

IMMUNOHISTOLOGICAL AND ELUTION STUDIES OF
THE HUMAN PLACENTA*

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The survival of the human fetus in a potentially hostile immunological environment is an established fact of mammalian evolution, but the immunological relationship of a pregnant mother to her developing fetus is not yet clearly defined. Apart from the histocompatibility antigens which have been demonstrated on the ovum (1) and on the developing trophoblast (2), the fetus is antigenically unique in the materno-fetal relationship in possessing embryonic glomerular basement membrane antigens (3), fetal myoglobin (4), transferrin (5), hemoglobin F (6), IgG H-chains (7), and endodermally derived digestive system epithelial antigens (8). At least some of these antigens may stimulate a maternal immune response as is shown by the presence of anti-embryonic gut antibodies in the serum of pregnant women (9). Continual migration of syncytial trophoblast into the maternal circulation during pregnancy is also well established (10) and an apparent maternal immune response to syncytiotrophoblast has been reported (11) and incriminated in the pathogenesis of pregnancy toxemia (12). However, the results of other work suggest that the reaction of maternal sera with syncytiotrophoblast is nonspecific.¹ Although antifetal (13) and anti-placental antisera (14) can induce abortion and congenital malformations, and xenografts of trophoblast are destroyed by preimmunized recipients (15), allogeneic antifetal antibody will home to specific fetal target sites without any pathological consequences (16). The passage of fetal blood elements into the maternal circulation undoubtedly occurs and erythroblastosis fetalis, anemia, leucopenia, and thrombocytopenia due to maternal sensitization are well docu-

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mented. Allotypic serum-protein variants in the fetal circulation may also be antigenic and it has been demonstrated that maternal anti-allotype antisera can suppress fetal immunoglobulin synthesis (17). Maternal antibodies against fetal Gm antigens have been described in hemolytic disease of the newborn (18) and maternal anti-fetal InV antibodies have been reported in congenital nephrosis (19).

However, the majority of pregnancies proceed without apparent complications and when considering the mechanism whereby the fetus can maintain its individual antigenic identity without any pathophysiological mishap, some workers have regarded the placenta as the bulwark of the fetal defences against maternal immunological aggression. Thus, protection from a hostile environment is implied by the observation that the placenta tends to be larger in relation to the degree of materno-fetal antigenic disparity (20, 21). A fibrinoid layer (22), and particularly its sialic acid component (23), between maternal and fetal cells in the hemochorial placenta has been suggested as the barrier which segregates fetal antigens from potentially aggressive maternal lymphocytes. If the placenta does protect the fetus from maternal humoral and cellular immune aggression, any materno-fetal immunological reaction which occurs in normal pregnancies should be manifest in the placenta. Some investigations (24, 25) have demonstrated the presence of albumin, gamma-globulin and fibrin in placental fibrinoid foci. The present study was, therefore, undertaken to characterize in more detail the gamma globulin deposits in the human placenta.

Materials and Methods

IMMUNOHISTOLOGY

Tissues.—A total of 26 normal full-term placentas were available and all but 3 of these were perfused with chilled Krebs's saline to remove blood cells and serum proteins as far as possible. Placentas were also obtained from two pregnancies associated with severe Rh-hemolytic disease resulting in fetal death. Placental tissue was also collected from 11 pregnancies terminated therapeutically at 10–18 wk gestation. No material was available from spontaneous or pathological abortions. Blocks of tissue were quick-frozen in a mixture of solid CO₂ and acetone and sections for immunofluorescence studies were cut at 4 μ in a cryostat.

Antisera.—In preliminary studies, globulin fractions of rabbit antisera monospecific for IgG, IgA, IgM, IgD, β IC, β IE, and fibrinogen/fibrin were conjugated with fluorescein isothiocyanate (FITC)^{2,3} by the method of Riggs et al. (26). However, even after repeated absorptions with rat tissue powder and a homogenate of fresh rat placenta, these conjugates continued to produce quite spectacular nonspecific staining of syncytial trophoblast (Fig. 1). Subsequently, all antiserum globulin fractions were labeled with FITC by a dialysis technique (27) which produces more uniform labeling of protein and less nonspecific reactions. Unreacted FITC was removed by Sephadex G25 gel filtration. Fluoresceinated IgG fractions with the optimal fluorescein:protein ratios were prepared from the crude globulin conjugates by elution

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³ *Abbreviations used in this paper:* FITC, fluorescein isothiocyanate; PBS, phosphate-buffered isotonic saline; F, fluorescein-labeled.

from DEAE-cellulose columns with 0.08 M phosphate buffer, pH 6.3 (28). The pH of each labeled IgG fraction was adjusted to pH 7.2 and heat-inactivated normal rabbit serum (20% v/v) was added to stabilize the dilute protein solution and to inhibit any subsequent non-specific binding of the labeled material in sections of placenta.

