A METHOD FOR THE PRENATAL DIAGNOSIS OF CHRONIC GRANU-547 LOMATOUS DISEASE (CGD). Peter E. Newburger, Susan B. Rothchild, and Harvey J. Cohen. (Spon. by David G. Harvard Medical School, Children's Hospital Medical Nathan). Center and Boston Hospital for Women, Departments of Pediatrics and Obstetrics/Gynecology, Boston, Mass. To provide a means for the prenatal diagnosis of CGD, we combin ed a modified nitroblue tetrazolium (NBT) slide test with quinacrine staining for Y chromosome fluorescence. Blood samples (10 μ) are applied to glass slides and the adherent cells incubated with NBT and phorbol myristate acetate, an activator of oxidative metabolism. Resultant metabolic activity produces micro-scopically observable formazan particles in 99-100% of adult and 95-100% of fetal granulocytes (PMN), in 0-1% of PMN from 4 CGD patients, and in 18-53% of PMN from 3 obligate CGD carriers. Since placental venipuncture samples are often contaminated with maternal blood, it is necessary to distinguish fetal and maternal cells in such mixtures. Quinacrine staining reveals a Y-body in 50-90% of male fetal PMN. Such identification of male PMN by Y-fluorescence allows detection and assessment of oxidative activity of CGD cells diluted 1:100 in maternal cells. Thus, the modified NBT slide test with quinacrine staining of blood obtained by placental venipuncture provides a method for the prenatal diagnosis of CGD in male fetuses at risk for the X linked or autosomal recessive forms of the disease.

548 PRENATAL DIAGNOSIS OF CONGENITAL ERYTHROPOI-ETIC PORPHYRIA. <u>Harold M. Nitowsky</u>, <u>Sigeru Sassa</u>, Sachiko Nakagawa and Nasseem Jagani. Departments of Pediatrics and Gyne cology-Obstetrics, Albert Einstein College of Medicine, and the Rockefeller University Hospital, New York.

Congenital erythropoietic porphyria (CEP) is a rare disorder of porphyrin metabolism in which uroporphyrinogen I (Uro I) and coproporphyr nogen I are found in great excess in tissues and excreta. This autosomal recessive disorder has been attributed to a partial deficiency of Uro III cosynthetase activity in cells of erythroid origin and other tissues. Studies of fibroblast cultures from skin of a 2 year old boy with CEP re vealed an accumulation of protoporphyrin after incubation with \triangle -aminolevulinic acid, but no increase in Uro I. A pregnancy of the mother of the patient with CEP was monitored by amniocentesis at 16 weeks gestation. The amniotic fluid had a pink-brown discoloration, and extraction of the porphyrins revealed a marked increase in fluorescence in compa rison with control fluids, with characteristic absorption and emission spectra. The presence of marked excess of Uro I was confirmed by thin layer chromatography. Prostaglandin termination of pregnancy 4 days later confirmed the presence of excess Uro I in fetal tissues. Although the diagnosis of CEP can be confirmed by demonstration of reduced Uro III cosynthetase activity in amniotic cell cultures, the marked derange ment of Uro I formation is evident in amniotic fluid thereby facilitating prenatal diagnosis of this disorder, (Supported by NIH Grant GM 19100)

VISUALIZATION OF HUMAN GLOBIN GENES BY RESTRICTION ENDONUCLEASE MAPPING: A NEW APPROACH TO THE PRENATAL 549 DIAGNOSIS OF GLOBIN GENE DELETION. Stuart H. Orkin by D.G. Nathan). Harvard Medical School, Children's Hospi (Spon. tal Medical Center, Div. of Hematology-Oncology, Dept. of Pediat rics, Boston, Mass. Analysis of the physical arrangement of globin genes in cellu lar DNA is now feasible. High molecular weight DNA is digested with site-specific restriction endonucleases, fractionated in agarose gels, and hybridized with radioactive complementary glo-bin cDNA either in situ or after transfer to nitrocellulose fil-ters. This technique permits direct, autoradiographic visualiza tion of DNA fragments containing globin gene sequences in DNA isolated from normal individuals and those with hemoglobinopa-thies. Comparison of the hybridization patterns of different DNAs provides a convenient, sensitive system for the detection of globin gene deletions or rearrangements. Study of homozygous α thalassemia (hydrops fetalis) DNA revealed complete absence of specific DNA fragments containing α globin sequences. The sensitivity and clarity of the visualization of this deletion indicate that this new approach will be especially useful in the prenatal detection of globin gene deletions or rearrangements in ammiotic cell DNA of fetuses at risk for severe thalassemia syndromes.

A NEW FAMILIAL DYSMORPHIC SYNDROME Dustan C. Osborn (), Philip Welch (Spon. by Richard B. Goldbloom), Dalhousie University, Department of Pediatrics, Halifax, N.S. A family is presented, members of which show a constellation of features similar to, but distinct from, the so-called Noonan Syndrome. The proband was an eleven year old boy admitted to hospital for an unrelated condition. Physical examination of the mother and six of seven sibs (2 female, 4 male) revealed some or all of the following in each: neck webbing, scleral telangiectasia, high arched palate, myopathic facies, low set ears, ptosis, mild mental retardation, pectus excavatum, short stature, unusual dermatoglyphics, and loose jointedness. All biochemical investigations to date have been normal. Cytogenetic studies have not shown an increase in the frequency of chromosome breakage. Typical features characteristically associated with the Noonan Syndrome. The father did not show any of these features and the parents are not consanguineous. The pattern of inheritance is most likely autosomal dominant with variable expressivity.

