Of course, before any portal substances can penetrate the systemic stream, they have to pass normal cells in the centre of the lobule, but these cells represent only a small fraction of the whole, as it is obviously mathematically correct that the cells in the periphery form the majority of the cells in the lobule.

Among its many functions the liver acts as a detoxicator of poisonous substances absorbed from the intestinal canal via the portal vein. Indole and phenol are examples of noxious substances carried by the portal vein: they are products of protein decomposition and are formed in the large bowel by bacterial action on the amino-acids tryptophane and tyrosine respectively. These are detoxicated in the liver by oxidation, and conjugation with sulphuric acid, and pass on to the body, from which they are eliminated by normal kidneys most probably within twelve hours. Indole is conjugated to indican, and consequently the proportion of indican in the urine forms a rough guide to the amount of putrefaction occurring in the large bowel. Thus indican is present in large quantities in the urine of a patient suffering from intestinal obstruction, but apart from such a grave lesion it is found almost invariably in the urine of constipated persons and can be made to disappear therefrom by purgation. The amount of indican in the urine might serve as a guide to the functional capacity of the liver for dealing with portal toxins, especially in subjects of constipation—a condition present in practically all pre-eclampsics or eclampsics. In constipation we have every reason to believe that indole is passing via the portal vein to the liver, which, if functioning correctly, will convert it into indican, and the latter substance will be detected in the urine. If the liver fails to function, no indican should be present in the urine. The absence of indicanuria in a patient who is purged obviously has a different interpretation, and in eclampsia may be due to failure of the kidneys to excrete it.

An interesting experiment was suggested by a Russian surgeon, Eck, and successfully carried out by Pavlov. An artificial opening was made connecting the lumen of the portal vein with that of the vena cava in a dog. The portal vein was then ligated above the anastomosis, so that the blood passed directly into the systemic circulation without passing through the liver. In some of the animals operated on in this way it was found that so long as their diet consisted only of carbohydrates they could be maintained in fair health. If they were given a large meal of meat, many of them became ill and suffered from convulsions which ended in coma. At the same time there was a large increase in the ammonia output of the urine. This condition was supposed by Pavlov to be due to ammonaemia, the liver being regarded as protecting the body from ammonia produced in the intestine by converting it into urea. In this condition—Eck's fistula—the speed and amount of conjugation of bodies such as indole and phenol is greatly reduced.¹

Slight injury to the liver by chloroform and phosphorus has little effect upon the phenol conjugation, but extensive injury reduces it greatly. Pelkan and Whipple² suggest that the fatal result of the Eck fistula experiment or even of chloroform poisoning may be due to the lack of conjugation of phenols. It has been pointed out by Gibbon FitzGibbon²—and I have personally confirmed this in my own experience—that the eclamptic patient usually suffers from constipation and indulges in dietetic excesses. Gibbon FitzGibbon lays great stress upon the intestinal overload, and certainly the success of the Rotunda treatment (purges and high colonic washes) confirms this belief. It is also interesting to note that the body weight of patients developing eclampsia increases more than the average.² This abnormal increase would be expected in a patient who is overeating. The seasonal variation, being highest in spring, could be explained also in this way, for in the months immediately preceding more meat and more food as a whole are consumed. An eclamptic patient therefore appears to be in a suitable condition to suffer from intestinal toxæmia. She is constipated and overeats, and her detoxicator—the liver—is damaged, which, on analogy with the kidney, may allow noxious substances from the portal vein to pass unchanged into the general circulation,

causing a condition closely resembling that found in any animal upon which Eck's experiment has been performed. In such a patient purging and colonic washes will obviously not only eliminate the primary toxin, but cut off the supply of the secondary toxin at its source.

From what has been said above, it will be clear that one might expect eclamptic women, even though constipated at the time, to exhibit either very little or no indicanuria, and this I have almost always found to be the case in the few eclampsics whom I have investigated in this manner.

Summary.