Immunofluorescence Techniques.—The techniques employed were based on those originally described by Coons and Kaplan (29). Sections cut at 4 μ in a cryostat were dried for 1 hr in the draught from an electric fan. No fixation was employed. The sections were exposed for 30–60 min to a drop of each conjugate in a moist chamber and subsequently washed repeatedly with 0.01 M phosphate-buffered isotonic saline (PBS), pH 7.2 before mounting in 90% glycerol,

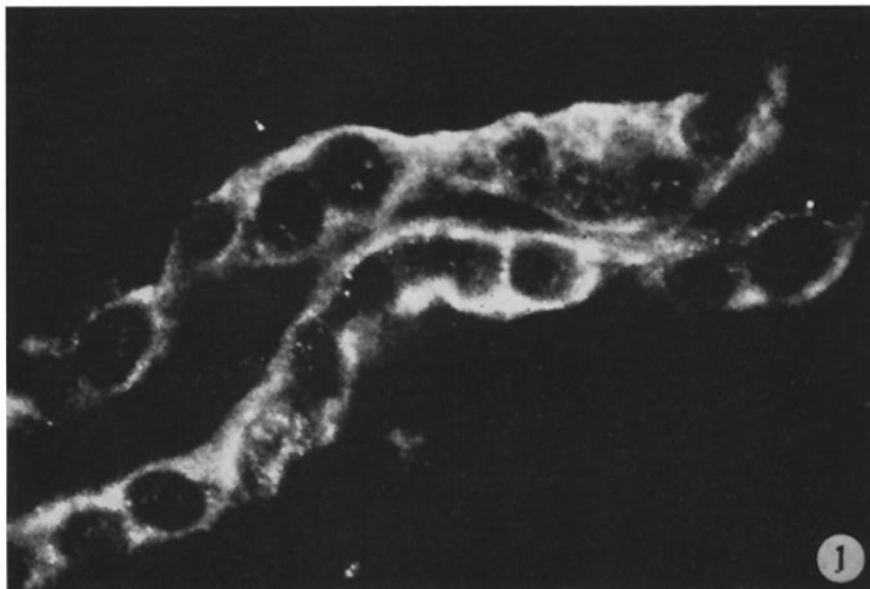


FIG. 1. Nonspecific staining of syncytial trophoblast by fluorescein-labeled (F)/anti-IgM.

buffered at pH 8.5. The stained sections were examined with a Zeiss fluorescence microscope equipped with a dark-ground condenser, UG5 primary filter, and 47/65 barrier filter.

Specificity of the staining reactions was confirmed by the following procedures: (a) *Inhibition:* Sections were pretreated for 2 hr with one drop of unlabeled antiserum globulin which was then mixed on the section with one drop of the corresponding conjugate and left for a further 20 min. Control sections were pretreated with normal rabbit serum before adding the conjugate. (b) *Absorption:* Sections were stained with a sample of each conjugate (except the anti-IgD conjugate) from which antibody activity had been absorbed completely by incubation with the appropriate antigen. The anti-immunoglobulin conjugates were absorbed with purified paraproteins coated on chromic chloride-treated erythrocytes (30), the anti-fibrinogen conjugate was absorbed with Cohn fraction 1, and the anti- β IC and anti- β IE conjugates with zymosan-C'3 and EAC'14 respectively. (c) *Displacement:* Sections were stained for 30 min with each conjugate and after washing with PBS were exposed for 2 hr to the corresponding unlabeled antiserum globulin. After 2 hr the drop of antiserum was carefully removed from

each section with a Pasteur pipette and a fresh drop of unlabeled antiserum was applied for a further 2 hr. This procedure was repeated once more before the sections were finally washed and mounted. Control sections were similarly exposed to three changes of normal rabbit serum after preliminary staining with conjugate. Under these conditions, labeled antibody was displaced by unlabeled antibody, which produced convincing diminution or almost complete abolition of fluorescence, whereas normal rabbit serum was without effect.

The displacement technique was introduced in this investigation because it was found initially that the inhibition technique alone could produce spurious confirmation of "specific" staining in studies of the placenta. Thus various conjugates, especially before purification on DEAE-cellulose, produced bright staining of the syncytial trophoblast which was obviously inhibited by unlabeled antiserum. However, prior treatment of the sections with normal rabbit serum also produced convincing inhibition of staining. Labeled antibody could not be displaced from the syncytial trophoblast by subsequent exposure to unlabeled antibody, indicating that the reaction was nonimmune by this criterion.

ELUTION STUDIES

Elution from Tissue Section.—Frozen sections were cut at $10\ \mu$ in a cryostat and thoroughly dried in an incubator at 37°C . The sections were then placed in a series of Coplin jars containing isotonic buffered saline ranging in pH from 7.2 to 2.3 and were left for 14 hr at 4°C . Subsequently the sections were washed in four changes of PBS and stained with the anti-fibrinogen, anti-IgG and anti- β IC conjugates, as previously described.

Elution from Bulk Tissue.—Approximately 100 g of six perfused placentas were separately homogenized with a Waring blender and washed repeatedly by stirring with chilled PBS until the washings were free of protein as judged by the optical density at $280\ m\mu$ (Fig. 2). Each washed homogenate was stirred for 2 hr at 4°C with isotonic saline buffered with 0.2 M sodium citrate/citric acid (pH 2.5), then was centrifuged and the supernate stored at 4°C . Washing of the homogenate at pH 2.5 was repeated twice more, the three supernates were pooled, the pH was adjusted to neutrality by the addition of a small quantity of solid tris(hydroxymethyl)aminomethane (Tris), and the pool was concentrated by ultrafiltration. After dialysis against PBS, each eluate was analyzed by immunoelectrophoresis (31).

