some symmetry, to realize the ideals of its founders, and only erred in evincing timidity in recognizing the need for an Imperial School of Science and research as distinct from a local institution. Something not dissimilar has previously occurred in Medicine.

Virtually a Science University.

I have described this confederation of colleges as virtually a science and technical university, and the phrase may stand. It has been taken to assume the formation of a uni faculty university, and is regarded as at once a heresy and a paradox. It is neither. The proposal is for a three-faculty university—science, mining, and engineering. I am not myself wedded to the phrase, but if an imperial ideal has been the thought fundamental which has all through led to the establishment of the College, the dependence of such an imperial institution upon other universities for its academic distinctions is surely destructive of the imperial ideal. Nor is the idea distinctive of the Imperial College. It exists elsewhere in other branches of work, and may find realization later by the coalescence of similar movements into an Imperial University. However that may be, this trend of thought has definitely influenced the character of the teaching and the research at Kensington, as was intended, and it would be folly to depart from a policy so thoroughly considered, and upon which so much money and effort has been lavished.

The institution has been established for the vocational training of men intended for the professions of chemistry, the various branches of engineering, economic biology, etc., and this vocational training requires for its essential substructure a wide general scientific training of such a kind that the special courses in the special professions are all founded on common courses in science. The system of training is that still known as the Huxley system. The tutorial and laboratory method characterizes it at every part. The students in the departments of physics, chemistry, geology, etc., learn the use of instruments by handling them until technique and scientific method become part of their very being. Set lectures are reduced to a minimum. The student may be said to discover for himself under the inspiration of his tutors. The applications of science serve as the models to illustrate the principles. The ample equipment renders possible the adoption of a system which avoids dependence for its teaching on textbooks and demonstrations.

A Lesson and a Model for Medicine.

In the daily round of my own duties as *servus professorum* it would be strange indeed if my thoughts did not frequently turn to my own profession and its splendid possibilities in the educational sphere, especially in London. It often strikes me that the parallel between medicine, chemistry, biology, mining, etc., is complete. The foundations are the same, and only the applications are different. At a particular period in his career at the Imperial College a student of any of the departments of knowledge could be diverted to medicine without delay or disadvantage, for, as I have said, the foundations are the same. The systems and methods of Kensington are applicable to medicine, and since they are costly they could only have been attained by combination of effort amongst the three constituent colleges.

Is there not in the history of the Kensington movements an example which may well be followed by the London medical schools? If the individuality of the separate schools here is retained while a combined effort for mutual assistance and support is sustained in the confederation of colleges, why should not the same system operate in medicine? It is true that combination of effort is difficult to secure in medicine, but, after all, in my experience, it is no less difficult in other professions. It must not be supposed that the path of the reformer at Kensington has been strewn with roses any more than it is anywhere else. All that can be said is that a sense of a common misfortune has proved stronger than vested interests. The tendency in medicine is centrifugal.

Combination, discipline, establishment of principles have carried Kensington as far as it has yet gone. Similar efforts in London medicine should lead to similar results, and one day perhaps we may see in London and elsewhere an Imperial School of Medicine, an Imperial School of Law, an Imperial School of Art, as we have to-day an Imperial School of Science and Technology. It may be the mission of the Universities Bureau to bring together the now scattered elements of such a confederation for the formation of a great Imperial University.

THE DEFENCE OF THE RESPIRATORY MEMBRANE AGAINST INFLUENZA, ETC.

BY

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In the account of a research on the action of ozone[1] carried out some years ago with M. Flack, after pointing out the poisonous action of too high concentrations on the lung, and the oedema and pneumonic condition produced thereby, and that very low concentrations could safely be used to add a quality to the air and take away offensive smell, we added the opinion "that ozone might possibly have some value in the treatment of disease of the respiratory tract if used in a concentration which produced a slight irritation and thus brought more blood and tissue lymph to the part.

Observations have demonstrated that the concentration which can safely be used in ventilation does not destroy bacteria in the air, and inhibits their growth on media slightly if at all. The respiratory membrane is much more easily attacked than the micro-organisms protected by their waxy or other resistant cuticle.

A poison gas like ozone, phosgene, or chlorine, when inhaled is concentrated by solution in the secretion covering the membrane, and the membrane defends itself by secreting fluid and so diluting and washing away the poison; hence the oedema of the lung, which increasing finally puts an end to the gaseous exchange and drowns the subject. The membrane responds in the same way to bacterial toxins.