In cases of toxæmia of pregnancy there is present in the circulation a toxin (or toxins) of unknown origin which affects the cells of many organs, interfering with their normal functions. The kidneys, if affected, no longer act as barriers to the passage of certain colloids from the blood into the urine. Should the liver be affected, it may no longer detoxicate portal poisons, but allow either all or some of them to pass into the general circulation, introducing a secondary toxæmia which may be the cause of the convulsions.

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INCIDENCE OF THE SEROLOGICAL TYPES OF THE PNEUMOCOCCUS IN LOBAR PNEUMONIA.

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THE incidence of the different serological types of the pneumococcus in lobar pneumonia has been studied extensively during the past seventeen years, and the original classification of Dochez, Avery, Gillespie, and others is now accepted by most bacteriologists. In the present article, in addition to a note of recent observations on the incidence of these types in Edinburgh, it is proposed to review briefly the findings of different observers during the past few years.

By protection tests and the agglutination reaction with antisera Dochez and Gillespie were able to divide strains of the pneumococcus into four groups, designated I, II, III, and IV. Groups I, II, and III were specifically differentiated in this way; Group IV comprised heterogeneous strains which could not be identified immunologically with the other three groups; Group III was also characterized by the possession of a thick mucoid capsule noticeable in the mucoid character of growths in culture media (*Pneumococcus mucosus*). More recently a number of constituent types referable to Group IV have also been identified by certain workers (Cooper, *et al.*), but, as will be shown, in this country such further serological subdivision seems unnecessary from a practical standpoint, though it may be of importance in other countries. The results of Dochez and Gillespie are noted in Table I.

TABLE I.—The Original Classification of *Pneumococci* by Dochez and Gillespie.

	Classification by Protection Tests.		Classification by Agglutination Tests.	
	No. of Cases.	Per cent.	No. of Cases.	Per cent.
Group I ...	28	45	22	41
Group II ...	12	20	11	20
Group III ...	9	14	9	17
Group IV ...	19	22	12	22

Classification by these two methods was carried out in the same series of cases. The similarity of both sets of results is at once apparent. Of the cases, 77 per cent. were due to pneumococci of the three typical groups, the remaining 23 per cent. being included in the heterogeneous Group IV.

Following on this work a number of other observers have recorded their results from time to time (Table II).

TABLE II.—*Type Frequency of Pneumococci in Lobar Pneumonia recorded by Various Observers.*

Observers.	Period.	Total No. of Cases.	Frequency Percentage.			
			I	II	III	IV
UNITED STATES OF AMERICA :						
Dochez and Gillespie ...	1913	74	47	18	13	22
Cole	1915	150	38	30	11	21
Thomas	1917-21	239	25	11	15	49
Schorer	1917-18	101	31	15	18	36
Cecil, Baldwin, and Larsen	1921-26	1,913	24	19	13	33
Bullowa	1928-29	368	24	9	3	55
GREAT BRITAIN :						
Glynn and Digby	1919-23	361	38	27	4	31
Griffith	1910-22	150	31	33	7	30
Davidson and McLachlan	1924-25	52	64	7	15	14
Ferguson and Lovell ...	1925-27	116	43	4	0	53
Alston and Stewart ..	1929-30	186	29	40	4	27
SOUTH AFRICA :						
Lister*	1917	148	22 (C)	16 (B)	1 (E)	61 (A, D, etc.)
INDIA :						
Malone	1923-24	106	28	17	8	47
DENMARK :						
Christensen	1923	110	33	27	8	32
NORWAY :						
Thjötta and Hanneborg ...	1924	100	44	33	6	17

These figures, though not a complete statement of pneumococcus type incidence since 1913, are sufficient to show that the incidence of the different types varies greatly from time to time, and in different parts of the world. Types I and II between them account for about 58 per cent. of all the cases, Type III for 9 per cent., while 32 per cent. of the cases are allocated to Group IV. It is interesting to note the relative infrequency of the Type III pneumococcus in lobar pneumonia. The fact that nearly two-thirds of all cases of lobar pneumonia are caused by either a Type I or a Type II pneumococcus is a point in favour of a more general therapeutic use of anti-pneumococcal serum, which is now prepared as a polyvalent serum, containing antibodies for both Types I and II pneumococci.

