

A comparison of the effects of these 2 penicillins with other penicillins^{2,13} and with 6-aminopenicillanic acid (6-APA)¹⁴ on this strain of *E. coli* is of interest. Thus, both cloxacillin and nafcillin are considerably less effective in inhibiting growth and inducing lysis and spheroplast formation than are benzylpenicillin, phenoxymethylpenicillin, propicillin, phenethicillin, phenbenicillin², ampicillin¹³ and 6-APA¹⁴. It has recently been observed⁵ that, in common with other penicillins, cloxacillin inhibited bacterial cell division (resulting in the formation of filaments) in an *Erwinia* species at concentrations far below those needed by nafcillin. According to ROLINSON⁸, differences in sensitivity of an organism to various penicillins could be related to the relative affinity of each antibiotic for a component of the bacterial cell wall.

The overall conclusion of these findings is to demonstrate that each penicillin has a similar mode of action against *E. coli*.

Résumé. Divers aspects de l'action de la cloxacilline et de la nafcilline sur *Escherichia coli* ont été étudiés. La

cloxacilline s'est montrée plus efficace que la nafcilline quand il s'agissait d'arrêter la croissance et d'amener la lyse et la formation de sphéropastes; par contre, elle s'est montrée moins efficace que plusieurs autres pénicillines (y compris l'acide 6-aminopénicillanique) à ces égards. Ces résultats tendent à démontrer que la cloxacilline et la nafcilline possèdent un mode d'action qui est typique des pénicillines sur cet organisme.

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¹³ T. D. TURNER and A. D. RUSSELL, *J. Pharm. Pharmac.* 14, 395 (1962).

¹⁴ A. D. RUSSELL, unpublished data.

Pregnancy Blocking Capacity and Inbreeding in Laboratory Mice

Blocking of luteal function and, hence, implantation, following a discrimination of pheromones in the urine of stud and strange males is a phenomenon that has been documented for a variety of types of laboratory mice¹⁻⁴, wild house mice⁵, and, a non-murid rodent, the deer-mouse⁶. MARSDEN and BRONSON⁷ were unable to detect any effect of exposure to strange males in any of the 5 highly inbred strains of mice they tested. Two experiments dealing with genetics and the blocking phenomenon are reported here: (1) an evaluation of blocking capacity in hybrid mice obtained from crossing 8 inbred lines and (2) separately testing males and females of one non-blocking, inbred strain to determine if the loss in blocking capacity in that strain could be traced exclusively to either sex.

Eight-way cross hybrids used in the first experiment were obtained from crossing the following lines at The Jackson Laboratory: SJL/J, BALB/cJ, C57BL/6J, CBA/J, 129/J, BDP/J, LP/J, and RF/J. The first 5 strains have been subjected to intra-strain, and some degree of inter-strain, testing for pregnancy blocking responses; all with negative results. Sixth generation hybrid offspring were evaluated for blocking capacity at 75-90 days of age. Females were paired with non-litter-mate males for 4 days. Stud males were removed when an insemination was detected and either the female remained isolated in her home cage as a control or a strange (8-way cross) male was put into her home cage for 2 days in an attempt to block her implantation. Autopsy on day 7 post insemination revealed the following pregnancy rates: control, 75% of 24; strange male exposed, 92% of 25. The strange male effect, therefore, could not be demonstrated.

