the operation of natural selection during racial experience of disease?

It matters just because the immunity reaction is a type of all adaptive response, and, since evolution is largely adaptation to a widening environment, a true solution of the immunity problem supplies the key to many other evolutionary problems also.

When narrowed down to essentials, there are only three ways of undergoing adaptation to environmental change, just as there are only three ways of becoming immune against disease:

1. Either adaptive change is entirely the result of external influence and the organism is as clay in the hands of the environmental potter.
2. Or the organism initiates and directs its own adaptation independently of outside interference.
3. Or adaptation is the result of the interaction of environmental influence and cell potentiality.

Now the immunity problem sheds some light here. We know that the toxin of the disease organism does not directly build up by chemical influence the immune response in the body cell. Nor does the body cell evolve the immune state in the absence of the stimulus of the disease organism.

The state of acquired immunity is the outcome of the exercise on the part of the body cell of a capacity to become different, to vary intracellularly, in not one only but in several directions, when stimulated by the toxin of the disease organism. When this hereditary capacity to become different, to vary intracellularly, is inadequate to meet the new conditions, "use acquirement" is impossible; the cell perishes, and the process of adaptation sinks from the intracellular to the intercellular level.

The problem for the social reformer is how to promote the adaptation of the social organism to its environment without sacrificing the interests or the lives of the individuals during the process of reform. The problem for the physician is how to bring about immunity and resistance to disease in the individual organism without at the same time injuring or destroying the body cells and so producing illness or disease itself.

The problem for both is how to raise the adaptive response to the intracellular level. Both must build on innate capacity for response, on capacity to vary or become different, in fact, on educability. Both alike should try to accomplish the result by stimulating the exercise of this capacity on intracellular and intraindividual lines, and should only resort to intercellular and interindividual struggle with its attendant destruction of competing units when intraorganismal methods have failed or are incompetent to produce progress.

Now this cannot be done by a return to older methods. A return to crude individual competition and natural selection would only serve to destroy the forces of co-operation and mutual protection, which are essential conditions for the exercise of the capacity of recovery and the production of acquired immunity from disease, just as they are essential also for the making of "use acquirements" in many other fields of human activity. Hope for future progress lies in the extension of the method of adaptation by "use acquirement" and environmental control, in the improvement of environmental conditions and the banishment of disease organisms from the human environment by measures of external sanitation, and in the destruction or the reduction of the virulence of disease organisms by vaccine- and chemo-therapy, if they should obtain a foothold in the body.

These are the methods of use acquirement and environmental control, and the methods by which more and more adaptation to disease on the part of the human race will be brought about.

And if, as I have already said, we may regard the great immunity reaction as a type of evolution and adaptation in other fields, if we may regard natural immunity through natural selection as a type of the earlier methods, and artificial immunity through the exercise of individual capacity to profit by experience and through environmental control as a type of the methods of the future, then, bearing in mind the success that has been achieved by these latter methods in the struggle against disease, we may look confidently to an extension of use acquirement and environmental control in other fields, rather than to a

return to innate preadaptation and natural selection, remembering always that both methods depend on innate capacity of some kind or other—capacity of being already adapted before experience, on the one hand, or capacity to become adapted and to learn by experience on the other.

Since innate capacity of recovery in the immunity reaction, like capacity to learn or educability in all adaptive responses are matters of heredity and breeding, it is essential in discarding the older method of natural selection that we take steps to safeguard the transmission and production of innate capacity by some measures of Eugenic control.

A Clinical Lecture

ON

AN ANALYSIS OF FIVE HUNDRED CONSECUTIVE OPERATIONS FOR ACUTE APPENDICITIS.

DELIVERED IN THE POST-GRADUATE COURSE AT THE MANCHESTER ROYAL INFIRMARY.

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IN the BRITISH MEDICAL JOURNAL of January 25th, 1908, I submitted an analysis of 100 consecutive operations for acute appendicitis. To these I have added 400 operations since performed, the present list including, therefore, all the operations I have undertaken in the acute stage of appendicitis between January 1st, 1906, and October 28th, 1911.

SEX.

