

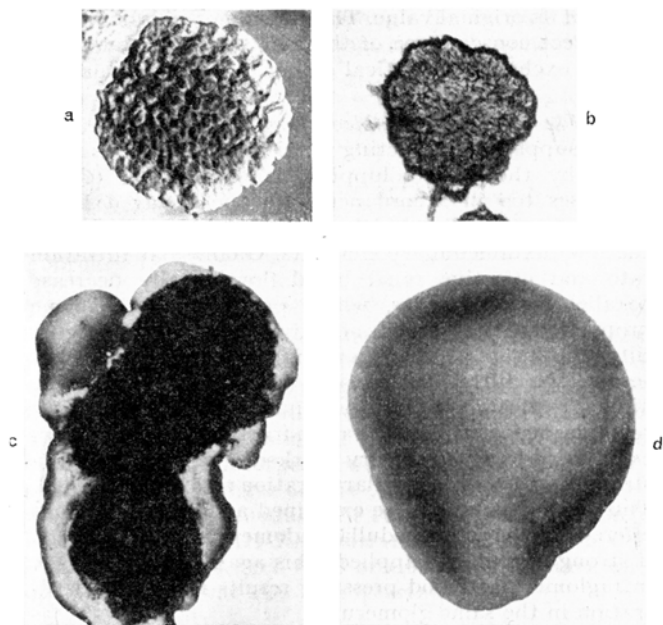


Abb. 1. 16stündige Kolonien auf Agarplatten (a bei Gegenwart von Kohlendioxyd, die übrigen bei gewöhnlicher Atmosphäre gewachsen). – a Kolonie von unbekapselten Milzbrandbazillen, b Kolonie von unbekapselten Kartoffelbazillen, c und d Kolonien von Milzbrandbazillen, die durch Behandlung mit Kartoffelbazillenextrakt bekapselt und begeißelt gemacht worden sind; c schleimige, zerfließende Kolonien mit dunklerer Mitte, ähnlich den Kolonien der bekapselten Urform des Kartoffelbazillus, d schleimige, zum Zerfließen neigende Kolonie von homogener Beschaffenheit. Vergr. 20:1.

Da die Versuche, unter Ausschluß der möglichen Fehlerquellen, soweit sie im positiven Sinne ausgefallen sind, stets zu demselben Ergebnis geführt haben, müssen wir annehmen, daß es tatsächlich gelingt, auf die angegebene Weise eine Mutation zu induzieren, wobei nicht nur die bezweckte Bekapselung der unbekapselten Milzbrandvariante, sondern auch ihre Ausstattung mit einem Geißelapparat zustande kommt. Wir sprechen hier absichtlich von einer Mutation, denn es handelte sich nicht um eine vorübergehende Variation. Zudem konnte auch dem Einwand begegnet werden, es könnten vielleicht in der ursprünglichen, unbekapselten Milzbrandkultur etwa latent vorhanden gewesene bekapselte Keime durch Einwirkung des Extraktes bekapselter Formen die Oberhand gewonnen haben. Die neue Mutante hat doch außer der Kapselbildungsfähigkeit eine durchaus milzbrand-

bazillenfremde Eigenschaft aufzuweisen, indem sie über einen Geißelapparat verfügt. Es ist zu betonen, daß die mutierten, bekapselten und begeißelten Milzbrandbazillen in morphologischer Hinsicht ganz den ursprünglichen Kartoffelbazillen entsprechen. Insbesondere ist hervorzuheben, daß die Kapseln kein so festes Gefüge zeigen wie die ursprünglich bekapselten Milzbrandbazillen. Sie erscheinen auffallend schleimig, mit ausgesprochener Neigung zum Zerfließen. Auch sind die einzelnen Bazillen etwas kleiner und gleichen auch in dieser Hinsicht den Kartoffelbazillen.

Die geschilderte Mutation läßt sich übrigens, wie spätere Versuche zeigten, auch auf einfachere Weise erzwingen, nämlich durch Beimpfung einer keimfrei filtrierten Bouillonkultur von bekapselten Kartoffelbazillen mit kapsellosen Milzbrandbazillen und Aussaat der Kultur auf Agarplatten nach einer Bebrütungszeit von 24 Stunden.

Auf die geschilderte Weise ist es uns später gelungen, durch Zusatz von Zellsubstanzen bekapselter Milzbrandbazillen zu einer unbekapselten Kartoffelbazillenvariante (Abb. 1b) bekapselte Kartoffelbazillen zu erhalten. Sie zeigten ein ähnliches Aussehen wie die ursprünglich bekapselten Kartoffelbazillen. Auch vermehrten sie sich, im Gegensatz zu bekapselten Milzbrandbazillen, selbst in gewöhnlicher Atmosphäre, in Form saftiger, glatter Kolonien, allerdings nicht auf gewöhnlichem, wohl aber auf Leberagar nach HUDDLESON.

