fluid in large quantities (higher than 8 U/l), it is indicative of tubular tissue destruction.

The detection of b -2 microglobuline would be considered in the same manner. (Figs 38.7 and 38.8) Corresponden a los dos esquemas de la nefrona).We found that the levels of biochemical markers are sensibly low in the physiological urine in comparison with the cases affected with irreversible renal disorder. The same outcome occurs with the tissular markers, NAG and b2 microglobuline(Table 38.3).

Table 38.3: Fetal Urinary Aspiration: Pathological Biochemical markers.

	Pathological Urine Values Weeks		
	18-20	*20-30*	*>32*
Na^+ (mEq/ml)	120.0	126.44±11.50	139.60
Cl^- (mEq/ml)	119.0	132.50±7.18	141.00
OsM (mOsm)	240	261.50±24.20	281.00
NAG (U/l)	18.0	25.83±0.85	25.73
b2mG (ml/l)	26.0	38.97±1.30	38.72
K^+ (mEq/ml)	3.1	3.41±0.66	3.90
Creatinine (ml/l)	1.2	2.54±0.83	3.70

When we compare the relationship between the ionic concentrations and the osmolarity (Na^+ and Cl) of the fetal urine, and those of the amniotic liquid, we do not find significant differences between fetuses

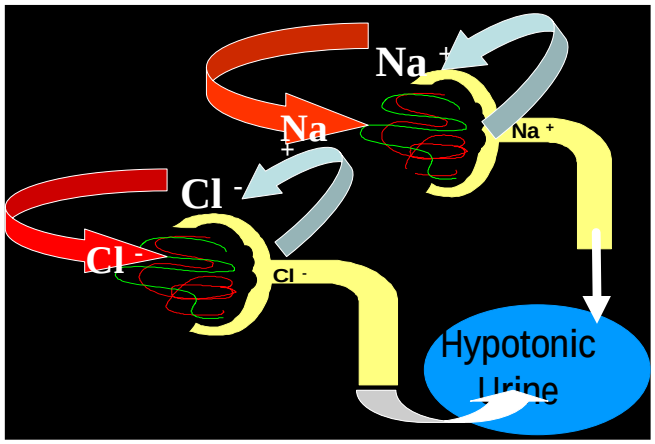

Fig. 38.7: Biochemical markers that have close relation with a renal function are defined by the NA+, Cl- and osmotic urine derived from the near high reabsorbative tubular activity. Fetal urine stays constant, practically through the pregnancy and with hypotonic characteristics.

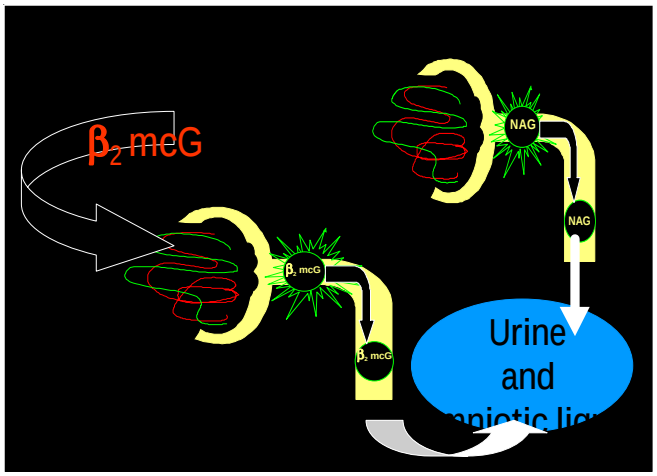

Fig. 38.8: Another determinating factors in the normal renal cleareance function correspond to lysosomial proteins exclusive of the proximate tubular structure (NAG), if it is presente in fetal urineand in the amniotic fluid in large quantities, it is indicative of tubular tissue destruction, Beta-2- microglobuline would be considered in the same manner.

with conserving and fetuses with patological functionalities. But comparing the levels of NAG and b2-microglobuline, a significantly greater concentrations of the two markers in the amniotic liquid of the affected fetuses have been observed (Tables 38.4 and 38.5).