The series comprised 285 males and 215 females. Much stress has in the past been laid upon and theories invented to account for the alleged great preponderance of appendicitis in the male over the female sex. I believe, however, that many slight attacks pass unrecognized in the female, in whom, owing to the menstrual function, slight abdominal pain is not held of so much account as in the male, where all abdominal pain is abnormal. Moreover, many attacks of appendicitis coincide in their onset with that of menstruation, and are, therefore, all the more likely to be overlooked.

AGE.

The average age was 26.3 years: of males 25.3, of females 28.1. The oldest patient was 77, the youngest 3.

Age Periods.	Males.	Females.	Total.
1 to 5 years ...	6	5	11
5 to 10 " ...	24	13	37
10 to 20 " ...	83	53	136
20 to 30 " ...	74	55	129
30 to 40 " ...	49	48	97
40 to 50 " ...	32	17	49
50 to 60 " ...	13	17	30
60 to 70 " ...	1	6	7
70 to 80 " ...	3	1	4
	285	215	500

PREVIOUS ATTACKS.

One hundred and forty-two patients gave a history of one or more definite previous attacks, that is, 28.4 per cent.

DURATION OF SYMPTOMS PRIOR TO OPERATION, WITH RESULTS.

In all cases the duration of the disease has been calculated from the first severe abdominal pain. It is well

known that this does not represent the real duration either of symptoms or disease, a preceding period of general malaise being very frequent, and corresponding to inflammatory changes confined, however, to the mucosa of the appendix. The onset of acute abdominal pain, which is almost always in the first instance referred to the "umbilical area," indicates the extension of the morbid process to the visceral peritoneum.

	Cases.	Deaths.	Mortality.
1. Under twenty-four hours ...	66	2	Per Cent. 3.03
2. Twenty-four to forty-eight hours	78	3	3.8
3. Third day ...	96	6	6.2
4. Fourth day ...	55	5	9.09
5. Fifth day ...	46	9	19.5
6. Sixth day ...	21	5	23.8
7. Seventh day ...	21	2	9.5
8. Second week ...	77	6	7.7
9. Third week or later ...	40	2	5.0
	500	40	8

The most instructive feature of this analysis is the progressive increase of mortality with each successive day of the disease up to the sixth day. Of the five deaths occurring in those patients operated upon within forty-eight hours the two on the first day and one of those on the second were due to the interesting but very fatal condition known as "delayed chloroform poisoning" or "fatty acid intoxication." One other case in this series died from the same cause, and as in all four chloroform was the anaesthetic administered, I believe it better to avoid this agent in these acute abdominal infections, especially in children. Though it is not impossible for the condition to follow upon the administration of ether, yet the recorded cases show this to be much less probable, and I believe that with "open ether" as the routine anaesthetic the mortality in these "early" operations can be materially reduced. The two remaining deaths in these cases operated upon within forty-eight hours were one from continued spread of the infection leading to general peritonitis, and one from acute pneumonia, developed on the eighth day, after complete subsidence of the abdominal symptoms.

Of the 35 deaths among the cases operated upon after forty-eight hours the causes were: Shock, collapse, or toxæmia 26, acute pneumonia 4, pulmonary embolism 1, sudden heart failure 1, acute nephritis with uræmia 1, and intestinal obstruction 2 (one of which occurred during the administration of an anaesthetic at a subsequent operation for the relief of the obstruction, and one after operation for obstruction developing three months subsequently to the opening of a large appendicular abscess from which the appendix had not been removed).

RESULTS CLASSIFIED ACCORDING TO THE PATHOLOGICAL CHANGES.

I have now relinquished the attempt made in my previous paper (January 25th, 1908) to differentiate between "diffuse" and "general" peritonitis, the true recognition of the latter being possible only either at a *post-mortem* examination or at a much more extensive operative procedure than is now my practice.

	Cases.	Deaths.	Mortality.
Group A.—Infection limited to the appendix	135	1	Per Cent. 0.74
Group B.—Circumscribed abscess ... (Appendix removed) ... (Appendix not removed) ...	213 (107) (106)	10 (2) (8)	4.64 (1.86) (7.54)
Group C.—Diffuse spreading peritonitis	152	29	19.07

Group A.—Infection Limited to Appendix.

The solitary death in this group was one of those already referred to, from "delayed chloroform poisoning."

With ether as the routine anaesthetic, the mortality of operations where the infection is still limited to the appendix will be reduced to a negligible quantity.