How much a poison gas may have to be concentrated is shown by some experiments we carried out in 1915 on ciliated epithelium. While 1 in 100,000 of chlorine by volume is too irritating to breathe, it took over 1 in 40,000 by volume of chlorine to stop the movement of the cilia when chlorine water was added to the preparation.

In the case of smells, while it is true of certain substances that 1 in 100 million parts of air may be smelt, yet concentration of unknown extent must in this case also take place in the fluid bathing the olfactory sense organ. The act of sniffing, by directing the air on to one part of the membrane, must bring about this concentration.

In researches on the influence of atmospheric conditions on the nose[2] I have put forward the important influence which cool air—cool and therefore of low vapour tension—has on bringing more arterial blood to the respiratory membrane, and increasing evaporation from and therefore flow of tissue lymph through it. Warm moist atmospheres are against this natural washing and immunizing defence. In this, I claim, lies one explanation of the good effect of open air treatment, and the ill effect of crowded tenements. Exercise in the open air, by increasing the breathing perhaps five times, greatly increases the blood flow through and evaporation from the respiratory membrane, and in this lies one of the good effects of exercise. At Alpine health resorts the air is not only cool, but owing to its tenuity a greater volume must be breathed.

By some observations made in the recent spell of frosty weather, breathing first in and out of the nose, next in by the nose and out through the mouth, then in by the mouth and out through the nose, lastly in and out through the mouth, and taking the temperature with a thermo-junction inserted far back in the nose, I find the cooling, and therefore the evaporative, power of the air is by no means spent in the nose, but acts on the deeper parts and probably right down to the smaller tubes of the lungs. Especially is this the case when the breathing is made deep and the lungs fully expanded. A man may in an hour easily evaporate an ounce and a half of water from his membrane when taking exercise in cold weather.

There is another thing to consider, namely, the actual cooling of the membrane, which may check the growth of sensitive pathogenic bacteria—for example, those of cerebro-spinal fever. Hence, again, the ill effects of crowded huts and tenements in spreading respiratory diseases. Mouth breathing, or a blocked airway on one side of the nose, keeps the nose (or one side of it) at a higher temperature, and makes it a better incubator for the growth of such bacteria, while it lessens blood flow through and evaporation from it.

There is some evidence (this is now being investigated) that workers in SO_2 factories are relatively free from colds, also those in commercial gasworks; chemical manufacturers, as a class, have a low phthisis mortality rate; the taking of ordinary snuff has been praised for keeping off influenza; nose-drill and the daily use of some mild antiseptic as a nasal wash, snuff, or spray are recommended for the same purpose; and recently evidence has come forth of considerable interest—namely, that the clerks in certain offices of the electric tube railways ventilated with ozone-air had 3 per cent. of absences in the late epidemic, while the clerks in the other offices, not so ventilated, had 10 per cent. All these agencies, just as the antiseptics used by surgeons in wounds, and Almroth Wright's salt treatment, have the effect of drawing out lymph, and so washing and cleansing the part. In the case of the respiratory membrane they take the place of the natural action of breathing the cool outside air. Probably tobacco-smoking in sedentary indoor workers brings about an increased outflow of lymph required by the membrane. The need for smoking is not felt when taking vigorous exercise in the open air. The smelling salts which used to be popular must play the same part.

To combat the influenza infection, then, I would urge the deep breathing of cool air, brought about by exercise, sleeping in open air, and as an adjunct any spray, gargle, or snuff which enhances the outflow of secretion from the respiratory membrane of the nose and throat.

The wearing of a mask by raising the temperature and humidity of the air breathed is against the natural defensive mechanism. People must eat and speak together, and will continue to kiss. The public may in time be taught to sneeze and cough into handkerchiefs or newspapers and not at large, and so lessen the dissemination of infected spray. Public conveyances, canteens, schools, cinemas, etc., require to be far more freely ventilated, but infection cannot be prevented by such means. The natural defence must be raised by the discipline of open-air exercise and by proper housing, and until this is brought about the public will continue to be scourged by diseases which kill, maim, and impoverish far more than the late war.

Experiments for Determining the Temperature of the Nose.

SUBJECT H.—Left side of nose largely blocked by deflected septum; right side of nose quite free. Temperature of air 1.5° C.

