compound containing ammonia is said to be formed by sea-urchin eggs during fertilization: Örström, 1935), and pyruvic acid.

Another line of investigation is to measure the respiratory quotient during activation, technically a very difficult experiment. There is evidence (Laser and Rothschild, 1939) that the respiratory quotient is rather low during activation, which suggests that activation is associated with the breakdown of fats or proteins rather than carbohydrates.

These facts and speculations about metabolism during the early phases of the fertilization reaction suggest that activation may be associated both with anaerobic processes and with aerobic ones involving the breakdown of fats or proteins. The latter may have an inhibitory effect on the former, including acid production. The inhibitory effects of aerobic processes on fermentation are well known, and the possibility of such a Pasteur effect in the fertilization reaction could be investigated by specific Pasteur-effect poisons such as ethyl carbylamine.

So far we have discussed only the fertilization reaction. There is the separate problem whether there is any metabolic difference between unfertilized and actually fertilized eggs. The researches of Runnström (1933) and Korr (1937) have led to the rather attractive theory that fertilization induces a cytochrome type of metabolism, while the unfertilized egg respires through a non-ferrous autoxidizable carrier of the flavin or pyocyanine type, the cytochrome being present but inactivated. The evidence for this theory is too complicated to discuss in detail here, other than to mention that cyanide is stated to have little inhibitory effect on unfertilized eggs, but a marked effect on fertilized ones. How is cytochrome inactivated in the unfertilized egg? It is well known that changes in the physical state of the egg protoplasm take place as a result of fertilization (Mirsky, 1936; Mazia, 1937; Monroy and Montalenti, 1946); these might result in the activation of cytochrome, but there is no evidence that they do. Korr and Runnström's results have recently been disputed (Robbie, 1946), and it is therefore urgently necessary to repeat the experiments, which, from a technical point of view, are comparatively simple.

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INFLUENCE OF PENICILLIN ON THE COAGULATION OF BLOOD

WITH ESPECIAL REFERENCE TO CERTAIN DENTAL OPERATIONS

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Certain minor operations in oral surgery depend for their success on the organization of a firm blood clot in a cavity in bone. This is particularly the case in the operation of apicectomy, where the excision of the end of the tooth root leaves a small but appreciable cavity in the bone covered only with a thin flap of mucoperiosteum. If the clot in this cavity breaks down the sinus which forms leads down to the cut surface of the tooth root and permits it to become infected.

Since penicillin has been available it has become a common practice to introduce the powder into the cavity before suturing. Such an amount of powder may, however, represent as much as 10,000 units or more of penicillin, and a marked tendency for the clot to break down has been observed in cases so treated. Because of this, experiments were made to see whether penicillin had any action on the coagulation time of blood or on the contraction of the clot.

The first experiment was carried out with an impure commercial penicillin (sodium salt) containing 361 units per mg. Of this, 100,000 units was dissolved in 0.5 ml. of normal saline, and serial dilutions (0.25-ml. volumes) were made in normal saline, leaving one volume of normal saline as a control. Normal human blood was then taken from a vein and immediately 0.25-ml. volumes were added to each tube and mixed. The tubes were then observed and the time which elapsed before clotting took place was recorded. A later examination was made to see whether or not the clot had contracted.

It was thought that the anticoagulant effect observed might be due to the impurities in the penicillin, so the same experiment was repeated using pure crystalline sodium salt of penicillin, and in the accompanying table the results are

Table showing effect of Penicillin on Coagulation Time of Human Blood

Final Concentration of Penicillin in Blood (Units per ml.)	Coagulation Time	
	Impure Penicillin	Crystalline Penicillin
50,000	No clot in 24 hours	No clot in 24 hours
25,000	" "	" "
12,500	" "	32 minutes
6,250	75 minutes	11 "
3,125	7 "	7 "
1,562	4 "	5¼ "
781	—	5 "
340	—	2¼ "
170	—	2 "
Control	2 minutes	2

contrasted with those obtained with the impure salt. It will be seen that the result with crystalline penicillin differed only in detail from that with the very impure commercial product, showing that penicillin itself has a considerable retarding action on blood-clotting.

Effect on the Contraction of the Clot

In the first experiment, with impure penicillin, it was noticed that in the tube containing 6,250 units per ml., in which clotting was much delayed, the clot did not contract. In the observation with pure penicillin the whole of the serum was drawn off after 24 hours and its volume measured. The amount of serum obtained from the control was considerably greater than that from any of the tubes containing penicillin, indicating that even so little as 340 units per ml. had some retarding effect on the contraction of the clot.