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Summary

Experiments have been carried out with strains of *Bacillus anthracis* and *Bacillus mesentericus* which in consequence of a mutation have lost their capsulas.

Non-capsulated living anthrax bacilli mixed with bacteria-free extracts of capsulated mesentericus bacilli may undergo a mutation which results in the appearance of constant strains of capsulated and flagellated bacilli with colony formation peculiar to *Bacillus mesentericus*. Similarly, after treatment of non-capsulated mesentericus bacilli with extracts of capsulated anthrax bacilli it is possible to isolate capsulated mesentericus bacilli.

It is pointed out that in both cases there is the question of the result of an induced mutation caused by the introduction of genes of the one species into the other.

Antibacterial Activity of *Penicillium divergens* Bainier

Among five hundred and thirty species of the genus *Penicillium* which we have tested on Czapek-Dox medium, *P. divergens* BAINIER showed no antibacterial activity. This mould, however, when grown on modified Raulin-Thom solution gave an antibiotically active filtrate inhibiting the growth of *St. aureus* and *Esch. coli*.

The active substance has been adsorbed on charcoal and eluted with a mixture of ether and acetone (2:1). The solution obtained was reduced to $\frac{1}{10}$ of its original volume by evaporation, diluted with ether and passed through a column of alumina. The following crystallization yielded 25 mg of antibiotic substance from 1,000 ml of culture filtrate. The isolated substance was found to be identical with patulin (clavacin, clavatin, claviformin,

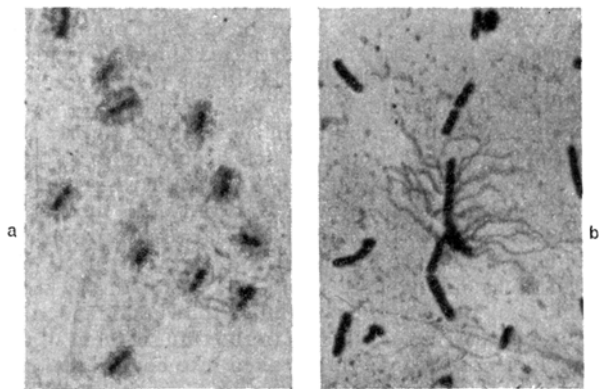


Abb. 2. Mit Zellmaterial von bekapselten Kartoffelbazillen behandelte Milzbrandbazillen. Bei a kapseltragende, bei b begeißelte Stäbchen (Färbung mit Karbolthionin bzw. nach ZETINOW). Vergr. 2000:1.

expansine) which has been previously obtained from culture filtrates of *P. expansum*¹, *P. claviforme*², *P. patulum*³, and *Asp. clavatus*⁴. Like *P. expansum*, *P. patulum*, and *P. claviforme*, *P. divergens* belongs to the group *Asymmetrica fasciculata* of the genus *Penicillium*.

Using the method described by BRACK, we found among other metabolites of this mould gentisinic acid and gentisin alcohol. The statements⁵ about their antibacterial activity have been checked⁶.

J. BARTA and R. MEČIŘ

Prague, March 14, 1948.

Zusammenfassung

Aus den Kulturfiltraten des Schimmelpilzes *P. divergens* BAINIER wurden drei antibiotische Stoffe – Patulin, Gentisinalkohol und Gentisinsäure – isoliert.

¹ A. VAN LUIJK, Mededelingen phytopath. Lab. Scholten 14, 43 (1938).

² W. H. WILKINS and G. C. M. HARRIS, Brit. J. Exp. Path. 23, 166 (1942).

³ E. CHAIN, H. W. FLOREY, and M. A. JENNINGS, Brit. J. Exp. Path. 23, 202 (1942).

⁴ S. WAKSMAN, E. S. HORNING, and J. SPENCER, J. Bacteriol. 45, 233 (1943).

⁵ A. BRACK, Helv. chim. acta 30, 1 (1947).

⁶ J. BARTA, M. KRAJNÍK, R. MEČIŘ, and V. PIČMAN, Chemický Obzor 22, 49 (1947). – J. BARTA and R. MEČIŘ, Chemický Obzor (in press) 23 (1948).