Temperature of left side of nose—

Inspiring through nose,	expiring through mouth ...	30.6° C.
,, ,, mouth	,, ,, nose ...	32.3

Temperature of right side of nose—

Inspiring through nose,	expiring through nose ...	30.0° C.
,, ,, nose	,, ,, mouth ...	28 0
,, ,, mouth	,, ,, nose ...	33.3

Very cold early morning, just after bath and dressing. Temperature of air −5° C.

Temperature of right side of nose—

Inspiring through nose,	expiring through nose ...	21.4° C.
,, ,, nose	,, ,, mouth ...	19.0
,, ,, mouth	,, ,, mouth ...	27.1
,, ,, mouth	,, ,, nose ...	27.1

After tobogganing:

Temperature of right side of nose—

Inspiring through nose,	expiring through nose* ...	28.5° C.
,, ,, nose	,, ,, nose† ...	26.6
,, ,, mouth	,, ,, nose ...	30.0
,, ,, nose	,, ,, mouth† ...	24.3

* Quiet breathing. † Deep breathing.

Warm after two hours' walking:

Temperature of right side of nose—

Inspiring through nose,	expiring through nose ...	31.1° C.
,, ,, nose	,, ,, mouth ...	31.1
,, ,, mouth	,, ,, nose ...	33.3

SUBJECT H. A.—Observations taken in open air, after resting in warm room. Temperature of air −1.2° C.

Temperature of nose—

Inspiring through nose,	expiring through nose ...	33.8° C.
,, ,, nose	,, ,, mouth ...	32.8
,, ,, mouth	,, ,, mouth ...	34.4
,, ,, mouth	,, ,, nose ...	34.4

After walking fast for forty-five minutes, but not heated by the exercise. Temperature of air −0.5° C.

Temperature of nose—

Inspiring through nose,	expiring through nose ...	29.6° C.
,, ,, nose	,, ,, mouth ...	26.8
,, ,, mouth	,, ,, mouth ...	32.8
,, ,, mouth	,, ,, nose ...	34.1

The nose was warmer in the fourth observation than in the third because it had had more time to warm up after being cooled during the second observation.

The same subject, very warm after an hour's skating and rapidly walking back.

Temperature of nose—

Inspiring through nose,	expiring through nose ...	37.4° C.
,, ,, nose	,, ,, mouth ...	37.4
,, ,, mouth	,, ,, mouth ...	37.4
,, ,, mouth	,, ,, nose ...	37.4

The membrane at the back of the nose in contact with the thermo-junction was sufficiently flushed with blood through hard exercise to keep the junction at blood heat whatever the manner of breathing was.

Estimation of the Water Evaporated, and Heat Lost from the Membrane, which Determine the Flow of Arterial Blood and Lymph through it.

Observations taken at open window. Fine, overcast, snow on the ground. Temperature outside window: Wet bulb, 1° C.; dry bulb, 1° C.

Temperature of nose—

Inspiring through nose,	expiring through nose ...	31.8° C.
,, ,, nose	,, ,, mouth ...	29.8
,, ,, mouth	,, ,, mouth ...	32.4
,, ,, mouth	,, ,, nose ...	32.4

Volume of air expired in 10 minutes, collected by means of a mouthpiece, suitable valves, and a bag = 68 litres (pressure = 759.5; temperature = 279 abs.).

$$\therefore \text{ Volume of air expired in 1 hour} = 408 \text{ litres} = 408 \times \frac{274}{279} = 401 \text{ at } p = 759.5;\ T = 274 \text{ abs.}$$

That is, volume of air inspired at 1° C. (274 abs.) = 401 litres; 401 litres saturated at 274 abs. contain 5.18 × 0.401 gram H_2O.

Now the 401 litres inspired at 274 abs. will at 304.8 abs. occupy a volume $401 \times \frac{304.8}{274} = 446$ litres, and will therefore contain 33.10 × 0.446 gram H_2O. (See tables of mass of water contained in saturated air at different temperatures.*)

$\therefore$ No. of grams H_2O evaporated per hour = 33.10 × 0.446 −5.18 × 0.401 = 14.76 −2.18 = 12.58.

Exercise might raise this to 60 to 120 grams per hour.

Heat required to evaporate 12.58 grams = 12.58 × 598 = 7523 gram calories.

Now the heat required to raise a volume V of air in c.c. at temperature T and pressure p through $t°$ C. is—

$$V \times \frac{273}{T} \times \frac{p}{760} \times C \times 0.622 \times S \times t.$$

Where C = density of dry air; S = sp. heat of air.