Table 38.4

Physiological Values: Urine vs. Amniotic Liquid

Urine / Amn. Liquid	*Weeks 18-20*	*20-30*	*>32*
Na^+ (mEq/ml)	42/137	42/140	47/140
Cl^- (mEq/ml)	23/109	47/109	41/108
OsM (mOsm)	98/267	102/273	102/271
NAG (U/l)	2.0/3.6	2.7/3.62	2.0/4.69
b2mG (ml/l)	4.7/4.5	5.1/5.0	5.3/5.8
K^+ (mEq/ml)		41/140	
Creatinine (ml/l)		1.9/.6	

Table 38.5

Pathological Values: Urine vs. Amniotic Liquid

Urine /Amn. Liquid	*Weeks 18-20*	*20-30*	*>32*
Na^+ (mEq/ml)	120/132	126.4/140	139.6/140
Cl^- (mEq/ml)	119/107	132.5/149	141/158
OsM (mOsm)	240/267	261.5/273	281/296
NAG (U/l)	18/16.9	25.83/20.34	25.73/20.8
b2mG (ml/l)	26/22.3	38.9/28.74	38.72/30.0
K^+ (mEq/ml)	3.1/138	3.4/140.6	3.9/148
Creatinine (ml/l)	1.2/0.7	2.54/0.82	3.7/0.9

The increase in concentration of NAG and β2 microglobuline increase possibly due to the cumulative effect of the amniotic clearance mechanism.

This opens the field of study of nephrouropathies through the determination of these and other parameters in the amniotic liquid, without the need for invasive study of the fetal urine [21].

The K^+ and creatinine concentrations are different in their predictive evaluation as there exists a great clearance effect in the placenta and great variability in its ionic charge, that makes the potasium filtration very disperse, in the other hand 90% of the K^+ concentration are intracellular [8,21].

Summarizing, we can adventure a prediction of renal viability in relation to those parametres expressed. In the Table 38.6 taking into account that these values are applicable to any gestational age.

The intrauterine determination of the characteristics of fetal urine offers absolute diagnostic possibilities about the normal renal clearance function.

Urine aspiration puncture with diagnostic aims is technically feasable, using conventional spinal needles

Table 38.6: Fetal Urine: Biochemical markers applicable to any gestational age and echographic image and amniotic liquid volume to determine a renal function status.

Prediction	*Bad*	*Good*
Echographic image	hyperecog. + Cyst.	Normal Echography
Amniotic Liquid	Oligoamnios	Normal.
	Fetal Urine	
Na^+	>100 mEq/ml	<100 mEq/ml
Cl^-	>90 mEq/ml	<90 mEq/mll
Osmolarity	>210	<210
NAG	>8 U/l	<8 U/l
β -2 microglob.	>4 mg/l	<4 mg/l
K^+	Indifferent	Indifferent
Creatinine	Indifferent	Indifferent

of 18g having an aspiration system connected to a 20 cc syringe.

The way to aproach this depends on the fetal position available.

If at the posterior back position we would not find any great inconviniences in punctioning the bladder whilst for a lateral or anterior back where a nephrostomic aspiration is chosen (Fig. 38.9)

In neither one nor the other, can any noticeable complications be found, at least in our experience.[8,21]

The nephrostomy aspiration allows us firstly to re-evaluate the echostructural characteristics of the expanded kidney parenchyma, and secondly, as long as we use the 16g *sure cut* aspiration system, to carry out at the same time a renal biopsy without any technical difficulties.