Immunofluorescence Reactivity of Labeled Eluate.—To determine whether or not the eluted material possessed antibody activity against some placental component, one of the concentrated eluates with a total protein content of 5.5 mg/ml, as measured by the Lowry technique (32), was selected for conjugation with FITC. A modification of the dialysis method was employed (27). After preliminary dialysis against 0.025 M carbonate/bicarbonate buffer (pH 9.0), 1.0 ml of the concentrated eluate was dialyzed for a further 18 hr against 10.0 ml of the same buffer containing FITC, 0.05 mg/ml. Unconjugated dye was removed by Sephadex G25 gel filtration and the labeled eluate was fractionated on a DEAE-cellulose column (28). Fluoresceinated IgG was eluted with 0.08 M phosphate buffer at pH 6.3. Finally, 20% v/v normal rabbit serum was added to the labeled IgG fraction after adjusting the pH to 7.2.

RESULTS

Immunohistology.—The most striking immunofluorescent staining was produced by the anti-fibrinogen antiserum (Figs. 3–5). This conjugate reacted primarily with fibrinoid foci in villi, with intervillous and perivillous fibrin aggregates, and also with segments of thickened trophoblast basement membrane. These features were constant for all the full-term placentas examined. The sites of fibrinoid change were demonstrated as intensely and homogeneously stained areas with occasional islets of slightly refractile unstained material. Some villi

seen in cross-section showed almost complete loss of structure and replacement with fibrinoid material, but such villi still retained a peripheral layer of apparently intact syncytial trophoblast which was unstained. Other villi, presumably at an earlier stage of pathological change, showed marginal crescents, irregular peripheral deposits, and peripheral linear zones of stained material, varying in degree from minimal to extensive. Fluorescent deposits were seen almost invariably in the fetal stem villi and were present to some extent in

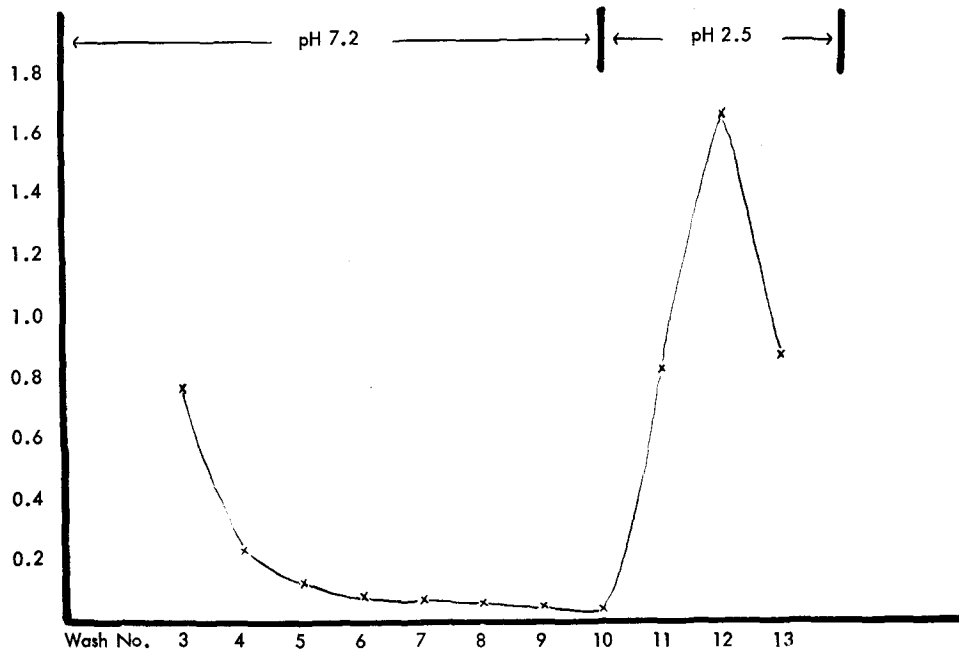


FIG. 2. Optical density (280 m μ) of successive washes of placental homogenate at pH 7.2 and pH 2.5.

10-35% of other villi. In the few placentas which were not perfused, fibrin or fibrinogen was also demonstrated within and around blood vessels and in a fine speckled distribution in the trophoblast stroma.

In as many as 35% of villi, the anti-fibrinogen antiserum also reacted with the trophoblast basement membrane, particularly in areas where the membrane was thickened. Commonly the immunofluorescent staining was intense and homogeneous but in other areas a "tram-line" appearance was produced. The peripheral layer of staining was sharply demarcated and in some areas seemed to split and encircle cytotrophoblast cells. The inner line of staining was less intense and tended to diffuse inwards in a tidal fashion or in a series of irregular projections extending a short distance towards the center of the villus. Some