$\therefore$ Heat required to raise 401,000 c.c. at 274° abs. and 759.5 mm. pressure through 31.8 − 1 = 30.8° C. is

$$401{,}000 \times \frac{273}{274} \times \frac{759.5}{760} \times 0.001293 \times 0.622 \times 0.242 \times 30.8$$
$$= 2393 \text{ gram calories.}$$

Total heat required to raise 401 litres of air saturated at 1° to 31.8° C. and saturate at that temperature is 2393 + 7523 = 9916 gram calories, or 10 kg. calories.

Exercise might raise this to 50 to 100 kg. calories per hour.

Observations taken sitting in a room, gas fire burning. Temperature of room: Wet bulb, 4.8°; dry bulb, 5.6°; dew-point, 3.7° C.

Temperature of nose—

Inspiring through nose,	expiring through nose ...	31.6° C.
,, ,, nose	,, ,, mouth ...	30.6
,, ,, mouth	,, ,, mouth ...	33.6
,, ,, mouth	,, ,, nose ...	33.8

Volume of air expired in ten minutes = 61·5 litres; (p = 759.5; T. = 279 abs.).

$\therefore$ Volume inspired in one hour = 369 litres, against 401 litres for the open air.

A difference is clear, without carrying through the full calculation, between the frosty open air and this very cold room. It is very great between cold and warm humid air, and the sudden change from one to the other obviously strains the functions of the membrane. The body is protected by clothes—not so the respiratory membrane. Hence the need to stay in a *uniform* atmosphere when infected with a catarrh.

A further discussion of this subject, and of the influence of open air and exercise on metabolism—a subject of no less importance—will be given in a report on "The Science

* Mass of water vapour in grams per c. metre of saturated air: 32° F., 5; 60° F., 13; 100° F., 45.

of Ventilation and Open-air Treatment," to be published by the Medical Research Committee, the first part of which is now in the press.

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[1] *Proc. Roy. Soc.*, 1911. [2] *Lancet*, May 10th, 1913 (with Muecke); BRITISH MEDICAL JOURNAL, April 16th, 1916.

CAUSE, PREVENTION, AND TREATMENT OF INFLUENZA.*

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DURING the first epidemic in Dublin last summer I isolated the *Bacillus influenzae* (Pfeiffer) without difficulty from the respiratory discharges of the first patients investigated. The culture medium I use as a routine is agar + 10 in reaction carefully made according to Eyre's directions and containing 1 c.cm. of fresh defibrinated unheated blood to each 10 c.cm. It will grow any aërobic pathogenic microbe with facility and profusion, not only the *B. influenzae*, but such difficult customers as *Micrococcus meningitidis*, *M. melitensis*, and even the gonococcus.

It appeared, therefore, very significant that in all my years of routine cultures of sputum I had not come across a microbe satisfying the cultural characteristics of the influenza microbe until the present epidemic.

There are several reasons why this bacillus has come under suspicion as the cause of the epidemic:

1. It has not been grown when present in the discharges.
2. It has often not been recognized when it has been grown.
3. Other microbes, ordinary catarrh-producing microbes, such as members of the pneumo-streptococcus group and *M. catarrhalis* group, always grow, and since none of them can conceivably be held to account for a pandemic, a filter passer is thought to be responsible.

1. Certain conditions are necessary for the cultivation of the influenza bacillus. It rapidly dies out if allowed to cool to room temperature. Therefore the discharges must be got to the laboratory in the shortest time and kept warm if possible. The medium must be suitable—such a one as I have described above, which for vaccine making purposes is far the most suitable owing to the hormonic influence of the fresh human blood on the bacillus. The commonly used blood smeared agar gives very poor results. Fildes, Baker, and Thompson,[1] when using this medium, failed to isolate the bacillus, but when they used a more suitable medium they succeeded constantly, and came to the conclusion that it was the cause. Others—for example, Macintosh—have isolated it in over 80 per cent. of cases. Has any one ever isolated this bacillus in such percentages from any series of cases of respiratory catarrh apart from an epidemic of influenza? On the blood smeared agar at the end of twenty-four to forty-eight hours the bacillus forms tiny dewdrop-like colonies which are very difficult to see. On my medium the colonies at the end of forty-eight hours may be several millimetres in diameter, are smooth, round, and have a ground-glass appearance.