Glomerular and Tubular Function in Experimental Renal Cortex Ischæmia

Recent studies by TRUETA, BARCLAY, DANIEL, FRANKLIN, and PRICHARD¹ opened new aspects in the research field of renal physiology and pathology. These authors were able to show that the application of certain stimuli (such as faradic stimulation of the sciatic nerve or of the nervous network of the renal artery, administration of pituitrin, staphylococcus toxin, various pathological events, etc.) results in a very marked circulatory change, i.e. the blood of the renal artery flows via "juxtamedullary" glomeruli (glomeruli of the deepest zone of the renal cortex) – vasa recta, directly to the renal vein, thus rendering the cortex ischæmic and the medulla hyperæmic. Consequently, the glomeruli and tubuli of the cortex, representing the vast majority of the filtering and excreting elements of the kidneys, are completely excluded from the circulation. So the blood of the renal artery, diverted by this shunt, traverses the kidney only through the juxtamedullary glomeruli, the number of which is inadequate to cope with the task of normal urine production, but on the other hand their larger size and, in the first place, the fact that their vas efferens is wider too especially enables them to act as shunters.

In our experiments (20 adult dogs in narconumal anaesthesia), the changes of glomerular and tubular functions in cortical ischæmia caused by bilateral faradic stimulation of the nervous networks surrounding the renal arteries were investigated, by the well-known and excellent clearance methods of H. SMITH².

Our results can be summarized as follows:

(1) *Glomerular filtration* as measured by the mannitol (Cm) and creatinine (Ck) clearances decreased in all cases of cortical ischæmia, in some cases even below one-

tenth of its original value. This phenomenon is obviously the direct consequence of the fact that the "by-pass" circuit excludes all cortical glomeruli from the circulation.

(2) *The effective renal blood flow* (i.e. the amount of blood supplying the acting renal parenchyma) as measured by the p-aminohippuric acid clearance (C_{PAH}) decreases too in accordance with the changed blood flow, being thus diverted from the numerous cortical to the few juxtamedullary elements. Glomerular filtration rate and effective renal blood flow usually decrease parallel to each other, which proves that the same proportion of the kidney's effective blood flow undergoes filtration in the still functioning glomeruli; in other terms, the filtration fraction (the proportion of the kidney's effective blood flow undergoing filtration, Ff) remains unaltered. The filtration fraction increased, however, in cases where a very marked effect, leading to a strongly reduced glomerular filtration rate, was obtained. This phenomenon can be explained as follows: The vas efferens of the juxtamedullary glomerulus contracts too if strong stimuli are applied; this again, by raising the intraglomerular blood pressure, results in increased filtration in the same glomeruli.

(3) *Urine flow* decreased significantly in every case; in some cases even temporary anuria occurred. This latter is in all probability the consequence of the ischæmia involving even the juxtamedullary glomeruli if very strong stimuli are applied. *Tubular* water reabsorption remained unaltered in some cases (pure glomerular oliguria) but increased in others.

(4) *Maximal tubular secretion* (tubular mass, Tm_{PAH}) greatly diminished as a consequence of the ischæmia, leaving the cortical tubuli unsupplied.

(5) *Maximal rate of tubular glucose reabsorption* of the kidney (glucose tubular mass Tmg) decreased too; this is only natural if the reduced or abolished function of the cortical glomeruli due to ischæmia is taken into consideration. Decrease of Tmg, however, is not proportional to that of glomerular filtration (Cm) as shown by the general and well-marked increase of the Tmg/Cm ratio after faradic stimulation of the periarterial plexuses. The Tmg/Cm ratio was 1.3 in general; after stimulation its highest value was 4.3 (in one case). Raised values of this ratio could be explained either by decreased filtration in the functioning juxtamedullary glomeruli or by the assumption of increased glucose reabsorption in the same nephrons. The first assumption can safely be discarded by recalling that increase rather than diminution of Ff has been observed in some of the experiments. Consequently it seems likely that the second assumption holds good and raised values of the ratio occur on account of increased maximal glucose reabsorption in the juxtamedullary nephrons (i.e. in the tubuli attached to the juxtamedullary glomeruli). This phenomenon is easily explained by considering that these tubuli lie in the medulla, tightly surrounded by the vasa recta in which, according to TRUETA and co-workers the blood flow greatly increases whenever cortical ischæmia occurs. Naturally this medullary hyperæmia is likely to increase tubular reabsorption to a considerable extent. Increased water reabsorption, observed occasionally, may set in as a result of the same mechanism. Besides, the possibility that under the same conditions passive re-diffusion in the thin segment of the Henle loops occurs has to be taken into consideration.

(6) The p-aminohippuric acid concentration of the renal vein's blood increases following faradic stimulation (*diminished extraction*), thus proving that a great proportion of the blood escapes the functioning parenchyma

¹ J. TRUETA, A. E. BARCLAY, P. M. DANIEL, K. J. FRANKLIN, and M. L. PRICHARD, Studies of the Renal Circulation (Blackwell Publ.; Oxford, 1947).

² H. W. SMITH, Lectures on the Kidney (Kansas, 1943).