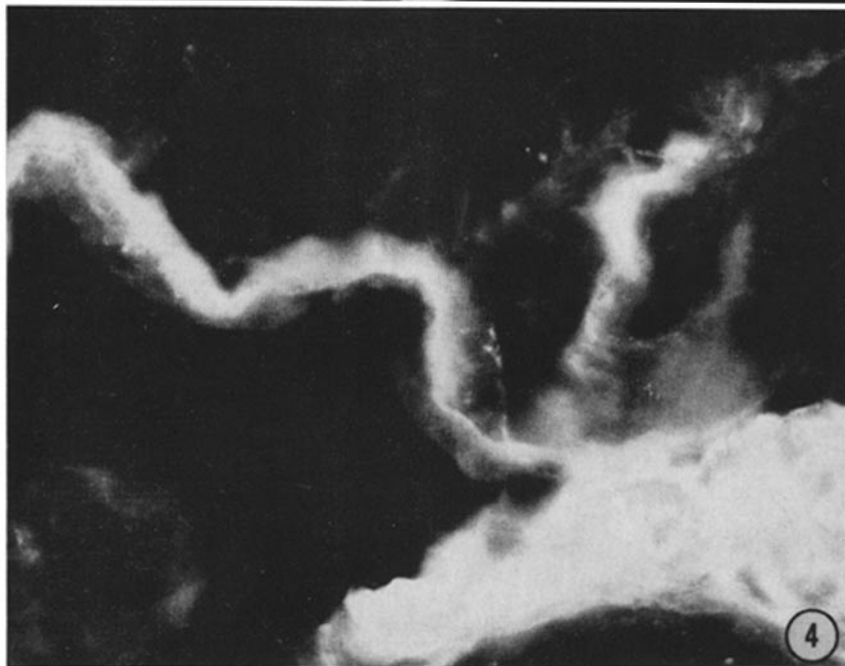
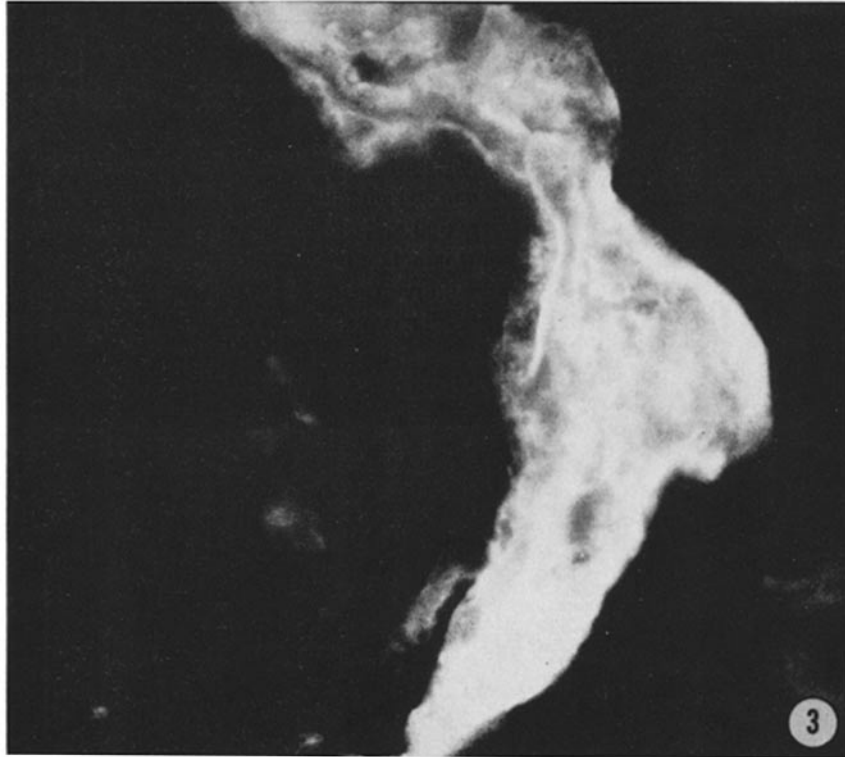


FIG. 3. F/anti-fibrinogen. Crescentic deposit of fibrinogen/fibrin at margin of villus.

FIG. 4. F/anti-fibrinogen. Intervillous fibrinogen/fibrin aggregate and deposition of fibrinogen/fibrin in a diffuse linear distribution along trophoblast basement membrane. The syncytial trophoblast is unstained.

villi showed continuous staining throughout the whole length of the basement membrane but in others the reaction was segmental or interrupted. Frequently the basement membrane staining extended into areas where fibrinoid material was deposited.

In general, a similar pattern of immunofluorescence was produced by the anti-IgG, anti- β 1C, and anti- β 1E conjugates (Figs. 6-8). The anti- β 1C antiserum, and to a lesser extent the anti- β 1E antiserum, reproduced the pattern of

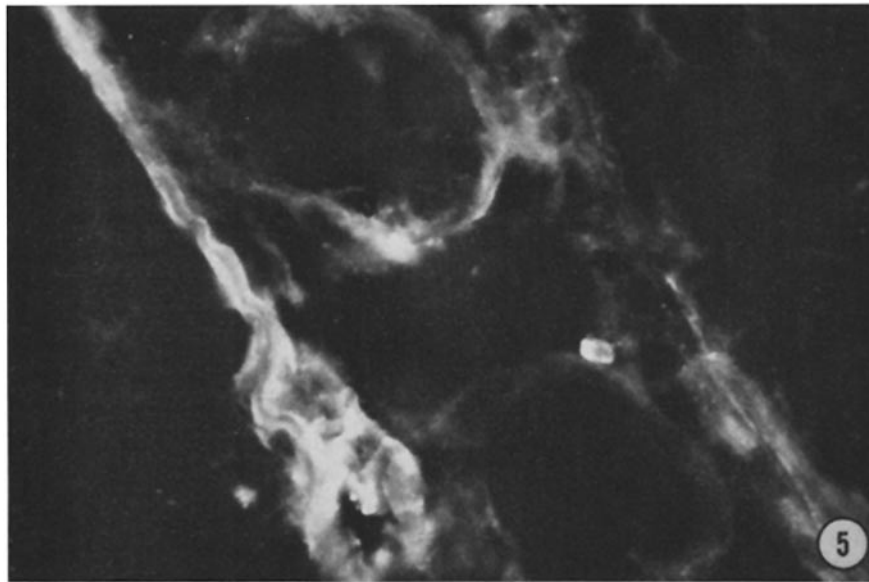


FIG. 5. F/anti-fibrinogen. Deposit of fibrinogen/fibrin along trophoblast basement membrane showing "tram-line" appearance.

