operated upon, 86.5 healed aseptically in 1906, and 92.8 in 1908. We hope that these statistics will prove useful and of interest to the practitioner and help him to give a patient a fair idea of the average chance of aseptic healing after the commoner operations. We have tried to make these records as accurate as possible and we have embodied in them the results of the work of four surgeons and three assistant surgeons.

In conclusion we must thank Dr. Slater, the head of the clinical laboratory of St. George's Hospital, for the kindly interest he has taken in our paper; and we are greatly indebted to him for the detailed description of the sterilising methods now in use.

THE RELATION OF ALCOHOL TO IMMUNITY.

By P. R. PARKINSON, B.A., M.B., B.C. CANTAB.

(From the Wellcome Physiological Research Laboratories.)

THE great amount of controversy which has arisen over the question of the action of alcohol on the human body has given rise to much experimental work on its action in animals. One of the chief interests of the question lies in the relation which alcoholism plays in the reaction of the body to infection. While much clinical evidence and general experience goes to show that large quantities of alcohol and the continuous use of moderate quantities in some individuals cause a lowering of the resistance to infectious disease, no definite evidence can be obtained as to its effect in small quantities. Experiments on animals have shown that there is in them a definite lowering of the resistance to infections when they are under the influence of alcohol.

The question as to how the alcohol acts does not seem to have been decided, though many statements have appeared to the effect that this drug lowers the resistance to disease by acting upon the phagocytes, and so inhibiting their activity. These statements have their foundation upon the fact discovered by Metchnikoff,¹ that drugs such as opium depress the activity of the white cells so that there is less phagocytosis than in normal animals. Since, however, it is now evident from the work of Wright² that phagocytosis is dependent upon substances in the serum it seemed that it might be of interest to determine by means of the opsonic index upon which factor—serum or phagocytes—the alcohol does act in an alcoholised animal. Delcarde³ showed that animals when given alcohol succumbed during a course of immunisation against anthrax while the controls lived. Abbot⁴ showed that animals alcoholised are more sensitive to harmful effects of several micro-organisms—e.g., streptococcus, staphylococcus, and bacillus coli. Laitmen⁵ gave anthrax vaccine subcutaneously to six alcoholised animals and all died, while of four control animals only one died. Friedberger⁶ has shown that one injection of alcohol increases the quantity of the antibodies while much alcohol diminishes them, but Fraenkel was not able to confirm this harmful influence.

Metchnikoff sums up the matter by saying: "Impairment of their [animals under alcohol] resistance was manifested by the inactivity of their white blood cells: alcohol therefore has a harmful action on phagocytes." Statements of a similar kind are quoted in the work by Horsley and Sturge.⁷ They say: "It is now proved that alcohol even in tiny doses paralyses more or less the white cells. . . . Alcohol renders the white cells less alert, so that they remain passive and motionless in the presence of dangerous microbes." Woodhead⁸ has stated that alcohol has an action on the antibodies in the serum, which are regularly but distinctly reduced. Kruschilin⁹ observed in alcoholised

rabbits a quicker course of infection and a quicker sprouting of spores than in control animals; he considers that the activity of the phagocytes is inhibited by the alcohol; he used staphylococcus, anthrax, and the hay bacillus in his experiments.

The experiments detailed in this paper were made with the object of determining the effect of alcohol, firstly, upon the phagocytes; and secondly, upon the production of antibodies which were gauged by taking the opsonic index.

Method.—The opsonic index was estimated in the usual way. The animals (rabbits), which were treated with alcohol (diluted), were injected by the vein of the ear. In the animals subjected to continuous alcoholism the treatment was commenced with small doses and gradually increased, the injections being made every other day and the treatment continued from two to four weeks; a tolerance is gradually established and the doses can be increased; the maximum dose obtained was once 2.5 cubic centimetres of absolute alcohol well diluted in normal saline. The minimum dose commenced with was 0.1 cubic centimetre. Rabbits should not be repeatedly injected subcutaneously with even dilute alcohol, as necrosis is apt to occur at the site of injection.

Action of alcohol upon the phagocytes.—In studying this action the following method was used: the blood was dropped into 1.5 per cent. sodium citrate and centrifuged down; the supernatant citrate was then drawn off and the corpuscles were mixed with normal saline made up with the required strength of absolute alcohol and this mixture allowed to stand, with occasional mixing, for about one hour. The corpuscles were then centrifuged down and immediately used.