2. At the end of twenty-four hours, when just isolated, the individual microbes are exceedingly small, and are often quite indistinguishable from cocci, especially if the magnification is not sufficiently high. Three times have I known the bacillus to be mistaken for cocci and the microbe said to belong to the *M. catarrhalis* group. Isolated from the cerebro-spinal fluid in a case of cerebro-spinal meningitis, I have known it to be mistaken at first for the meningococcus. In this respect the bacillus is not singular; for many years the bacillus of Mediterranean fever was thought to be a coccus, hence its name, *M. melitensis*; on suitable medium it invariably grows as a bacillus. So, too, young colonies of *B. coli* consist often of solely coccal forms, which become bacilli on further growth.

3. The microbes well known as catarrh-producing, such as members of the *M. catarrhalis* or the pneumo-streptococcus groups, can at once be dismissed as causes of the pandemic. None of them have ever been known to produce a pandemic. All of them are, of course, capable of producing epidemics and are responsible for the annual occurrences of pseudo-influenza. More recently certain very minute Gram-positive anaërobic microbes have been isolated in France in trench fever, polyneuritis, influenza, measles, rose measles, and two cases of typhus. They all appear to be similar and to have produced illness of very much the same type when injected into animals. They have also been isolated from the excreta of infected lice. I have no doubt such microbes do exist and do produce disease, but do they produce influenza? Quite similar microbes have been isolated from epidemic cerebro-spinal meningitis, from which the meningococcus can always be isolated. Does the filter passer produce this disease? If it does, we must stop using antiserum. It is important to remember that filter-passing Gram-positive cocci have before been isolated from cases of anterior poliomyelitis, and have been proved to be a phase in the life-history of streptococci and to have produced the disease in monkeys. Further, anaërobically and otherwise, strepto cocci can be grown so small that they pass through the Berkefeld and the coarser porcelain filters. I have made experiments with such a stolid microbe as the *Staphylococcus aureus*, and by varying the constitution of the medium have been able to make it vary in size from minute almost invisible dots to giant forms. It is well recognized that the tubercle bacillus can infect by such minute forms. Now streptococci of various sorts are constant inhabitants of the mouth and respiratory passages; they are always prepared to become pathogenic and complicate other infections. I suggest that in these cases these filter passers may be forms of streptococci or complicating infections *sui generis*.

The result of prophylactic inoculation with the antigen of the pure influenza bacillus adds great weight to the evidence for it as the cause. It is extremely easy to deceive oneself in this respect, because the incidence of the infection cannot absolutely be known. For instance, I know of one school of over 150 boys, all of whom got prophylactic injections, and none of them got the disease although it was raging in the vicinity. Dr. Parsons relates his experience of a school in which 30 per cent. of the boys got the disease. Half of the rest of the boys were then inoculated and half not. None of them, either inoculated or uninoculated, got the disease. Dr. Cremin, of Newcastle West, informs me that he inoculated 52 people in the midst of the epidemic, and only two mild cases occurred amongst them. On the other hand, much more significance is to be attached to the following results, because we have an indication of the extent of the infection. Dr. Keelan, of Mullingar, inoculated four members of the staff of forty-one of a racing establishment—all the uninoculated got the disease, not one of the inoculated. Among the students of University College, Dublin, of 182 uninoculated, 43.95 per cent. contracted the disease; of 113 inoculated, 21.2 per cent. contracted the disease, and of these all but 14.42 per cent. contracted it within twenty-four hours of inoculation; 14 per cent. as against 44 per cent. is a very remarkable contrast. If I had eliminated those who contracted it outside the three or four days' incubation limit the contrast would be still more remarkable. Among the attendants at Mullingar District Asylum only 4 per cent. of the inoculated developed the disease, over 50 per cent. of the uninoculated.

I think, then, it is certain that this pure influenza antigen had a marked prophylactic effect. The doses used were only 25 million in those who had colds and 50 million in those who felt normal. If I were doing it again I should not give more than 10 million to those who felt tired or had a slight headache, as they probably have the disease, and 25 million is too large a dose.

It is interesting to relate that several apparently quite normal persons have reacted to different doses and have had symptoms, lasting usually only an hour or two, exactly like those of influenza—namely, frontal and occipital headache, pains in the back and limbs, and severe malaise. I know of no other antigen which produces symptoms quite like these.

It is very important that the stock influenza vaccine should be potent. Making large quantities involves extensive subculturing. If the medium does not contain a substance—for example, fresh human blood—to induce the microbes to produce their specific toxins, they lose to a

* Read before the Medical Society, University College, Dublin.