staining seen with the anti-fibrinogen antiserum, being particularly reactive with fibrinoid deposits and also staining trophoblast basement membrane in a segmental or continuous distribution. The anti-IgG conjugate also reacted with thickened basement membrane and deposits of fibrinoid material but the intensity of fluorescence was less impressive. From a comparison of adjacent sections it was evident that IgG was not always detectable at basement membrane and fibrinoid sites where fibrinogen/fibrin, β 1C, and β 1E were present. In the placentas which were not perfused, IgG was also present in the trophoblast stroma and around blood vessels, but β 1C and β 1E were not detected in these situations.

These findings were consistent for all the full-term placentas examined. Traces of IgG and β 1C, and deposits of fibrinogen/fibrin were also detected in



FIG. 6. F/anti-IgG. Irregular linear deposit of IgG along trophoblast basement membrane showing spiky projections encircling cytotrophoblast cells (bottom center). Syncytial trophoblast is unstained.

FIG. 7. F/anti- β IC. Wavy linear deposition of β IC along basement membrane in three villi. A fibrinoid deposit is also stained (right).

occasional fibrinoid areas and thickened basement membranes in each of the 11 placentas obtained by therapeutic termination of normal pregnancies after 10–18 wk gestation. Traces of IgM were also detected on segments of basement membrane and in some fibrinoid areas in 18/28 full-term placentas (Fig. 9) but

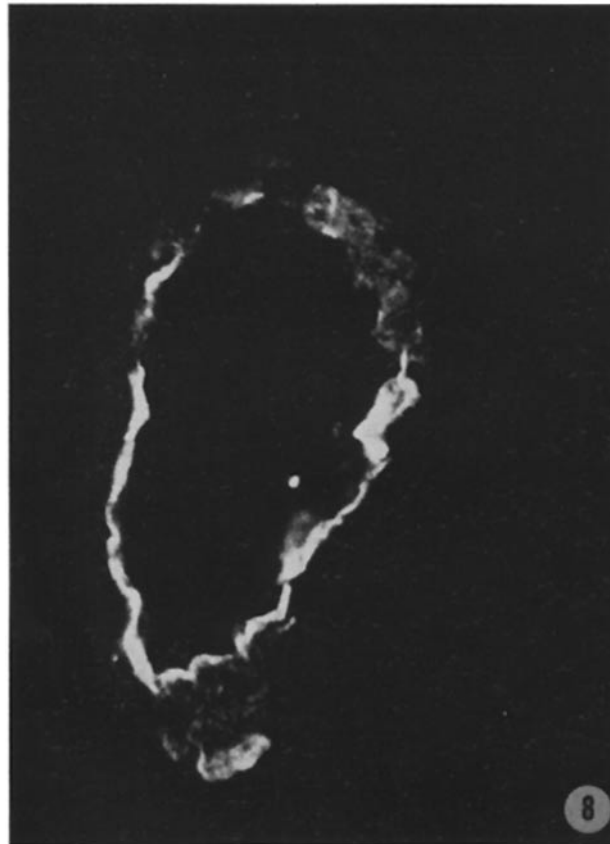


FIG. 8. F/anti- β IE. Staining along thickened trophoblast basement membrane and traces in peripheral cap of fibrinoid material.

IgM was not detected in any of the placental material from 10–18 wk gestations. In the two cases of severe Rh-hemolytic disease which resulted in fetal death, examination of the placentas revealed no unusual immunofluorescent features. Similarly, in another two cases of Rh-incompatibility without hemolytic disease, the placentas were indistinguishable on immunofluorescence criteria from those obtained from mothers without any recorded immunological complication.

In all the material examined the anti-IgA and anti-IgD conjugates produced no specific reaction. In many of the placentas various conjugates produced bright staining of Hofbauer cells, but although this staining was partially inhibited by unconjugated antiserum, it did not satisfy the absorption and displacement tests of specificity. In the 10-18 wk placentas but rarely in the other material, all conjugates produced some nonspecific staining of syncytial tropho-