Group B.—Circumscribed Abscess.

It is interesting to note that of the 213 cases in this group, with a total mortality of 4.64 per cent., the appendix was removed in addition to opening the abscess in 107, with a mortality of 1.86 per cent., whereas in 106 cases where it was left the mortality was 7.54 per cent. This does not, apparently, support the view so frequently advanced, that removal of the appendix materially increases the risks of operation, though it must be admitted that the cases in which I left the appendix were usually the more serious prior to operation—either of very large abscess or whose general condition rendered any prolongation of the operation inadvisable. My tendency is undoubtedly towards a more frequent removal of the appendix in abscess cases. Thus in the first 200 cases in this series the appendix was removed in 35.4 per cent. of the abscess cases; in the remaining 300 in 61.6 per cent.

The advantages of removing the appendix are certainly considerable: (1) The patient is spared a subsequent operation for its removal (and this I urge unless, as sometimes happens, the appendix has been recognized as a slough coming away with the discharge), or, failing this, the risk of further attacks. (2) The wound heals more quickly when the appendix has been removed, and drainage may be dispensed with earlier; consequently there is less chance of subsequent ventral hernia. (3) Persistent sinus and faecal fistula are less common. About two years ago, on opening an appendicular abscess in a youth, I found the appendix hanging freely into it, apparently about 3 in. long, and perforated. Fearing to break down the deep wall of the cavity by separating the base of the appendix freely, I merely ligatured it flush with the wall, cutting off just distal to the ligature, but well above the perforation. A small faecal fistula persisted for some months, which at a second operation by another surgeon was found to lead directly to the stump of the appendix, the rest of which, 1½ in. in length, was removed, the fistula then closing. (4) Remote troubles are less likely. Only very recently I have operated upon a man for acute intestinal obstruction, in whom four years ago an appendicular abscess had been opened by a colleague without removal of the appendix. This I found practically normal, except that from its inner aspect, close to the tip, a short but strong band of adhesion extended to the mesentery of the ileum, and under this 2½ ft. of small intestine were strangulated and completely gangrenous, the case ending fatally.

In deciding, during the course of an operation for appendicular abscess, upon the advisability of searching for the appendix, the point that weighs most with me, granting that the general condition of the patient is sufficiently good to allow of the necessary prolongation of the operation, is whether the abscess has been reached through the general peritoneal cavity or not. If the former (and this I prefer) then the abscess will have been carefully packed off with gauze from the rest of the peritoneum, and, having wiped the cavity as clean as possible, I have no hesitation in separating its walls and searching carefully for the appendix. Where, however, prior to operation the abscess has become adherent to the anterior abdominal wall and is opened into directly, and where, therefore, protective gauze packs cannot be placed around it, I hesitate to interfere materially with its deeper walls lest I break through into unprotected and uninfected peritoneum.

Concretions.

Fruit seeds were found in the appendix in a few instances, and in several small thread worms were present. Faecal concretions occurred in 21 per cent. of the cases. Their presence is interesting in relation to the site of perforation or gangrene. Perforation of an appendix which does not contain a concretion usually occurs near to the tip and on the free border, just distal to the termination of the attachment of the appendix-mesentery. Perforation of one containing a concretion is more probable opposite the concretion. The practical application of this is that if a perforation be found elsewhere than near the tip of an appendix in which no concretion can be felt

careful search should be made for one which may have escaped through the perforation, and which, if overlooked, may lead to a persistent sinus.

A consideration of the above two mortality tables at once renders evident the advantage of early operation, with limited infection. This advantage is also very manifest when we take into account the *morbidity* of the cases that recover. Thus, if only we can secure the appendix while the infection is still limited to it no drainage is requisite, primary union is the rule, no risk of subsequent hernia arises, and the patient may be allowed up within a few days—that is, the convalescence is exactly comparable to that after an “interval” operation. And even if the infection has but recently extended beyond the appendix, nevertheless these advantages can, in many cases, be still obtained. Where, however, a definite abscess has been allowed to form, drainage is essential, and has to be carried out for many days, and sometimes weeks, convalescence is prolonged, complications more likely to supervene, and the chances of subsequent yielding of the scar greatly increased.