Conclusions

These results have no bearing on the systemic application of penicillin, as the concentration of the drug in the blood is then in the region of only 1 unit per ml. or less. However, it is quite easy to introduce locally sufficient to interfere seriously with coagulation and contraction of the clot.

It would appear, therefore, that the local use of penicillin in an operation where the formation of a firm blood clot is of importance should be limited to washing out the cavity with a solution of the drug not exceeding 100 units per ml. This could, of course, be combined with intramuscular injections if there is any reason to fear wound infection by penicillin-sensitive organisms.

IRRADIATION OF GASTRIC CANCER*

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While encouraging progress has been made in dealing with cancers in more superficial and accessible sites, cancer of the stomach still remains a problem. It is responsible for 13,000 deaths annually in Great Britain, and 40,000 in the U.S.A. (Wilbur and Shenson, 1942)—that is, 33% of all cancer deaths in America (Mullen, 1941). But, worse still, its highest incidence in men and women is between 40 and 60 years, when they have established a place in life, a home, and a reputation ; when they are most useful to their profession and their country, and most necessary to their families (Ogilvie, 1945). It is the commonest type of cancer, with the worst results from treatment, for on the average only 1–4% of all cases are alive after five years following curative surgery, and only about four months' prolongation of life can be obtained by palliative operations (Livingston and Pack, 1941).

What can be done to decrease this annual toll of valuable lives ? Apart from the possibility of prevention, about which we are able to do little until we know more of the causal factors, the problem is one of diagnosis and treatment. Early diagnosis is particularly important, for we know the vast majority of patients can be cured if treated by radical surgery when the disease is localized to the stomach. But at present some 80% of cases of gastric cancer are beyond any hope of cure by surgery alone when first brought to the surgeon (Ogilvie, 1938). In spite of the tremendous advances that have been made in the surgical treatment of this disease during recent years, radical surgery can hardly become more radical, for physiological or technical reasons. Its limitations are set by Mayo's dictum that a live patient is one of the essentials of a successful operation, and not by timidity and lack of enterprise by surgeons (Ogilvie, 1945). But what of irradiation—for post-mortem findings show that over 20% of people dying of gastric cancer have the disease still confined to the stomach and immediately adjacent lymph glands (Livingston and Pack, 1939) ? Owing to the impossibility of a surgical cure in such a vast number of cases, many other forms of treatment, including irradiation, have been tried in the past, but without striking success. Hardly had Roentgen discovered *x* rays in 1896 when Despeignes applied them to the external irradiation of a gastric cancer.

There is no need for us to recall the different forms and combinations of irradiation applied to this viscus from then to the present day. It should suffice merely to make some general remarks on their limitations and shortcomings.

External irradiation fails because of the deep situation of the gastric tumour and its close relation to other vital organs—both factors tending to prevent adequate tumour dosage—and because of the high but variable radio-resistance of gastric cancer cells, possibly increased by infection. This high resistance may be only apparent, owing to limitation of the tumour dose by severe general and skin reactions. Movements of the tumour make accurate centring of the *x*-ray beam at repeated exposures difficult to obtain. Livingston and Pack (1941) stated that most patients will not survive long enough to benefit from prolonged external irradiation alone because of the profound state of malnutrition many of them attain.

Contact therapy with the Chaoul tube covers a relatively small area (2 cm. diameter) in each field with very little penetration at low voltage. Pack (1939) found that only 22% of the surface dose penetrated to 1 cm. below the surface. For comparison, Fairchild finds that 32% of the surface dose of high-intensity irradiation penetrates to 10 cm. below the surface with the technique he has been using. With the Chaoul tube bulky tumours could not be destroyed by single surface doses at one operation, but needed repeated exposures. This could be done only through some kind of fistula or pouch formation. With such a small field of 2 cm., repeated applications would be required for most inoperable tumours, with the obvious difficulty of adequate and uniform dosage. Also, such localized irradiation would have no appreciable effect on any glandular or other local spread, the presence of which is the usual reason for inoperability.

Radon seed implantation has the same difficulty of uniform and adequate dosage (as shown by subsequent radiography) when introduced at operation from either serous or mucous surface, or through a gastrostomy opening or the oesophagoscope. There are also dangers of haemorrhage and infection and perhaps perforation due to massive necrosis of the tumour, while the adjacent field of spread does not receive adequate irradiation.

Intracavity irradiation with the five-way tube described by Livingston and Pack (1941) has, they claim, the advantages of easy application, fractionation of doses, avoidance of damage to adjacent vital organs, freedom from dangers of haemorrhage, infection, and perforation, and no interference with food intake. But they had not at that time determined how effective a total dose patients would stand, the most effective fractions into which to divide the total dose, or the results as regards palliation or cure. Used

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