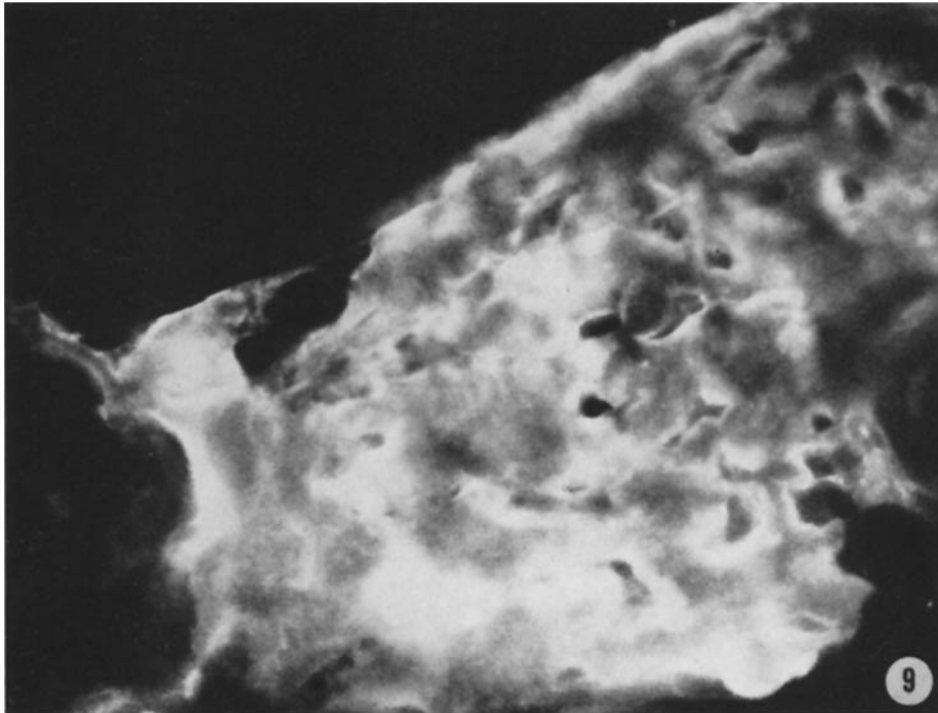


FIG. 9. F/anti-IgM. Tram-line staining of trophoblast basement membrane extending into large fibrinoid mass.

blast despite purification on DEAE-cellulose. All other staining reactions recorded above satisfied the three criteria of immunofluorescence specificity.

Elution Studies.—It was found that after pretreating $10\ \mu$ sections at pH 3.5 there was some loss of β 1C and IgG from the basement membranes, as shown by thinning of the linear deposits, especially at their internal margin. At a pH above 3.5 there was no obvious loss of staining reactions. At pH 2.3, IgG and β 1C were almost completely removed from the basement membranes although staining of the fibrinoid deposits elsewhere was only slightly diminished (Table I). There was also less staining of basement membranes with the anti-fibrinogen

conjugate in sections prewashed at pH 2.3, but there was no obvious change in the intensity of immunofluorescent reaction with the larger deposits of fibrinoid material and the intervillous fibrin aggregates. Presumably more complete removal of bound proteins might have been achieved with thinner sections, but in practice it was found that sections cut at 4–6 μ , tended to fragment after prolonged soaking in acidic buffers.

All six eluates from bulk placental homogenates were shown to contain appreciable concentrations of IgG, fibrinogen, and fibrin split products (Fig. 10).⁴ Complement components and IgM were not detected by immunoelectrophoresis, but IgM was demonstrated in three of the eluates by an agglutination-inhibi-

TABLE I
Effect on Immunofluorescence Reactions in Placenta Sections Prewashed at Varying pH

pH	Anti-IgG		Anti-fibrinogen		Anti- IC		Eluate-IgG	
	BM*	Fibrinoid	BM	Fibrinoid	BM	Fibrinoid	BM	Fibrinoid
7.2	++	++	+++	+++	+++	+++	—	—
5.8	++	++	+++	+++	+++	+++	—	—
5.3	++	++	+++	+++	+++	+++	—	—
4.7	++	++	+++	+++	+++	+++	—	—
4.3	++	++	+++	+++	+++	+++	—	(+)
3.8	++	++	+++	+++	++	+++	(+)	+
3.2	+	++	++	+++	+	+++	+	++
2.8	+	+	++	+++	+	++	++	++
2.3	(+)	+	+	+++	(+)	++	+++	+++

+++ = Strong immunofluorescence reaction; ++ = moderate immunofluorescence reaction; + = weak immunofluorescence reaction; (+) = trace immunofluorescence reaction.

* BM = Trophoblast basement membrane.

tion technique employing a monospecific anti-IgM antiserum and chromic chloride-treated erythrocytes coated with purified IgM (30). Gm typing of the IgG in the six eluates was attempted but the results were equivocal. In three eluates the Gm type was apparently (a — b — f —) and in the other three (a + b — f —). Gm data on the corresponding maternal, paternal, and fetal sera were not available.

When the labeled eluate-IgG fraction was applied to routinely prepared frozen sections of placenta, no significant staining reaction was observed unless the section was exposed to the labeled IgG for at least 4 hr. After 4 hr, quite definite staining of some basement membrane sites and fibrinoid area was apparent. On the other hand, when the labeled IgG was applied for only 20 min to sections prewashed in buffers at pH ranges of 7.2–2.3 as already described,

⁴ Albumin was detected in only one of the acidic eluates, having been removed completely from the other five homogenates by preliminary washing at pH 7.2.

faint but definite staining of fibrinoid areas and segments of thickened basement membrane first became apparent in the series of sections prewashed at pH 3.8 (see Table I). At this pH, staining of fibrinoid areas was streaky and granular, suggesting that some inhibitor has been only partially removed. In sections prewashed at lower pH values, and particularly in the pH 2.3 series, staining of the fibrinoid areas was more intense and homogeneous. Segments and continuous loops of basement membrane were also more sharply demarcated by bright fluorescence in the pH 2.3 series of sections (Figs. 11, 12). Intervillous fibrin