F	221	David C	. Peakman rthur Rob	ICISM IN AMNIOTIC FLUID CELL C , Marilyn F. Moreton, Barbara , Inson. University of Colorado	<u>J.</u> School
ю	f Medicine	, Depart	ment of B	Biophysics and Genetics; Nation	ai
IJ	awich Hosp	ital and	Pecearch	h Center, Denver,	
1	The abil	ity to d	li fferenti	iate true from pseudomosaicism	is of
١,	aior conce	rn in pr	renatal di	iagnosis. Of 1000 amniotic th	ulas
I.	processed h	v in sit	u methods	s, a total of 26 demonstrated :	some
Ľ	learee of c	hromoson	al mosai	cism. Two, which had more than	n one
Ľ	alony poss	essing t	he came a	abnormality, were interpreted	as true
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Ľ	1050101511. 10 VV/17 VV	10 000	cluses c	o be present in the newborn or	fetus.
Ľ	+0 ,/// +/ ,//		s shown c	luding 10 with trisomy 2, were	inter-
I.	ine resiaini	ng 24 ca	ises, inc	ince only a single colony or p	artial
μ	preted as p	seudomos	dicisii s	rrant chromosome complement.	No
ľ	colony demo	instrated	l the abe	ve been noted in the babies de	livered
μ	phenotypic	abnorma	illies na	ve been noted in the bubies de	
Į	following a	alagnos	SIS OT PS	eudomosaicism. Chromosome	No. of
				Chromosome Constitution	Cases
1	Constitut	tion	Lases	47,XX,+20	1
	47,XX(or X)	() , +2	ių	47,XY,t(1;13),+t(1;13)	i
	47,XY,+3		1	$46_XX_t(5;5)$	i
	47,XX,+4		1	46,XX,t(9;14)	i
	47,XX,+6		!		i
	47,XY,+11		1	46, Y, t(X; 15)	1
	48,XY,+14,		1	46,XX,i(Dq)	1
	47,XX(or X	Υ),+16	2	46,XY,-G,+mar	1

	REACTION OF 4-METHYLUMBELLIFERYLGUANIDINOBENZOATE
	552 (MUCB) WITH SKIN FIBROBLASTS FROM PATIENTS WITH CYS- TIC FIBROSIS (CF). M.Walsh Platt, Girimaji S. Rao,
	JJZ (HOOD) WITH SHOFT (CF), M. Walsh Platt, Girimaji S. Rao,
1	Stacy J. Simpson and Henry L. Nadler, Northwestern U. Med. Sch.,
	Children's Mem. Hosp., Dept. of Ped., Chicago, Illinois.
1	Plasma of patients with CF has been shown to have reduced
	Plasma of patients with of has been shown to have feature 1975
	protease levels as measured by rate assays (Pediat.Res.9:739,1975)
	and by "titration" with MUGB(Am.J.Hum.Genet.29:111A,1977). In
	order to study whether the reduction in protease activity is a
	generalized phenomenon in CF, we have quantitated proteases in
	cultivated skin fibroblasts derived from patients with CF.
	Fibroblasts were grown in MEM and fetal calf serum and harves
	ted by scraping. The cells were homogenized in 0.01M veronal HCl
	and 0.15M NaCl, pH 8.3 and centrifuged at low speed. The super-
	natant was assaved for reactivity towards MUGB by following the
	liberation of 4-methylumbelliferone(4-MU). The activity was par-
	ticulate inhibited by benzamidine, and not inhibited by p-hydron
	Immeduribenzoate The mean "titre" values (nmoles 4-MU released
	per mg protein) corrected for nonspecific hydrolysis of MUGB were
	$ \begin{array}{c} \begin{array}{c} \text{Samples} \\ \text{Controls (N)} \end{array} & \begin{array}{c} n \\ 8 \end{array} & \begin{array}{c} \underline{\text{Mean "titre" Level}} \\ 1.27 \pm 0.11 \end{array} & \begin{array}{c} \underline{\text{Range}} \\ 1.09 - 1.50 \end{array} $
	0.66 + 0.10 0.47-0.82
	CF 14 0.66 ± 0.10 $0.47-0.82$ CF Heterozygotes (H) 8 0.82 ± 0.12 $0.66-1.06$
	The differences were significant for N:H and N:CF($p < 0.001$)
	and H:CF($p < 0.01$). Cultivated normal human amniotic fluid cells
	and $H:CF(p < 0.01)$. Cultivated normal numan anniotic right certo
	gave values in the range of those observed for control skin fib-
	roblasts.
	These data suggest that the reduction in protease levels in
	patients with CF is a generalized phenomenon.