

reported by others suggests that the plaque technique in our experiments detects only immunoglobulin M (5).

Our data suggest that two types of antibodies with different specificities were produced by a single cell. The alternate possibility is that a new cross-reacting antigen was formed between bacterial and red-blood-cell components and that this antigen stimulates production of cross-reacting antibodies which are both hemolytic and bactericidal. However, the available data do not support the latter conclusion, because all antibodies were absorbed specifically either by erythrocytes or by bacteria. The apparent antibodies with two specificities were formed only when the test antigens were closely associated; this was achieved by coating the erythrocytes with the somatic antigen. The antigens responsible for the production of bactericidal and hemolytic antibodies are quite complex and probably of polysaccharidic nature.

Several investigators obtained evidence that single cells can make antibody of only one specificity (1). With fluorescent antibody preparations of different colors and specificities, others determined the quantitative and qualitative distribution of heavy and light chains in antibody-forming cells. In general, single cells were found to contain only one kind of heavy chain and one kind of light chain (6). On the other hand, few reports suggest that an individual cell can produce antibodies of two or more specificities (2). Although the wide variations in the results can be ascribed to the use of different techniques, it is quite possible that an antibody-forming cell may recognize a limited number of structurally similar antigens. The surface antigens of red blood cells and several gram-negative bacteria may cross-react. Although this was not evident in our system, the relation between these two types of antigens is well proved (7).

The suppressive effect of initially administered antigen upon the substance later injected indicates the phenomenon of antigen competition (8); interpretation of this phenomenon varies widely. The mutual suppression may be the result of competition of antigens for pluripotential antibody-forming cells or for some early nonspecific products needed for antibody formation (9).

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Incidence of Gross Chromosomal Errors among Tall Criminal American Males

Abstract. *Chromosome studies on 129 tall men surveyed in four different institutions for the care of criminal males in Pennsylvania showed that 1 in 11 subjects displayed aneuploidy of the sex chromosomes; specifically, five cases of 47,XYX and seven cases of Klinefelter syndrome were identified. All the aneuploid subjects were mentally ill; none had been cytogenetically diagnosed.*

The prevalence of aneuploidy among criminal males who are mentally ill, mentally retarded, or criminally insane is a phenomenon well appreciated in Great Britain (1, 2) but little recognized in the United States. In the course of a recent search for 47,XYX males among several criminal populations in Pennsylvania, we were impressed by the fact that 1 in 11 tall males displayed a gross chromosomal error but that all the affected individuals had gone undiagnosed despite frequent arrest and review (Table 1).

As a first step, inmates of four institutions for the detention of criminals were screened according to height, those 71 inches tall or over being selected for study. With the explicit permission of the subject, a buccal smear was made according to the method of Sanderson and Stewart (3) and 2 ml of venous blood was drawn into a heparinized syringe for the purpose of leukocyte culture (4). Two culture vials were set up for each subject. Chromosome counts were made of 25 well-spread metaphases; the unique morphology of the human Y chromosome makes the identification of XYX males by microscopic inspection quite satisfactory. Six clear metaphases were photographed on 4- by 5-inch (10- by 12-cm) film and karyotypes were constructed for each aneuploid subject. Individuals whose cultures failed were eliminated from the study. Mosaicism was not observed but cannot be ruled out as a possibility without parallel analyses of other tissues.

Individuals who displayed sex chromatin in the buccal smear or who dem-

onstrated aneuploidy on chromosomal analysis were revisited for further study. The cytogenetic studies were repeated; in each instance the initial finding was confirmed. A physical examination was performed at this time and the prisoners' social, educational, and medical records were carefully reviewed.

As shown in Table 1, 1 in 11 subjects proved to be aneuploid. Seven of the 129 subjects were Klinefelter males with positive sex chromatin and palpably atrophic testes. Five others were 47,XYX males, including one Negro, apparently the first to be reported in the literature (5).

The incidence of gonosomal aneuploidy among tall American males in a facility for the detention of juvenile delinquents proved to be 1:14; in a

Table 1. Incidence of gross chromosomal errors among tall criminal American males, 71 inches or more in height. Abbreviations: N, number of subjects studied; JD, detention center for juvenile delinquents; MDDA, penal institution for mentally defective delinquent adults; UDA, penal institution for unselected delinquent adults; and CI, mental hospital for the criminally insane.

| Type of facility | N | No. of subjects with chromosomal disorders | | Overall incidence |
|------------------|----|--|--------|-------------------|
| | | Klinefelter males | 47,XYX | |
| JD | 14 | 0 | 1 | 1:14 |
| MDDA | 30 | 2 | 0 | 1:15 |
| UDA | 35 | 1 | 2 | 1:12 |
| CI | 50 | 4 | 2 | 1:8 |
| Total | | | | 1:11* |

* Probability that this incidence is due to chance alone, $P = .001$.

penal institution for mentally defective delinquent adults, 1:15; in a penal institution for unselected delinquent adults, 1:12; and in a mental hospital for the criminally insane, 1:8. The comparable incidence of sex chromosome errors among tall men at large is estimated to be 1:80, if one assumes that 20 percent of American males attain a height of 6 feet or over (5), that sex chromosome errors result in extreme body height, and that the incidence of 47,XYX is 1:2000 (6) and of 47,YYY is 1:500 (7) adult males.