Incidence of Pneumococci Types in Edinburgh, 1929-30.

During the period January, 1929, to June, 1930, the types of pneumococcus in 186 cases of acute lobar pneumonia were ascertained. In the majority of cases sputum was obtained immediately after the admission of the patient to hospital. In a number of patients with no sputum, where for therapeutic reasons it was necessary to ascertain the type of pneumococcus as soon as possible, lung puncture was performed (Stewart, 1930) and the organism isolated from the "lung fluid." Our method of determining the type was as follows.

One cubic centimetre of a saline emulsion of sputum was injected intraperitoneally into a white mouse of standard weight, and the type of pneumococcus determined according to the usual

* Lister (1917) in South Africa classified 148 strains of pneumococci from cases of pneumonia, allocating them into eleven groups, each indicated by a letter. The major groups A, B, and C accounted for 31 per cent., 16 per cent., and 22 per cent. of the strains respectively, leaving 31 per cent. in the remaining groups. According to the present methods of classification Lister's Group C would be identical with Type I, Group B with Type II, Group E with Type III, and the other groups, including the large Group A, would all be included in Group IV.

method of macroscopic agglutination, by the addition of standard typing serum to saline dilutions of peritoneal fluid. The agglutinating serums for the three standard types which we have consistently used were obtained in the laboratory of the Department of Health, City of New York, U.S.A., and were kindly sent to us by Dr. Bullowa of the Littauer Pneumonia Fund Hospital, New York. After a series of titration experiments it was found that the optimum dilutions of these serums for the test were as follows: Type I, 1 in 20; Type II, 1 in 10; and Type III, 1 in 5. Equal parts of peritoneal fluid washings and typing serum were added together, giving final dilutions of Type I, 1 in 40; Type II, 1 in 20; and Type III, 1 in 10. When no agglutination was observed with any of the three typing serums a separate test was made with undiluted Type II serum for the so-called "atypical" strains of Type II, which have been stated to agglutinate only with the maximum concentration of the serum. It has to be noted, however, that in no case have we been able to demonstrate the presence of this atypical Type II pneumococcus by serological methods. In addition, bile solubility tests were performed to exclude streptococci by adding two or three drops of 10 per cent. sodium taurocholate to 1 c.cm. of peritoneal emulsion, and in every test a control tube of emulsion without serum was included. In quite a number of cases agglutination was observed immediately after the addition of serum—in several cases it could be actually observed while the serum was being added—but in every case incubation at 37°C. for a period of time varying from fifteen minutes to two hours was sufficient to enable readings to be taken. In any doubtful case, and in all cases where no agglutination was observed after two hours, further readings were made at varying intervals up to twenty-four and thirty-six hours; the original reading, however, has always proved sufficient.

The results of typing pneumococci in 186 cases of lobar pneumonia admitted to the Royal Infirmary, Edinburgh, are noted in Table III.

TABLE III.—*Type Incidence of Pneumococci in 186 Cases of Lobar Pneumonia, Edinburgh, 1929-30.*

Type.	No. of Cases.	Percentage.
I	53	29
II	75	40
III	7	4
IV	47	27

From these figures it will readily be seen that Type II pneumococci have been most frequently found, that the incidence of Type I and Group IV organisms is about the same, and that Type III pneumococci are not commonly demonstrated in cases of lobar pneumonia. Stewart and Gibson, in a study of 43 cases of lobar pneumonia in Edinburgh, found that the incidence of the types was as follows: Type I, 19 per cent.; Type II, 48 per cent.; Type III, 9 per cent.; and Group IV, 23 per cent. These 43 cases are included in the present series, being among the earlier ones examined in 1929, and it may be seen that Type II pneumococci at that time were even more commonly found than during the year 1930.

It is interesting to compare our findings with the observations of Davidson and McLachlan. They found, during 1924-25, Type I pneumococci in 60 per cent. of the cases, and Type II in only 12 per cent. The type incidence has therefore changed very considerably in this particular area during the last five years, as the Type II pneumococcus is the organism most commonly associated with lobar pneumonia.