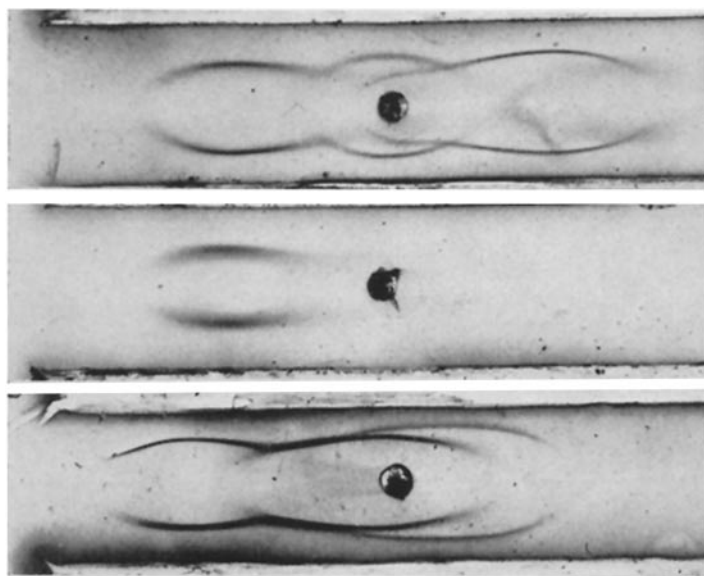


FIG. 10. Immunoelectrophoresis of placental eluate. (a) Anti-whole serum; (b) anti-IgG; (c) anti-fibrinogen/fibrin.

aggregates were unstained and there was no reaction in the trophoblast stroma or around blood vessels. Otherwise, the pattern of staining produced by the eluate-IgG was virtually indistinguishable from that already observed with the anti-fibrinogen, anti-IgG, anti- β 1C, and anti- β 1E conjugates. It should be noted, however, that the eluate-IgG reacted at the most with only 15% of the villi and there was no evidence of a general anti-placental basement membrane specificity nor was there any reaction with basement membrane or reticulin in sections of normal human kidney, thyroid, or lung. There was also no reaction with sections of rat or rabbit placenta.

The labeled eluate-IgG staining reactions were completely inhibited by each of the six unlabeled placental eluates available and the labeled IgG was convincingly displaced from sections by the unlabeled eluates. Human Cohn fraction

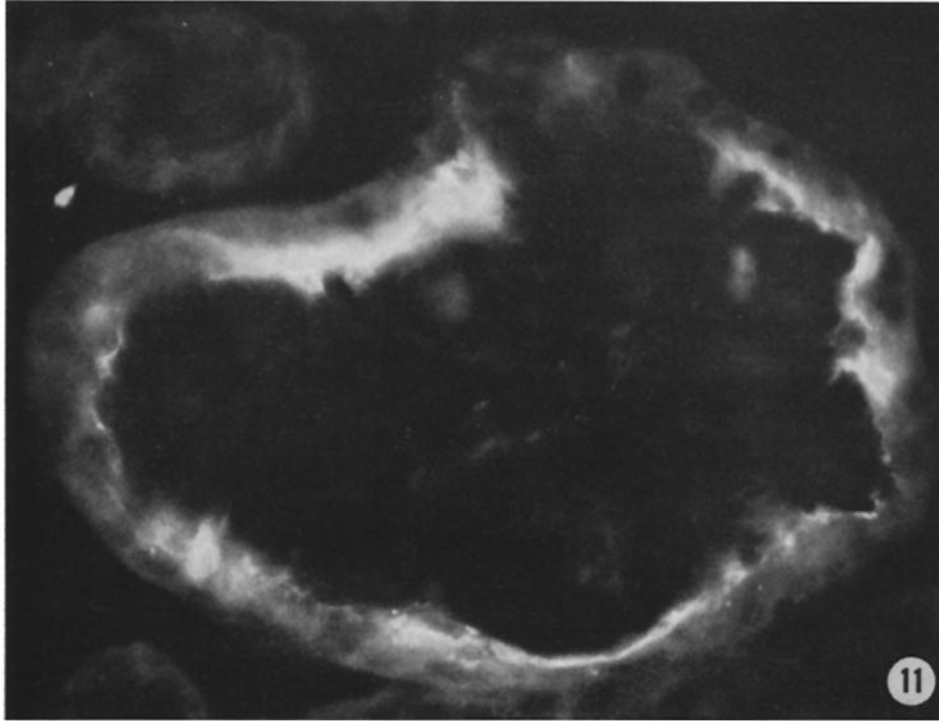


FIG. 11. F/eluate-IgG. Irregular staining around most of trophoblast basement membrane. Syncytial trophoblast is unstained. (Section prewashed at pH 2.3.)

FIG. 12. F/eluate-IgG. Staining along basement membrane and in fibrinoid deposit. (Section prewashed at pH 2.3.)

2 was completely ineffective in the inhibition and displacement techniques. In addition, a series of 22 cord sera, 36 maternal sera obtained immediately postpartum, and 36 sera obtained 3-7 days postpartum were examined for any ability to inhibit or displace the labeled eluate-IgG. None of these sera showed any significant inhibition or displacement.

Finally, to determine whether or not the eluate-IgG would fix complement after reacting with basement membrane and fibrinoid sites, sections prewashed at pH 2.3 were exposed to unlabeled eluate for 1 hr, followed by exposure to fresh guinea pig serum for 1 hr at 37°C. When subsequently exposed to labeled anti-guinea pig β 1C, no reaction with basement membrane or fibrinoid areas was observed. In a parallel study, where fresh human serum was used as a source of complement, the results were inconclusive because of residual in vivo-bound β 1C which could not be removed completely, particularly from the fibrinoid deposits, by prewashing the sections at pH 2.3.