The results of this limited survey appear to confirm British observations that gross chromosomal errors contribute, in small but consistent numbers, to the pool of antisocial, aggressive males who are mentally ill and who become institutionalized for criminal behavior. Our data show, furthermore, that these men are to be found in general prisons as well as in mental hospitals for the "hard to handle."

To this we would add the observation that despite good physical care and much psychiatric attention throughout repeated incarcerations, these individuals are not being identified in the institutions we have surveyed. The implications of gross chromosomal errors for the intellectual, emotional, physical, and social development of the individual, for his legal status before the law (8), for the psychiatrist who treats him, for the society that must provide either care or parole are fundamental and deserve serious attention by professionals in many related disciplines.

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Pathogenesis of a Local Graft versus Host Reaction: Immunogenicity of Circulating Host Leukocytes

Abstract. *A local invasive-destructive reaction typical of that seen in allograft rejection occurs when Lewis rat spleen cells are inoculated under the capsule of Lewis kidney freshly grafted into F₁ hybrid hosts. Thus the donor lymphoid cells can be immunogenically stimulated by circulating host leukocytes and the interaction of these two cell populations results in nonspecific damage to kidney parenchyma. The results indicate that passenger leukocytes in organ allografts may be important immunogenic agents.*

Lymphocytes from normal adult parental strain rats give rise to a local invasive-destructive lesion when inoculated under the kidney capsule of genetically tolerant F₁ hosts (1). The local lesion is a massive one which depends on immunologically specific activation of donor cells (1, 2) and is marked by their continuing proliferation for periods in excess of 1 week (2). In terms of time course and histopathology this local graft versus host reaction mimics that of the acute rejection of primary renal allografts (1, 3), hence one could surmise that the infiltrating mononuclears are engaged in an immunological attack on the renal parenchyma.

However, when hosts that had previously been exposed to total body irradiation were employed, it was found that the graft versus host reactions were progressively inhibited in proportion to the dose of radiation administered (4). The donor lymphoid cells appeared to be powerless to generate an invasive-destructive lesion in allogeneic kidney when the host was profoundly leukopenic. One of several possible explanations for this phenomenon would be that host leukocytes rather than kidney were necessary to provide an immunogenic stimulus to the donor lymphoid cells. In order to study whether the invasive-destructive process depended upon the antigenicity of the renal parenchyma, or whether, on the other hand, the immunogenic stimulus could be provided by host leukocytes, we sought to confront the donor cells with

isogeneic kidney that was perfused by allogeneic blood.

Lewis (L) rat kidneys were transplanted orthotopically by the microvascular surgical technique of Fisher and Lee (5) into genetically tolerant (L/BN) F₁ hybrid hosts. Within 24 hours 50 million spleen cells (6) from L, BN, and F₁ donors (7) were inoculated under the capsule of the graft, and the results were assessed by histologic examination on the 8th day. When Lewis spleen cells were employed the kidney parenchyma was of course non-antigenic, but circulating host leukocytes or free subcellular transplantation antigens of the F₁ hybrid host could provide the necessary immunogenic stimulus.

Typical invasive-destructive lesions were observed under these circumstances, as shown in Table 1 and Figs. 1 and 2. Therefore, it is reasonable to conclude that the kidney need not provide the stimulus. Moreover, because the ability of inocula of whole blood to induce transplantation immunity resides exclusively in its leukocyte fraction (8), it seems likely that the donor lymphocytes were stimulated by circulating host leukocytes. Polymorphonuclear leukocytes are but rarely noted in the interstitial infiltrate or in the peritubular capillaries within the reaction site by either light or electron microscopy (1, 9), so the host cells involved are probably lymphocytes or monocytes or both.

The role of circulating leukocytes as the effective source of antigen in local graft versus host reactions was first un-

Table 1. Induction of graft versus host reactions in antigenically relevant and irrelevant kidney grafts from Lewis donors in genetically tolerant (L/BN) F₁ hosts.

| Derivation of spleen cell inoculum | No. | Histologic evaluation* | | | Kidney relevant? | Blood leukocytes relevant? |
|------------------------------------|-----|------------------------|------------|----------|------------------|----------------------------|
| | | No. pos. | No. equiv. | No. neg. | | |
| L | 4 | 4 | 0 | 0 | — | + |
| BN | 3 | 3 | 0 | 0 | + | + |
| (L/BN) F ₁ | 5 | 0 | 1 | 4 | — | — |

* Positive = mononuclear cell invasion through cortex at least to depth of peripheral glomeruli, and distinct signs of tubule degeneration. Equivocal = sparse mononuclear cell interstitial infiltrate, no sign of tubule destruction. Negative = no infiltration or destruction of outer cortex.

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