Further improvement in the mortality statistics of operations in the acute stage of appendicitis is to be looked for chiefly upon the lines of earlier diagnosis, and of a more general recognition of the advantages of early operation. I believe also that the adoption of less heroic measures in the operative treatment of diffuse peritonitis than were formerly in vogue will diminish the mortality of the “delayed” cases. Flushing the abdominal cavity is almost a thing of the past. In the most desperate cases a rapid incision under nitrous oxide anaesthesia through the lower part of the right rectus muscle, and the insertion of a large rubber tube to the bottom of the pelvis is all that is advisable at the time, and may save life where any further procedure would have turned the scale against it. Secondary abscesses may form, but can be more safely dealt with when the immediate danger of “toxaemia” is passed.

EARLY DIAGNOSIS.

In this connexion a factor which is not yet, I believe, sufficiently appreciated is the great frequency of the disease. If called to a case of acute abdominal pain and sickness, the probabilities are in favour of appendicitis before one reaches the patient at all. Most of the cases of acute abdominal pain occurring in definite attacks, and of doubtful origin, are proved in course of time to be due to the appendix.

The early symptoms of acute appendicitis and their characteristic order of onset have been well described many years ago by Murphy. They are:

1. Abdominal pain, usually referred at first to the “umbilical area,” later to the right iliac fossa.
2. Nausea, and in many cases vomiting.
3. Localized tenderness.
4. Localized muscular rigidity.
5. Rise of temperature and rise of the pulse-rate.

The importance of this order of onset cannot be too strongly insisted upon, and if the symptoms present in any acute abdominal crisis have not conformed to it, then a diagnosis of acute appendicitis should not be made without considerable hesitation. So far as the last group (5) is concerned, I believe it would have been better omitted from the list. I feel strongly that fewer cases would pass unrecognized in their early stages were it to become the universal rule never to take the temperature nor count the pulse in a suspected case of acute appendicitis; they are only too apt to mislead. The temperature is of no value as a guide, and though the pulse-rate may possibly possess some prognostic worth, it is certainly of no assistance in early diagnosis. It seems difficult for men to convince themselves that dangerous pathological changes, such as gangrene, perforation of the appendix, and rapidly spreading peritonitis can coexist with a normal temperature and pulse, yet this is a by no means infrequent occurrence, and one which it is important should be widely known. Moreover, Murphy's fourth symptom—muscular rigidity—need not be waited for to complete a diagnosis, since it indicates that the infection has already spread from the appendix, and that there is either toxic irritation or actual inflammation of the parietal peritoneum overlying it. So long as the infection does not extend

beyond the visceral peritoneum, rigidity of the abdominal muscles of the true involuntary type is not met with.

It is, then, upon the first three of Murphy's symptoms that we have to rely for the early diagnosis of acute appendicitis:

1. *Abdominal Pain.*—It is important to remember that the early pain is usually not felt over the appendix at all, but is referred to the area around the umbilicus—that is, to the peripheral distribution of the spinal nerves arising from those segments of the spinal cord with which the appendix and small intestine are connected through their sympathetic nerve supply—eighth to eleventh dorsal. The later transference of pain to the right iliac fossa indicates extension of the irritation to the parietal peritoneum (or rather to the rich nervous plexus in the connective tissue immediately underlying it), and inasmuch as this is supplied by the cerebro-spinal as distinct from the sympathetic nerves, accurate localization of the irritated area is possible. Thus the closer the situation of the appendix to the parietal peritoneum the earlier will the latter be irritated, and the sooner will the pain be localized. It must, however, be remembered that the appendix is sometimes placed deeply among the coils of small intestine or among the pelvic viscera, so that there may be no local pain at any stage, the initial “umbilical area” pain becoming steadily generalized. Absence of local pain may be, therefore, either a favourable sign, indicating that the infection is so slight as never to irritate the parietal peritoneum (and the appendicular origin of many of these cases is overlooked), or an unfavourable sign, indicating an appendix deeply placed among the viscera. When well marked local pain appears in the right iliac fossa early on in the attack one may confidently expect to find the appendix not far removed from the parietal peritoneum.

2. *Vomiting* is relatively more frequent in children than in adults, many of whom do not proceed further than the stage of nausea. The initial vomiting is a purely reflex phenomenon, and usually disappears within twenty-four hours. Persistence of vomiting, and its recurrence after having once definitely ceased, are strongly suggestive of spreading peritonitis.