DISCUSSION

The presence of "fibrinoid" material in the villi of immature and full-term human placentas is a well recognized phenomenon but the nature of this material has not been fully defined. On the basis of histochemical (33) and immunohistological studies (25) fibrin and fibrinogen have been demonstrated in this fibrinoid material. The results of the present investigation also indicate the presence of fibrin and/or fibrinogen. In electron micrographs, fibrils with the electron density and cross-striation indicative of fibrin have been defined, but the number of such fibrils is less than would be expected from the total distribution of fibrin as demonstrated by histochemical techniques (33).

The presence of IgG, IgM, β 1C, and β 1E in relation to the fibrinoid deposits suggests that some immunological reaction may be involved in the formation of these deposits. Although albumin has also been demonstrated in the fibrinoid deposits (24, 25), it seems unlikely that the immunoglobulins and complement components detected in this study were deposited by nonspecific precipitation of plasma proteins. The immunological nature of this deposition is suggested by the removal of bound proteins only at a low pH which would be expected to dissociate antibody from antigen, whereas albumin could be removed by preliminary washing at pH 7.2. The recovery in placental eluates of an IgG which reacts with thickened basement membrane and fibrinoid deposits again suggests the immunological nature of this process. Furthermore, the apparent inhibition of eluate activity by in vivo-bound material and the removal of such inhibition by prewashing sections at low pH would also indicate a specific immunological reaction.

Thus, the fibrinoid material with its content of immunoglobulin, complement, and fibrin may represent the "immuno-debris" of an immunological reaction with some undetermined placental or fetal antigen. It is unlikely that placental

basement membrane, or at least unmodified basement membrane, can be the antigen involved since the placental eluate reacted only at the sites where the basement membrane by its thickened appearance was demonstrably abnormal. Also, the eluate did not show cross-reaction with normal kidney, lung, or thyroid, which might have been expected if the eluted antibody activity were directed against normal basement membrane antigenic determinants. Alternatively it seems more likely that the antibody activity of the eluate and, therefore, of the deposited immunoglobulin seen in tissue sections, is directed against some component of the fibrinoid material laid down in relation to the basement membrane. A carbohydrate component in placental fibrinoid material can be demonstrated by the periodic acid-Schiff reaction (34), and it has been reported that there is an antibody in some maternal sera which will react with polysaccharide material extracted from the human placenta (35).

In the present investigation, antibody activity could not be demonstrated in maternal or fetal sera by inhibition of labeled eluate activity. It could be argued that antibody was already totally bound by the placenta and therefore not demonstrable in the serum. If this were the case, then by analogy with the appearance of anti-renal basement membrane antibody in the serum of glomerulonephritic subjects following nephrectomy (36), circulating antibody might be expected to appear in the serum of postpartum mothers. However, no antibody activity was detected in maternal sera obtained up to 7 days postpartum. Thus from the examination of maternal and fetal sera it was not possible to determine whether the antibody activity in the placental eluate was derived originally from the maternal or fetal circulation. Gm typing of the IgG in the placental eluates was not helpful in this respect but the apparent lack of Gm determinants might have resulted from damage to the immunoglobulin molecule during the elution procedure or from local enzymatic digestion *in vivo*. That the Fc portion of the molecule might have been deficient is suggested by the inability of the eluted IgG to fix complement in sections of placenta although presumably this IgG had previously fixed complement *in vivo* before elution.

It is known that maternal IgG is transferred selectively across the placenta and there is little if any transfer of IgM (37), but passage of maternal IgA across the placenta resulting in intrauterine isoimmunization has been reported (38). Synthesis of IgG and IgM by the human fetus has been observed at 20 wk gestation (39) while synthesis of β 1C and β 1E has been demonstrated as early as 10-14 wk gestation. In the 10-18 wk placentas examined in the present investigation, the β 1C detected in the fibrinoid areas may presumably be of fetal origin. Although the IgG in the most immature placentas is likely to be of maternal origin, the presence of fetally synthesized IgG cannot be excluded in the older abortion material (e.g. at 18 wk gestation). In the full-term placentas, it should be noted that IgM in addition to IgG was detected in 18 or 28 cases. It seems most likely that the IgM in this situation is entirely of fetal origin

although concentration by the placenta of trace amounts of maternal IgM cannot be excluded. From the present evidence, therefore, it cannot be determined with certainty whether the deposits of immunoglobulins and complement in the human placenta are entirely of fetal or maternal origin, or a conglomerate of materno-fetal derivation. The significance of this phenomenon is as yet unknown.

SUMMARY

An immunohistological survey of 28 full-term human placentas has demonstrated deposits of IgG, β 1C, β 1E, and fibrinogen/fibrin in areas of fibrinoid necrosis and on the trophoblast basement membrane in approximately 35% of placental villi. Traces of IgM were detected at similar sites in 18 of 28 full-term placentas. In 11 specimens of immature placentas (10–18 wk gestation) traces of IgG and β 1C and deposits of fibrinogen/fibrin were also present, but IgM was not detected in this material.

IgG was recovered in acidic eluates from an homogenized placenta which behaved as an antibody reactive with unidentified material present in fibrinoid deposits and on the thickened trophoblast basement membrane of some villi. It could not be determined whether this IgG was derived from the maternal or fetal circulation.

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