Small quantities of alcohol.—The first experiments were made with small quantities of alcohol in order to see if this had any effect, either stimulant or depressing, upon the action of the phagocytes. Dilutions of alcohol 1 in 100, 1 in 50, and 1 in 25 were made: human serum and staphylococcus aureus were employed, and in all the experiments human corpuscles were used.

				50 cells. Index.
Normal corpuscles		+ serum + cocci	= 220	= 1
Alcoholised "	(1-25)	+ "	+ "	= 218 = 1
" "	(1-50)	+ "	+ "	= 221 = 1
" "	(1-100)	+ "	+ "	= 198 = 0.9

The conclusion from this experiment is that by treating white cells with the quantities of alcohol given no effect on phagocytic activity is apparent.

Stronger solutions of alcohol.—Dilution 1 in 5: The corpuscles were next treated with a very strong solution of alcohol, 1 in 5, with the following result:—

			50 cells.
Normal corpuscles	+ serum + cocci	= 212	
Alcoholised "	+ "	+ "	= 0

The white cells were here obviously much damaged by the alcohol and probably actually killed as the majority were broken in appearance and very granular.

Experiments were then made to determine at what concentration of alcohol the corpuscles are affected, and for this purpose two dilutions of alcohol were used for treating the corpuscles, 1 in 8 and 1 in 10.

				50 cells.	Index.
Normal corpuscles		+ serum	+ cocci	= 269	= 1
Alcoholised "	(1-10)	+ "	+ "	= 260	= 1
" "	(1-3)	+ "	+ "	= 132	= 0.5

The phagocytosis in the last case is lowered to half the normal, and though the corpuscles were not broken up there was some evidence that the alcohol of this strength had acted upon their structure in that the outline of the nucleus in many cases was becoming irregular as though small "streamers" of nuclear protoplasm were projecting into the cytoplasm.

From these experiments it may be concluded that alcohol has no effect upon phagocytic activity until it is of such a concentration as to seriously injure the vitality of the cells. Moreover, it is practically impossible that it could occur in such quantities in the blood as to be in a solution of 1 in 8, at which dilution it begins to exert its effect upon the cells.

Effect of alcohol on the opsonic index.—1. *Non-toxic dose of alcohol.* A cubic centimetre of alcohol was injected subcutaneously and caused no apparent clinical effect. Blood was withdrawn 24 hours and three days after the injection and tested against staphylococci.

¹ Metchnikoff: Immunity in Infectious Diseases (Cambridge, 1905).

² Wright: Studies of Immunisation (London: Constable, 1909).

³ Delcarde: Annales de l'Institut Pasteur, 1897, p. 837.

⁴ Abbot: Journal of Experimental Medicine, vol. i., p. 447.

⁵ Laitmen: Zeitschrift für Hygiene, 1900, vol. xxxix., p. 206.

⁶ Friedberger: Quoted by Metchnikoff, Harben Lectures, Hygiene of Tissue, 1906.

⁷ Horsley and Sturge: Alcohol and the Human Body.

⁸ Woodhead: Recent Researches on the Action of Alcohol in Health and Sickness, quoted by Horsley and Sturge.

⁹ Kruschilin: Zeitschrift für Immunitätsforschung, Band 1, 1909, S.407.

24 hours—	50 cells. Index.
Corpuscles + normal rabbit serum + cocci = 211 = 1	
„ + alcohol „ „ + „ = 285 = 1.3	
Three days—	
Corpuscles + normal rabbit serum + cocci = 283 = 1	
„ + alcohol „ „ + „ = 279 = 0.98	

A small non-toxic dose of alcohol causes a rise in the opsonic index of short duration.

2. *Toxic dose of alcohol.*—The effect of this was studied by giving a rabbit a single large dose (4 cubic centimetres) subcutaneously. The clinical effect of this was respiratory distress and some collapse. The symptoms appeared in half an hour and lasted about four hours. The animal's serum was tested four hours and 24 hours after the injection.

Four hours—	50 cells. Index.
Corpuscles + normal rabbit serum + cocci = 380 = 1	
„ + alcoholic „ „ + „ = 294 = 0.77	

24 hours—	
Corpuscles + normal rabbit serum + cocci = 248 = 1	
„ + alcoholic „ „ + „ = 269 = 1.08	

A toxic dose of alcohol lowers the opsonic index for a few hours, but recovery has taken place in 24 hours.