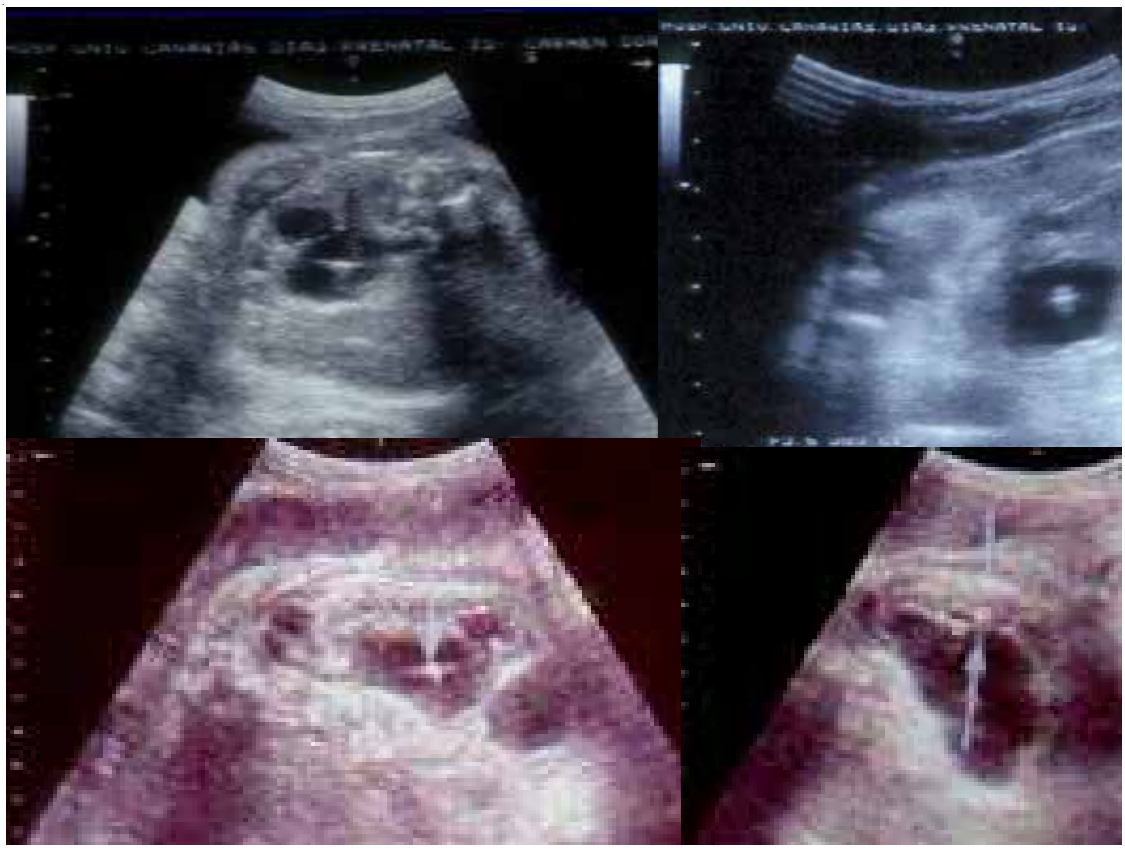

Fig. 38.9: Aspirative nephrostomy: echographic monitoring

For this, once the nephrostomy urine aspiration has been done, without taking the needle out move it towards the renal parenchyma and carry out the aspiration with a *swing* movement over the corticomedular area

The obtaining of samples of 2mm in length is enough for the detection of the histological characteristics that define a kidney dysplasia [8,9,21-23] .

But the use of 16g catheters Aspiration Biopsy Set (Fig. 38.3), once the technical problems of involving tissues have been solved, allowes to obtain samples in the 65% of the cases If conventional 18g catheters are used but inocuous, only 30% of the cases are obtained. (J. Troyano, Ian Donald, School Interuniversity of Medical Ultrasound, Dubrovnik August 1996, unpublished observations).

SKIN BIOPSY

As already stated in the generalization section about fetal biopsies, the skin biopsy entails the most serious difficulties in the obtaining of adequate or sufficient samples that would allow correct histopathological diagnosis or prediction.

The most important aspect is the obtention of valid samples, for this we need at least 1 mm strips of skin and no smaller in surface area and that also include a thickness of the epithelial stratum, and comprising of conjunctive areas and basal membrane. Only by this can an acceptable reading be obtained [24] .

The second aspect to be taken into account is the surgical biopsy material. We have already exposed previously that the use of section 2.5 mm clipping tongs (forceps/clippers) introduced into the amniotic eviroment by trocar, will allow the obtention of skin samples in 100% of all cases, and it is true that the residual skin lesions and any pregnancy complications there maybe, will not render any noticeable benefits in relation to the diagnostic data.

The use of conventional needles and isometric aspiration practising the *slice* technique, that consists in inserting the needle sidelongly over the skin and make *scratching* or *scraping* movements, as this will allow us to obtain skin strips of optimum quality with minimum damage to the integrity of the pregnancy (Fig. 38.10) [25-28] .