The second experiment substituted C57BL/6J males and females separately into a proven blocking system to determine if the loss in blocking capacity previously reported for this strain⁷ could be exclusively traced to either sex. All C57BL/6J mice were reared in Bar Harbor and shipped to Burlington where the senior author tested them in a system known to result in a strange male blocking response: insemination of Swiss-ICR albino

females by males of the same strain, removal of the studs, and exposure for 7 days to a wild house mouse male in the female's home cage^{5,8}. Averaging several experiments for appropriately aged females under these conditions shows a reduction in implantation rate from 92% for control (isolated) ICR females to 49% following exposure to one strange wild male (Table). A lower pregnancy rate (as low as 15%) is possible by simultaneous exposure to more than 1 male⁸. Substituting C57BL/6J females into this system revealed a complete lack of response to the strange wild male; pregnancy rate being lowered by only

Pregnancy blocking attempts in ICR or C57BL/6J females (ICR studs used throughout)

Inseminated female	Test exposure	No.	% Pregnant
ICR	no male ^a	225	92
ICR	wild male ^a	218	49
C57BL/6J	no male	27	74
C57BL/6J	wild male	51	69
ICR	C57BL/6J male	60	80
ICR	ICR male	60	75

^a Data in part from CHIPMAN and Fox⁸ to illustrate the normal degree of blocking found in the standard test system.

¹ H. M. BRUCE, *J. Reprod. Fert.* 1, 96 (1960).

² H. M. BRUCE, *J. Anim. Sci.* 25 (Suppl.), 83 (1966).

³ A. S. PARKES and H. M. BRUCE, *Science* 134, 1049 (1961).

⁴ R. K. CHIPMAN, J. A. HOLT and K. A. FOX, *Nature* 210, 653 (1966).

⁵ R. K. CHIPMAN and K. A. FOX, *J. Reprod. Fert.* 12, 233 (1966).

⁶ F. H. BRONSON and B. E. ELEFThERIOU, *Gen. comp. Endocr.* 3, 515 (1963).

⁷ H. M. MARSDEN and F. H. BRONSON, *Nature* 207, 878 (1965).

⁸ R. K. CHIPMAN and K. A. FOX, *J. Reprod. Fert.* 12, 399 (1966).

5% from the 74% control value. It should be noted that these figures are based only on inseminations occurring on days 2–4 after pairing due to a high rate of out-of-phase (midday) inseminations occurring during the first day that ICR males were paired with C57BL/6J females. Exposure of inseminated ICR females to either ICR or C57BL/6J males resulted in slight, if any, depression of implantation success when compared to the long-term control value of 92% (Table). The figures are, of course, not directly comparable but it is difficult to construe pregnancy rates of 80% and 75% as anything other than a trivial depression regardless of control values.

The negative results of these experiments document the widespread loss of the blocking phenomenon among inbred mice. Both male and female wild house mice are capable of playing their respective roles in either evoking or responding with an implantation failure⁸. Blocking capacity has been demonstrated in several random-bred as well as in one inbred line^{9,10}. Many highly inbred strains, on the other hand, are deficient in this capacity and, as shown in this paper, the loss may be traceable to both sexes in at least one strain. BRUCE⁹ has previously demonstrated some degree of strain differences for both sexes in ability to promote or respond with a blocked pregnancy. KRZANOWSKA¹⁰ has reported that exposure to hybrid males results in a greater degree of synchrony of oestrus than does exposure to inbred males (also due to a urinary pheromone). It might, therefore, be suspected that homozygosity per se is a contributing factor in the loss of blocking capacity among many inbred strains. Such is not the case as shown in the first experiment where a heterogeneous stock developed from inbred lines also failed to show the block. The loss in blocking capacity must, therefore, be traceable to the intentional or unintentional selection for reproductive efficiency which normally accompanies intensive inbreeding¹¹. The pregnancy blocking phenomenon may be lost by only one sex (for example, ICR males do not block ICR females, but these females can be blocked by wild males). Thus loss of the phenomenon in one sex would effectively remove the phenomena from a laboratory colony.

The results of these experiments also bear on another problem in pheromone research. Urine of C57BL/6J males is apparently incapable, or only slightly capable, of blocking pregnancy, yet this urine is capable of accelerating oestrus¹². This would seemingly indicate that separate urinary factors control the appearance of the 2 phenomena. This statement cannot be made with any great degree of strength because of the complexity of the problem¹³, yet it can be stated that the data do not lend support to the concept that one pheromone in male urine acts to both accelerate oestrus and block implantation¹⁴.