Effect of chronic alcoholism on the opsonic index.—A rabbit was treated with gradually increasing doses of alcohol, the injections being given intravenously every other day. Serum taken at various intervals of time gave the following results:—

<i>Eleventh day—</i>	<i>Three weeks—</i>
Index to staphylococcus = 0.72	Index to staphylococcus = 0.72
„ tubercle bacilli = 0.78	„ tubercle bacilli = 0.69
<i>Stateventh day—</i>	<i>Four weeks—</i>
Index to staphylococcus = 0.76	Index to staphylococcus = 0.78
„ tubercle bacilli = 0.77	„ tubercle bacilli = 0.70

Chronic alcoholism produces a marked lowering of the opsonic index, although no toxic symptoms are produced.

Effect of alcoholism on reaction to vaccination.—A rabbit which was under the influence of chronic alcoholism was injected with a vaccine of 1,000,000,000 staphylococcus aureus and its reaction compared with that of a normal rabbit similarly treated.

<i>Before the vaccine—</i>	50 cells. Index.
Alcohol rabbit =	0.79
Normal „ =	1

<i>24 hours after the vaccine—</i>	
Normal rabbit =	218 = 1
Vaccinated alcohol rabbit =	206 = 0.94
„ normal „ =	288 = 1.32

<i>Third day after vaccination—</i>	
Normal rabbit =	302 = 1
Vaccinated alcohol rabbit =	229 = 0.7
„ normal „ =	308 = 1

<i>Sixth day—</i>	
Normal rabbit =	203 = 1
Vaccinated alcohol rabbit =	136 = 0.6
„ normal „ =	207 = 1

The effect of this vaccine on the rabbits shows that where a normal rabbit would respond to a vaccine with a considerable rise on the opsonic index a rabbit under the influence of alcohol shows reaction, the index not rising above normal. The injections were repeated, using a much thicker emulsion of killed organisms.

<i>Before vaccination—</i>	50 cells. Index.
Normal rabbit =	203 = 1
Alcohol „ =	136 = 0.6
Rabbit to be vaccinated =	207 = 1

<i>24 hours after the injection—</i>	
Normal rabbit =	342 = 1
Vaccinated alcohol rabbit =	268 = 0.78
„ normal „ =	395 = 1.15

<i>Third day—</i>	
Normal rabbit =	570 = 1
Vaccinated alcohol rabbit =	382 = 0.67
„ normal „ =	352 = 0.61

<i>Sixth day—</i>	
Normal rabbit =	4 = 1
Vaccinated alcohol rabbit =	357 = 1.06
„ normal „ =	436 = 1.3

<i>Ninth day—</i>	
Normal rabbit =	387 = 1
Vaccinated alcohol rabbit =	352 = 0.8
„ normal „ =	476 = 1.26

<i>Twelfth day—</i>	
Normal rabbit =	284 = 1
Vaccinated alcohol rabbit =	197 = 0.7
„ normal „ =	296 = 1

The large dose was sufficient to produce a marked negative phase followed by a positive one; the negative phase brought the normal vaccinated rabbit's index down to the level of the alcoholised one after a slight rise in each case; from this point the reactions show a marked difference, the normal vaccinated rabbit's index mounts up to 1.3 while the alcoholised rabbit's index starting from the same level mounts up only to about normal. The reaction lasts rather longer in the case of the normal vaccinated rabbit.

These results show that one of the effects of chronic alcoholism on the animal's body is to act upon the mechanism which produces the anti-bodies in such a way as to render it less sensitive to the invasion of killed micro-organisms so that the reactions are not so great as in a normal animal; it is interesting to note also that the negative phase is less marked in the alcoholised rabbit. It would naturally be inferred from such results that animals under the influence of alcohol would show less resistance to infections by living organisms than the normal animal, as has been shown by experiments referred to previously.

The next experiment therefore was to try the effect of such living cultures upon the reacting mechanism. A rabbit under the influence of alcohol was infected intravenously with a living culture of staphylococcus aureus and at the same time a normal animal was treated with an equal quantity of the same emulsion of staphylococcus; the variations in their opsonic indices were followed for several days; the rabbits showed no clinical signs except a slight loss in weight in each case. The opsonic index of the alcoholic rabbit before infection stood at 0.7. 50 cells were counted in each case.