The third aspect to consider is the place selected to proceed for the taking of the sample, as depending on the disorder that we aim to diagnose prenatally, the biopsy area would be different. Not always the

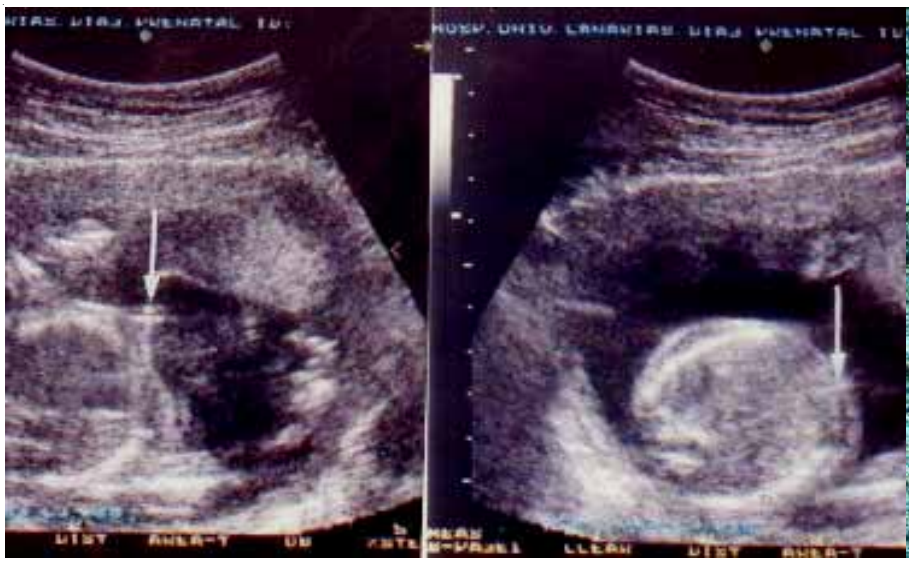

Fig. 38.10: Left: skin biopsy in fetal abdomen, sidelongly scratching. Right: mature histologycal cutaneous samples where keratohyalin and hemidesmosomes are detected

same area of the fetal skin wrap will be valid, or will suit the purpose of the biopsy.

Technique

Skin samples should, if possible, be taken from different areas of the fetus.

The pregnancy stage recommended for this is around 20 weeks, as after this time, the pilose folicles and keratinization mechanisms begin to develop. The study of the elements involved in the keratinization (keratohyalin and tonofibers), initially give suspicions of the disorder.

On the other hand, at this stage in the pregnancy the dermoepidermical junction has definitively been established, and the gradual rise of intercellular desmosomes, is a great help for the diagnosis of different forms of epidermolysis

The sequence should follow the following steps:

- Echographic monitoring.
- If it is possible, the placenta must be avoided
- Take into consideration the fetal position as on some ocassions it will be necessary to obtain samples from different skin areas.
- Rigorous sterilization.
- Optional local anaesthesia, depending on the surgical timing.
- Oblique needle incidence in the thickness and surface of the skin, making a scraping or scratching movement without pulling back.
- Try to obtain at least 1mm strips. The use of the vacum needles allow the collection of various fragments from the interior without the need of withdrawing the needle.
- Immediately proceed to swim the samples in saline serum for their histological staining and fixing process or for electronic microscopy analysis.

Indications

They are most frequently based on the diagnosis of some type of genodermatosis or congenital dermoepidermic disorders, of dominating autosomic transmission as well as recesive types, the majority being lethal in short or medium terms.

These disorders can be classified as follows :

- Bullous epidermolisis: Fetuses with large scale blistered areas that once the blisters break, set off intensive erosive zones with a fast loss of electrolytes are affected [6,10,29,30].
- Anhidrotic ectodermic dysplasias: Recessive disorder linked to the sex. The fetuses are born without pilose follicles, without any hair or sudoriparous glands. They develop hyperthermic affectation by disregulation and general dryness syndromes [31] .
- Keratinization disorders: Also called *Colodion baby syndrome*, characterized by the appearance of *reptile skin* due to epidermic membranes that are of quick *shedding*. Severe and lethal dehidrating disorders.[32,33]
- Pigmentary atopies: Ocular syndromes with severe intolerance to light and early or premature development of skin cancers [31,34,35].