3. *Local tenderness* should be searched for not only through the abdominal wall but also by rectal examination, since the appendix is frequently a pelvic organ. I have frequently detected local tenderness on rectal palpation when no trace whatever of a tender spot could be obtained on abdominal examination.

TREATMENT.

At the onset of acute abdominal pain the patient should be at once placed in the semi-recumbent or Fowler position, and this should be consistently maintained throughout any removal to hospital or nursing home, throughout the subsequent operation, and for several days afterwards. During the operation the limbs and chest should be wrapped in wool and flannel bandages and the theatre maintained at as high a temperature as can be comfortably borne. A good light is essential, and I always have at hand an electric forehead lamp, the use of which has frequently enabled me to remove the appendix from an appendicular abscess which otherwise I should have been compelled to leave. For the majority of cases (76 per cent. of this series) I use the lateral “gridiron” incision, reserving one through the lower part of the right rectus for those where I have reason to believe, either from the situation of the local tenderness or the presence of any palpable swelling, that the appendix is situated nearer to the middle line than usual. In either case the muscle fibres are separated, never divided, and at the conclusion of the operation the wound is sutured in layers with iodized catgut, either completely or around a drainage tube, if such be requisite. On opening the peritoneum I palpate carefully with my gloved left index finger for any swelling, having located which I introduce a retractor beneath the inner lip of the wound and instruct my assistant to make strong traction upon it in a direction vertically upwards, so as to lift the abdominal wall away from the intestines as far as possible, while I introduce the gauze packing. This step I consider the most important of the whole operation and one worthy of the expenditure of considerable care. I generally use from 4 to 6 yards of “roll” gauze, 6 in. wide and four layers thick, and pass it in in four pieces—north, south,

east, and west of the inflammatory swelling—leaving a forceps attached to each. The "south" piece is the longest and extends well into the pelvis; if the appendix is closely adherent to the outer part of the iliac fossa, there may be no room for more than a short "west" piece. While introducing the gauze I always keep my left index finger placed lightly upon the swelling to prevent traction being exerted upon it while the gauze is pushed into place with long dressing forceps. Unless this precaution is observed, it is easy for the gauze to carry along with it a portion of intestine constituting the wall of the inflammatory mass, and so to break down limiting adhesions and flood the area with pus before packing is completed. Having, then, securely isolated the inflamed area from the rest of the peritoneal cavity, I open up the mass with my finger, wiping away any pus as fast as it escapes until the abscess cavity is dry, or, if no pus be present, searching for the appendix itself. The factors which influence me in deciding when to search for the appendix in the presence of a localized abscess have already been referred to. Wherever possible I prefer to treat the appendix as I do in "interval" operations—that is, crush and ligate its base and bury the stump in the caecal wall with a purse-string suture. In many cases, however, where the base of the appendix is situated deeply, it is not advisable to draw up the caecum sufficiently to pass a purse-string suture, and I have no hesitation in leaving the stump simply ligated, though here I invariably employ drainage. The gauze packs are next removed in the inverse order of their insertion, the "east" piece usually bringing with it a little of the omentum, which I tuck snugly around the drainage tube when such is used. Flushing with saline I now never employ except for cleansing large abscesses which have been reached without exposure of the general peritoneal cavity. I have already referred to the treatment of desperate cases of diffuse peritonitis and the importance of not attempting too much.

THE INGUINAL OPERATION FOR THE RADICAL CURE OF FEMORAL HERNIA.

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THE inguinal method of operation for the cure of femoral hernia seems now to be very frequently employed. My attention was first called to it by the paper of Mr. T. E. Gordon in the *BRITISH MEDICAL JOURNAL*, 1900, vol. i, p. 1338, at a time when I was myself planning some method for closing the crural canal at its upper end, and I began to perform the operation of radical cure of femoral hernia by this method in January, 1903. Since then I have operated on 27 cases in this way up to the end of June, 1911, and I have endeavoured to trace the first 12 of these cases. They were all operated on more than six years ago, and therefore there has been plenty of time for late relapse. It is stated that when relapse occurs after operation for femoral hernia it is usually late.