<i>24 hours after infection—</i>	50 cells. Index.
Normal rabbit serum + staphylococci =	107 = 1
Infected alcoholic rabbit serum + „ =	70 = 0.6
„ normal „ „ + „ =	140 = 1.3

<i>Third day—</i>	
Normal rabbit serum + „ =	349 = 1
Infected alcoholic rabbit + „ =	106 = 0.3
„ normal „ + „ =	161 = 0.4

<i>Fifth day—</i>	
Normal rabbit + „ =	465 = 1
Infected alcoholic rabbit + „ =	240 = 0.5
„ normal „ + „ =	358 = 0.77

<i>Seventh day—</i>	
Normal rabbit + „ =	316 = 1
Infected alcoholic rabbit + „ =	89 = 0.25
„ normal „ + „ =	162 = 0.5

<i>Ninth day—</i>	
Normal rabbit + „ =	335 = 1
Infected alcoholic rabbit + „ =	212 = 0.63
„ normal „ + „ =	385 = 1.15

<i>Eleventh day—</i>	
Normal rabbit + „ =	467 = 1
Infected alcoholic rabbit + „ =	486 = 1.04
„ normal „ + „ =	668 = 1.42

<i>Thirteenth day—</i>	
Normal rabbit + „ =	284 = 1
Infected alcoholic rabbit + „ =	247 = 0.87
„ normal „ + „ =	388 = 1.36

<i>Fifteenth day—</i>	
Normal rabbit + „ =	312 = 1
Infected alcoholic rabbit + „ =	225 = 0.72
„ normal „ + „ =	364 = 1.16

These results show as would be expected from the previous ones that the production of antibodies as represented by the opsonins is very much feebler in an alcoholised rabbit than in a normal rabbit when both are infected with living micro-organisms. In this case both animals survived the injection, and though they suffered from a prolonged negative phase both eventually showed a positive phase; the difference of reaction is marked, the alcoholised rabbit shows a much lower index during the negative phase and a less marked rise during the positive reaction, thus proving again that the alcohol has interfered with the reactive mechanism.

Though these results are definite for animals and probably show the method by which alcohol lowers resistance to disease in man the conditions under which the experiments are performed are not strictly the same in the two cases. The alcohol present in alcoholic liquors is not pure alcohol alone, but contains other substances which may in large quantities be equally deleterious; at the same time it is probable that such toxic substances would act in the same

way as the alcohol does, by depressing the activity of the reacting mechanism.

Another important difference to be remembered in applying these results to the case of man is that of tolerance. The experiments were carried out after a few doses of alcohol had been administered and such doses were given in gradually increasing quantities. In man, however, there may be the same dose, roughly speaking, continued over a great number of years, in which case it is probable that a high degree of tolerance being induced no abnormal condition of the reacting mechanism is incurred.

In those cases in man in which alcohol does lower the resistance to infections it is probable that it acts in the same manner as it appears from these experiments to act in rabbits, by its action on the production of antibodies and not from any action directly upon the phagocytic activity of the white cells.

Conclusions.—1. Alcohol in small quantities has no action upon the phagocytic activity. 2. It has no action on the phagocytic activity until it is present in 12·5 per cent. strength. 3. Small quantities of alcohol injected into rabbits may stimulate the production of antibodies temporarily. 4. A large dose of alcohol lowers the opsonic index for 24 hours. 5. Continuous moderate doses of alcohol cause a permanent lowering of the opsonic index. 6. The reacting mechanism to vaccines is much less effective in alcoholised rabbits than in normal rabbits; the difference is still more marked when living micro-organisms are used.

SOME COMPLICATIONS AND DANGERS OF NASAL SURGERY.¹

BY H. BELL TAWSE, M.B., CH.B. ABERD.,
F.R.C.S. ENG.,

LATE HOUSE SURGEON AND CLINICAL ASSISTANT, HOSPITAL FOR
DISEASES OF THE THROAT, GOLDEN-SQUARE, LONDON, W.

DURING the last 20 years nasal surgery has made very rapid advancement, the technique has much improved, and areas which at one time were deemed inaccessible and dangerous can now be reached with comparative safety, while the vulnerable parts of the ethmoidal labyrinth, for instance, have been more clearly defined. In recent years the attention of the medical profession has been drawn to the importance of surgical procedure in many of the cases previously treated—and very often unsuccessfully treated—by douches, snuffs, &c. Medical men, as a rule, did not hanker after such cases, which seldom did credit to their treatment; and often the patients, in a miserable condition from headache, foul nasal discharge, cough, and expectoration, &c., dispensed with medical advice, and either resigned themselves to their condition or gave themselves up, body and soul, to the remedies of the unscrupulous quack. Nowadays there are few diseases of the nose that we cannot in some way ameliorate, and there are many sufferers that we can reasonably promise to restore to perfect health. Naturally the increased number and the magnitude of nasal operations have produced complications and dangers unheard of in pre-operative days, and it is on these more particularly that I propose to dwell, completing the imperfect record of personal experience by cases which I have observed under the care of others.