The diagnostic problems faced with these dermatosis are due to the development of the lesion has different topographic origins, so the need to select the punture spot has to be in accordance to the illness that one is traying to detect.

The diagnostic possibilities of skin biopsies are summarized as shown in Table 38.7.

Table 38.7: Diagnoses possible from fetal skin biopsies

- Keratinization disorders:
Harlequin fetus.
Colodion baby.
Sjögren-Larsson syndrome.
Congenital icthyosis.
The puncture spot is in trunks and buttocks (Fig. 38.11)
- Ampollous diseases:
Herlitz ampollous junctional disease.
Hallopeau-Siemens ampollous dermolytic disease.
Inverse dystrophic ampollous disease.
Cockayne-Touraine dystrophic ampollous disease.
The puncture spot is in waist, skin folds, abdomen and buttocks (Fig. 38.12)
- Pigmentary disorders:
Negative tirosinase oculocutaneus albinism.
Chediak-Higashi disease.
Anhidrotic ectodermic disease.
The puncture spot in the skin-head (scalp) (Fig. 38.13)

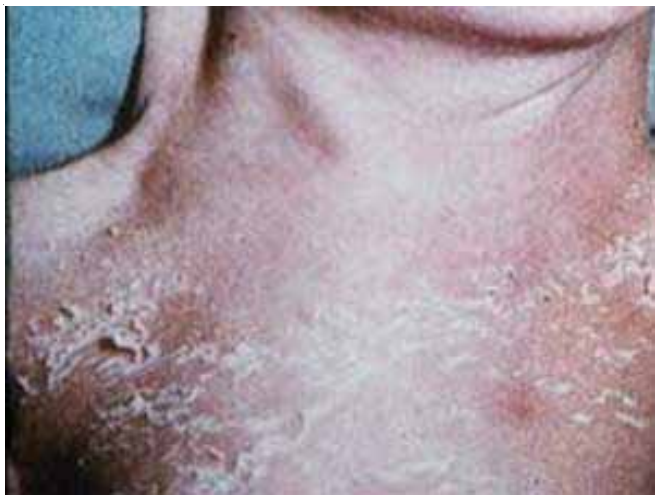

Fig. 38.11: Keratinizationdisorder

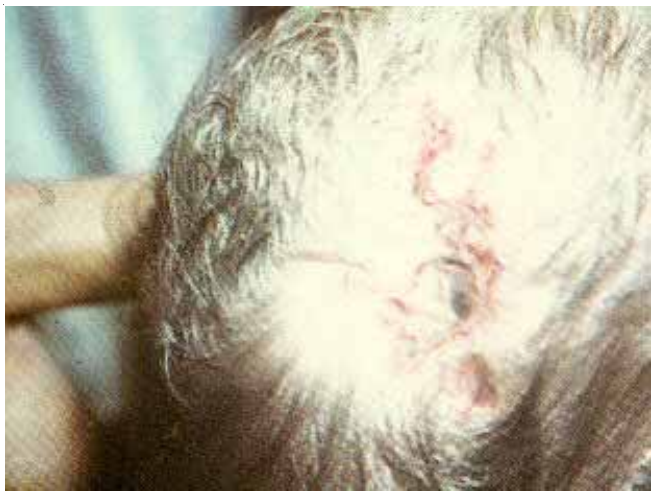

Fig. 38.13: Pigmentary disorder (scalp lesions)

It is fundamental to have objective family history in order to determine the biopsy spot [34,36,37].

Complementary Requirements

The study of the samples will be based on the ultrastructural features stated beforehand. A great deal of experience in fetal dermatology using electronic microscopy is required to make the diagnosis.

It is fundamental to have objective family history knowledge in order to determine the prenatal dermoepidermic structural markers.