The statistics given to show the results of operation for radical cure of hernia are not usually satisfactory. We are generally told that so many cases have been operated on by some special method and only so many relapses are known; or if the cases are examined and found free from relapse, the time after operation at which such an examination is made is not given for all cases. What we really want to know is not whether few cases returned to the surgeon with relapse, for, of course, relapsed cases might quite likely not return to the surgeon who had operated, or whether so many cases were found free from relapse when examined shortly after the operation, but what proportion of patients have been found free from relapse some years after the operation. Even if they are free from relapse many years after the operation, that does not, of course, prove that they will never get a relapse, but we must have some time limit. But every one who has tried to obtain the result of treatment years after an operation knows how extremely difficult it often is to trace such cases amongst hospital patients.

They move so frequently, and where they move to is not generally known in the neighbourhood where they previously lived. I have been more fortunate in tracing my first twelve patients operated on by this method of radical cure than I expected. Two out of the twelve died; one of them was an elderly man who died a week after the operation (which was for strangulated hernia followed by "radical cure") from bronchitis, and the other died nine months after the operation, of heart disease and without any recurrence of the rupture. In three cases my letters were returned through the "dead letter" office and seven replied. All these seven stated that they were free from recurrence, though one male had developed an inguinal hernia on the same side. I was able to examine four myself. Thus all the cases (seven) it was possible to trace, out of the twelve, were free from recurrence six years after the operation. In looking through the records of these cases, I have been struck with the small proportion of radical cures of femoral hernia which I have done, compared with inguinal hernia. I find I have only done radical cure for femoral hernia in 47 cases, and in no less than 27 of these the radical cure was done after herniotomy had been done for strangulation, leaving only 20 cases of operation for the radical cure of femoral hernia apart from strangulation. Some of the seven cases found free from recurrence after six years were radical cures done at the end of a herniotomy. I have not looked through my records to see in how many cases of inguinal hernia, which I have operated on for strangulation, I have done a radical cure, but I find that, whereas I have only operated in 20 cases of non-strangulated femoral hernia for radical cure, I have done so in 156 cases of non-strangulated inguinal hernia.

Although when considering the best method of closing the crural canal I came across the paper by Mr. Gordon, yet a little more than a year later, and before I began to practise the operation, Mr. Parry of Glasgow advocated it in a paper published in the *BRITISH MEDICAL JOURNAL*, 1901, vol. ii, p. 1136. I do not remember reading the paper at that time, but Mr. Parry had practised the method for four years before he published his paper—that is, he performed it for some time before Mr. Gordon did so. But unknown to both these surgeons, Lotheissen¹ described a similar operation several years before, and both he and Parry were led to adopt this method for the radical cure of femoral hernia after they had employed it in the operation for inguinal hernia. Parry brought the cord out through the crural canal and fixed the internal oblique and transversalis to Cooper's ligament, so as to form a barrier against descent of both forms of hernia. Lotheissen also fixed the conjoint tendon to Cooper's ligament in operating for combined inguinal and femoral hernia, and was thus led to adopt the method for femoral hernia alone.

The operation which I perform is not quite the same as the method described by Lotheissen, Gordon, or Parry, and I think it will be well first to describe it and then to point out how it differs from them. I make an incision parallel to and very slightly above Poupart's ligament, in the position of the neck of the sac, and then carry it downwards at the inner end at almost a right angle to the part parallel with Poupart's ligament, but where the horizontal joins the vertical portion it is curved, not angular. Each limb of the incision is about 2 in. long. The flap of skin which is thus cut is then dissected up in the outward direction, exposing the sac, Poupart's ligament, and the lowest part of the aponeurosis of the external oblique above it. The sac is now opened and the contents reduced. It is better not to tie the neck in the thigh, as it can be tied higher up from above Poupart's ligament, when later on it is reached through the incision through the external oblique; but if the sac is large it may not be easy to pull it up through the crural canal, and thus it may be necessary to tie the neck of the sac in the thigh, and after removal of the rest of the sac simply return the tied neck through the crural canal. In any case, whether tied in the thigh or above Poupart's ligament, the sac is always removed. If it is removed from above Poupart's ligament, it should, I think, be separated from its surrounding fat and fascia by dissection in the thigh before it is drawn up through the crural ring. Hence the incision should be carried over the sac in the thigh by means of a vertical limb, in the way I have described. Having, then, separated the sac ready to be drawn up