Résumé. Des expériences sur l'inhibition de l'implantation normale de l'œuf fertilisé dans la paroi utérine (l'effet BRUCE), faites avec plusieurs générations de souris consanguines ainsi qu'avec un groupe hétérosanguin, indiquent que la disparition de cette inhibition est due à la sélection plutôt qu'à l'homozygosité. L'odeur provoquant cette inhibition et celle qui favorise la synchronisation oestrogénique (l'effet WHITTEN), semblent être des émanations urinaires différentes.

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⁹ H. M. BRUCE, *J. Reprod. Fert.* 6, 451 (1963).

¹⁰ H. KRZANOWSKA, *Folia biol.*, Kraków 12, 415 (1964).

¹¹ D. S. FALCONER and R. C. ROBERTS, *Genet. Res.* 1, 422 (1960).

¹² H. M. MARSDEN and F. H. BRONSON, *Science* 144, 1469 (1964).

¹³ W. K. WHITTEN, in *Advances in Reproductive Physiology* (Ed. A. McLAREN; Logos and Academic Press, New York 1966), vol. 1.

¹⁴ This investigation was supported by research grants HD-01141 and HD-00767 from the National Institute of Child Health and Human Development.

STUDIORUM PROGRESSUS

Berechnung von Konzentrationsprofilen in Blutkapillaren und Nierentubuli unter Verwendung der GRÄTZ-NUSSELTschen Differentialgleichung

Zur Vereinfachung von Berechnungen des Stoffaustausches zwischen biologischen Gefässen wie Blutkapillaren und Nierentubuli und ihrer Umgebung gehen zahlreiche Autoren (DOLE¹, THEWS², BLUM³, HUDSON und CATER⁴ u.a.) von der Voraussetzung konstanter Konzentration und Strömungsgeschwindigkeit im Querschnitt der Gefässe aus. Diese Voraussetzung ist aber streng genommen nie vollständig erfüllt: Die Strömungsgeschwindigkeit ist parabolisch verteilt, und durch die Penetration der Moleküle in die Umgebung entstehen Konzentrationsunterschiede im Kapillar- und Tubulusquerschnitt, die nochmals von der Geschwindigkeitsverteilung der Strömung beeinflusst werden. Die Frage nach Grösse und Einfluss der Konzentrationsprofile auf den Stoffaustausch ist in neuerer Zeit wiederholt untersucht worden. Insbesondere haben POLLOCK und BLUM⁵ Gleichungen abgeleitet, die es erlauben, die Ausbreitung einer gelösten, durch die Wandungen diffundierenden Substanz im Hagen-Poiseuille-Profil eines durchströmten

Gefässes zu berechnen. Sie haben dabei gezeigt, dass unter den geometrischen und physikalischen Bedingungen, die in Blutkapillaren herrschen, das Massenzentrum einer gegebenen Menge gelöster Substanz sich mit einer Geschwindigkeit ausbreitet, die der durchschnittlichen Flussgeschwindigkeit im Gefäss entspricht; hieraus leiteten sie das wichtige Ergebnis her, dass die gelösten Substanzen – d.h. Substanzen mit Diffusionskoeffizienten, die zwischen denen des O₂ und des K⁴² liegen – die Kapillare mit einer Geschwindigkeit verlassen, die nur von den Permeabilitätskonstanten der Kapillarwand und

¹ V. P. DOLE, *Am. J. Physiol.* 139, 504 (1943).

² G. THEWS, *Acta biotheor.* 10, 105 (1953).

³ J. J. BLUM, *Am. J. Physiol.* 198, 991 (1960).

⁴ J. A. HUDSON und D. B. CATER, *Proc. R. Soc. [B]* 161, 247 (1964).

⁵ F. POLLOCK und J. J. BLUM, *Biophys. J.* 6, 19 (1966).