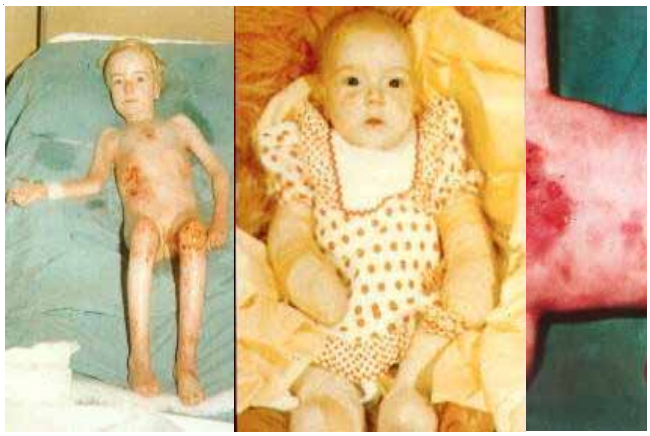

Fig. 38.12: Ampollous disease

It is recommended to have kept previous samples in order to be used as a *study bank*.

Complications

Now the tendency is to propose minimally invasive techniques by the use of conventional needles **7** .[38]

The use of conventional needles does not withhold more risks than the amniocentesis. On the other hand, the trocar techniques and the 2.5 mm sectio biopsy provoke around 5% of miscarriages due to iatrogenic amniorexis, although similarly some indelible fetal skin lesions have been described (Fig. 38.14). This does not occur in cases where the *scalp* technique is carried out with the use of conventional needles.

MUSCLE BIOPSY

This is carried out preferably for the prenatal diagnosis of Duchenne's muscular dystrophy (DMD), although it is also possible to detect other heredetary miopathies as long as there is some clinical family history of these disorders [11,38,39] .

For the diagnosis of Duchenne's muscular dystrophy, it is usual for the DNA analysis to be used. When the recombinations within the DMD gene or the DNA analysis are not sufficiently informative, or if from the family history it is not clear if there are possible carriers, so the direct examination of the muscle and its analysis is the only way to give the basis of an objective prenatal diagnosis.

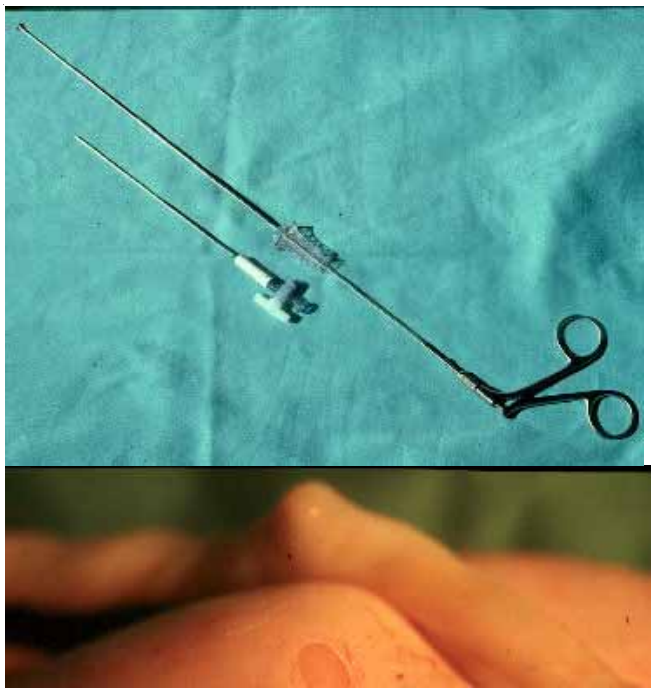

Fig. 38.14: Residual cutaneous lesion after biopsy with clipper system

The marker used is the dystrophine, its determination by means of immunoflourescence allows to differenciate the features of affected muscles from those of the healthy ones. The absence of this protein from the skeleton muscles is practically pathognomonic of DMD [11,14,39,40] (Fig. 38.15).

Some other times the prenatal diagnosis of DMD may be impossible when there is only one previously affected male in the family, and there is no identificable delection.

The absence of dystrophine in a skeleton muscle, is worth in itself the determination of the screening of the DMD. Nevertheless this diagnosis can be reinforced by detecting a rise in fosfocreatinkinase of more than 10 times its normal value in fetal blood.

Within the possibilities that can reinforce a prenatal DMD diagnosis or prediction we have:

- Sex linked.
- High values of fosfocreatinkinase.
- Absence of dystrophine.
- Degenerated muscle.
- Fat infiltration.