Death Rate in Relation to Types.

Certain observers have tabulated their mortality rate in lobar pneumonia in relation to the different types of organism. Although most series are small in number, an analysis of the combined results show Type III infections to have a high fatality rate—between 40 and 70 per cent. Type II infections come second, Type I infections next, and it has been fairly well established that pneumonia caused by organisms in Group IV tends to be associated with a relatively low mortality rate.

Of the 186 cases in our series, 45 died, giving a death rate for all types of 24 per cent. The death rate in relation to types is given in Table IV.

TABLE IV.—*Death Rate in Relation to Type Incidence, Edinburgh, 1929-30.*

T. ps.	No. of Cases.	No. of Deaths.	Death Rate (Percentage).
I	53	12	23
II	75	23	31
III	7	5	71
IV	47	5	10

It is to be observed that the order of severity is similar to that of other workers. The numbers, of course, are small, and may be insufficient for an exact statistical statement, but it is interesting to note that the death rate in Group IV is as low as 10 per cent.

Summary.

1. A brief review of the incidence of the different types of pneumococci in lobar pneumonia according to a number of observers from 1913 to date is given.

2. The incidence of pneumococcus types in 186 patients suffering from acute lobar pneumonia in Edinburgh during

the past eighteen months is recorded, and also the mortality rates associated with the different types.

The authors gratefully acknowledge facilities granted to them by the physicians to the Royal Infirmary, Edinburgh, and thank Professor T. J. Mackie for valuable assistance. The expenses of this work were met in part by a grant from the Moray Fund, Edinburgh University. One of us (J. M. A.) was in receipt of a grant from the Medical Research Council.

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A CASE OF OSTEOGENESIS IMPERFECTA.

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L. M., aged 34, a coloured woman, was admitted to the Holberton Hospital on July 3rd with a fracture of the left radius just below the insertion of the pronator teres, and a fracture of the right olecranon. Both fractures

which seems to suggest that the pain was not of a degree usually associated with fractures even in an infant. Her first recollection was of a fractured femur, which was followed by many fractures of the lower limbs up to the age of 16. These frequently occurred at school, if she fell or was pushed about by other children. She stated that the fractures were painful, and used to swell.

According to the hospital records, she was admitted in 1904, at the age of 7, with a fractured femur, and was in hospital from May 2nd to June 13th. The following year she was again

were the result of direct violence—by being beaten with a walking-stick. She was unaware that the olecranon was fractured, and complained only of the left arm, which she knew was broken, and a contusion of the left leg. Her complaints of pain in view of pending legal proceedings were not very convincing, as she showed little sign of distress on manipulation. There was also a remarkable absence of swelling, ecchymosis, or muscular spasm.

Family History.

The patient's father was a tailor, who died of senile decay three years ago. He had had no serious illnesses or fractures. Her mother, whose legs were deformed, died some years ago, probably from pneumonia. The mother's sister, thought to be in America, also had deformed lower limbs. A sister and two brothers are normal.

Patient's History.

The patient's mother told her that her legs were broken many times when a baby before she was old enough to feel pain,

in hospital, from March 27th to May 23rd, with a fractured femur. In 1909 she was in hospital from February 19th to March 11th, the diagnosis being fragilitas ossium. On this occasion fractures were not specifically mentioned, but in view of the diagnosis and her good health in other respects, it is probable that she had a fracture on this occasion also. For some years she was an inmate of the poorhouse, reserved for the destitute and very chronic cases. She did not at any time appear to have been destitute. From the age of 16 until the present time she had had no fractures.

Clinical Examination.

The only thing of note about the patient, apart from the deformities, was the blue colour of the sclerotics, which is very striking in a coloured person. Her height was 4 ft. 10 in., reduced by the shortening of the lower limbs. All the long bones of the lower limbs were grossly deformed, particularly the left femur, which was bowed forwards and outwards, and the right tibia and fibula bowed forwards and inwards—well shown in the accompanying photographs. The anterior superior spines