DISEASES OF THE MIDDLE TURBINATE.

The middle turbinate, by far the most interesting and important of the spongy bones, is very commonly the site of disease of varying forms and intensity, and from its close proximity to the openings of the anterior group of sinuses it will be obvious to you that alterations in its size must materially influence the drainage of those sinuses. Fortunately, in many of the cases of acute inflammation of those sinuses the inflammatory products force a way out and recovery speedily follows, but occasionally—and I venture to say more commonly than we think—the sinuses only partially empty themselves, and one is face to face with the beginning of a chronic sinus suppuration.

Diseased conditions of the middle turbinate require its

partial or complete removal. It is said that fracture of the cribriform plate of the ethmoid has been caused by the use of the cold wire snare in this procedure. This I very much doubt, but I have seen post mortem a case where this structure showed a perforation supposed to have been caused by Walsham's scissors in removing the anterior end of the middle turbinate, death being due to suppurative meningitis. A point which I should like to strongly emphasise is the importance of having free access to the middle turbinate before attempting its removal. I refer to the correction of deviations and obstructing spurs, which not only occlude the view but very frequently conceal an enlargement and prevent its complete removal. If this is not done the mucous covering of these deviations is almost certain to be damaged and troublesome adhesions between the septum and turbinates are extremely likely to follow and will be very difficult to cure. The surgery of the nasal septum was until a few years ago in a most unsatisfactory state. The operations were manifold and the armamentarium employed was a most extensive one, and the results in many cases were deplorable. Adhesions to the turbinates were common, perforations and sloughing of the septum were frequent, and I know of a case where collapse of the tip of the nose occurred and transformed a well-shaped into an ugly snubnose. A few years ago Killian introduced his now famous operation of submucous resection of the septum, and I can unhesitatingly recommend it to you for practically all cases of septal deviation. Carefully and skilfully done it has no equal. It will afford easy access to the diseased middle turbinates, it will render any after-treatment simple, and it will make it possible for you to obey the golden rule for successful nasal surgery—namely, to have efficient drainage.

By far the most important disease of the middle turbinal region requiring surgical intervention is polypoid degeneration, commonly called nasal polypi, and there is no pathological condition in the nose which demands such careful, thorough, and patient treatment. Associated as it often is with suppuration and sinus infection, it will be at once apparent to you that it is a prolific source of the complications which occur in nasal surgery.

Ethmoidal curetting, the only operation worth doing for nasal polypi and apparently a dangerous procedure, is one which in skilled hands is attended with brilliant results. The dangers I shall enumerate to you, but only the most important will be reviewed at length. They are: (1) hæmorrhagic effusion into the eyelids and orbits; (2) orbital abscess; (3) necrosis of the frontal bone; (4) necrosis of the superior maxilla; (5) fracture, puncture, and laceration of the cribriform plate, suppurative meningitis; (6) suppurative meningitis apart from injury; (7) severe hæmorrhage; and (8) optic neuritis and blindness.

The first of these, effusion into the eyelids and orbit, is very common and of no moment. Orbital abscess, very rare, requires external incision, as do necrosis of the frontal bone and superior maxilla, but such unfortunate occurrences should not deter one from thoroughly clearing out the disease. To be timid with ethmoidal curetting will certainly deprive the operation of much of its success.

I had the good fortune to see a case which well illustrates all the complications I have discussed and a few more. Double ethmoidal curetting was performed on a woman rather over 30 years of age, who was the subject of old-standing nasal polypi and ethmoidal suppuration. A few hours later both eyes were closed with hæmorrhagic effusion, and, as is usually the case, she had severe frontal headache. At night the temperature was 101° F., being 99·5° in the morning. This febrile condition persisted, although at the end of the first week the effusion had left the eyelids, and the headache was merely a dull aching heaviness. Four days later puffiness appeared over the right nasal bone and the nasal process of the superior maxilla, and in a few days fluctuation was made out. The abscess was freely incised; a little thin pus escaped, and some necrosed bone was scraped away; it was drained. A week after, during which time the temperature had varied from 99° to 102°, a similar but larger swelling appeared along the lower orbital margin and was similarly treated. A week later just the same happened in the right frontal sinus region and subsequently on other parts of the skull. By this time the headache had become intense, optic neuritis was diagnosed, the eyelids were oedematous, and drowsiness had developed. At night she was delirious, and occasionally in

¹ Founded on an address delivered before the Nottingham Medico-Chirurgical Society.