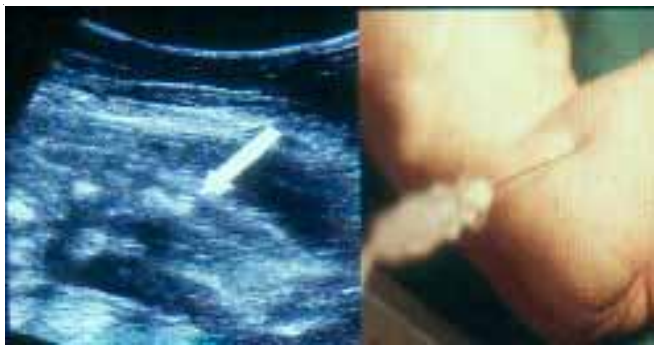

Fig. 38.15: Subtrochanteric muscle biopsy; the detection of dystrophin by inmunofluorescence determines healthy muscle

- Connective infiltration.
- Nuclear and cellular morphological alterations (Fig. 38.16).

Technique

Any muscular skeleton area is good, preferably of the external face of any of the thighs or nuckle areas, avoiding topographic places with inervation or vital vascularization, in this manner indelible functional lessions will not be provoked. Preferably using 18g conventional needles or even better, the *sure cut* method that have already been described [8,38,41-43] (Fig. 38.2).

Carrying out subtrochanteric punctures in a descending obliquest manner as possible, orientated towards the fetal femur (Fig. 38.2).

The puncture success rate is of 75%.

It is essential to determine muscle dystrophy by immunoflourescense, being advisable but not determining the detection of phosfocreatinkinase and the study of the muscular structure at a morphological muscular level, fat and connective infiltration.

No complications are described.

The fetus is susceptible to being studied by invasive techniques. These techniques are only justified by the seriousness of a possible inherited illness, or by any other disorder detected during pregnancy; in the latter the need for biopsy diagnosis is exceptional, as the thoracocentesis, pericardiocentesis and punctures of other thoracoabdominal, primary seek a therapeutic attitude, using the

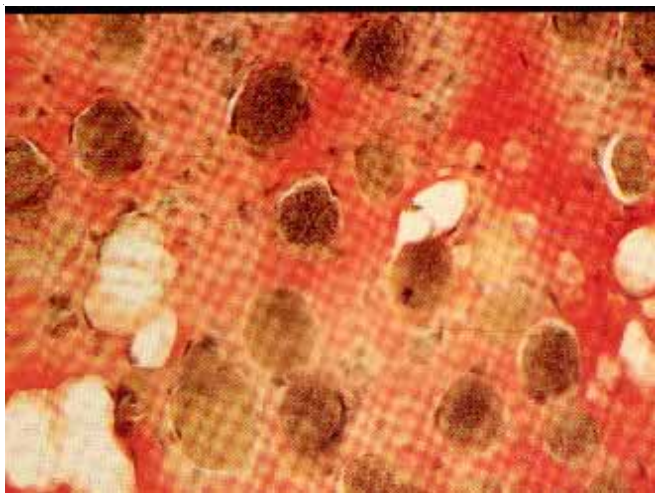

Fig. 38.16: Duchenne´s muscular dystrophy; degenerated muscle as an associated sign: fat and connective infiltration, and morphological cellular alterations and leucocytes infiltration.

extracted material for studying its analytical components.

Other punctures on fetal tumor formations (sacrococcygeal teratomas, solid cervical teratomas, etc...), or liquid colections, such as pericariocentesis, do not have an acceptable justification from a therapeutic or diagnostic point of view, as the echographic evaluation and the present application of biophysical methods (Colour Doppler amongst them) give an acceptable identification of their vascularization and origin, including those of suspicious neoplasm.[44,45]**.** (A. Kurjak, In: Ian Donald., University School of Medical Ultrasound 16th Course, - Granada, Spain, June 14th-16th 1993, Unpublished)

In agreement with our conduct, we wolud like to express this thought: The fetus has been endowed by nature to surpass several inconvenientes provided by its forty weeks of developing. It is a "Real Titan" front any adversity and, its adaptability is exceptional.

Don´t we disturb it!

Don´t we invade its privacy agressively!

Let´s observe it minutelly and, only when it need us, which generaly happens in few occations, it will advise us, then, let´s help it.

J.M.Troyano-Luque (1993)

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