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SOME MEDICAL ASPECTS OF TOBACCO-SMOKING*

BY

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Of all the imports for which the Old World is indebted to the New, none equals in medical interest two which anticipated the Lease-Lend Act by nearly 450 years—syphilis and tobacco. It is of the second, the only drug to which addiction is universally considered respectable, that this paper treats.

Historical

So far as Western civilization is concerned, the history of tobacco begins on October 13, 1492, when Christopher Columbus landed on the island he named San Salvador. The natives sought to propitiate their visitors with rare gifts, including among them some dried leaves, which the Spaniards later threw away with smiles of condescension at the artless generosity of the savages. Nevertheless, within fifty years these leaves were eagerly sought in Europe, and were recommended for their medicinal properties by the French Ambassador at Lisbon, Jean Nicot, who later gave his name to nicotine. A century later the habit of pipe-smoking had firmly established itself in England. It survived the fulminations of James I, who published his *Counterblaste to Tobacco* within a year of coming to the throne, stigmatizing smoking as a "custome loathsome to the eye, hatefull to the nose, harmfull to the braine, dangerous to the lungs, and, in the black stinking fume thereof, nearest resembling the horrible Stygian smoke of the pit that is bottomlesse." The milder strictures of Charles II, who forbade Cambridge men to "wear periwigs, smoke tobacco or read their sermons," were equally ineffective. In Continental countries, where deterrents were more vigorous, the habit spread less rapidly: in Russia, smokers were discouraged by amputation of the nose, and in the Swiss Canton of Berne the offence was ranked as only one degree less odious than adultery. A prohibition against smoking in the streets was rigidly enforced by the police in Berlin up to 1848.

The habit has now become so universal that the occasional non-smoking compartment in railway carriages, which has long since replaced that formerly labelled "smoker," seldom contains more than one old lady. The increase has been due to the cigarette, a South American invention of the 1750's, which reached Europe through the Peninsula and was made fashionable by Louis Napoleon after the Crimean War. So vast has the consumption of tobacco become that the duty paid on it affords the Chancellor of the Exchequer one of his main sources of revenue, providing him in 1950 with £601,651,432. The moralist will find matter for reflection in the thought that over one-quarter of the country's income is now derived from the addiction of its inhabitants to tobacco and alcohol.

Much ingenuity has been expended in efforts to explain the attraction of tobacco-smoking. "I cannot imagine what pleasure they derive from this practice," wrote Oviedo in 1526, "unless it be the drinking which invariably precedes the smoking." He continues: "I am aware that some Christians have already adopted the habit, especially those who have contracted syphilis, for they say that in the state of ecstasy caused by the smoke they can no longer feel their pain." Of recent years less naive reasons have been postulated: the atavistic lure of fire worship, a pleasurable stimulation of the vagal nerve endings, and a rise in the blood-sugar level have all had their champions (Finnegan, Larsen, and Haag, 1945). The psychiatrists have made their characteristic contribution to the problem. "Getting something orally," one asserts (Bergler, 1946), "is the first great libidinous experience in life"; first the breast, then the bottle, then the comforter, then food, and finally the cigarette. More mundane, but perhaps better founded, is the suggestion that a true addiction to nicotine is at least part of the explanation (Finnegan, Larsen, and Haag, 1945; Johnston, 1942).

The Pharmacology of Smoking

The pharmacology of tobacco-smoking is more complex than at first appears; nicotine is the only alkaloid of importance in the leaf, but at least eleven others are recognized, although their biological actions are uncertain. Estimates of the quantity of nicotine entering the mouth during smoking vary: earlier reports claimed amounts as great as 3.6 mg. per cigarette, of which 90% was said to be absorbed (Pierce, 1941). More dependable assays are in the region of 1 mg. per cigarette weighing 1 g., 2.69 mg. per gramme of pipe tobacco, and 0.7–1.6 mg. per gramme of cigar (Ling and Wynn Parry, 1949). The proportion absorbed varies directly with the "wetness" of the smoker and inversely with the length of the cigarette-holder or pipe-stem. In the case of a cigarette smoked without a holder, it is estimated at about 0.5 mg., and this is borne out by comparing the antidiuretic effect of one cigarette with that of 0.5 mg. of nicotine given by injection (Burn, Truelove, and Burn, 1945). After smoking 20 cigarettes in seven hours the quantity of nicotine in the blood reaches an average of 0.14 mg. per litre; lower levels result from pipe or cigar

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smoking. It is remarkable that traces of nicotine can still be found in the blood ten hours after the last cigarette has been smoked (Wolff, Hawkins, and Giles, 1949).

Doses of 1–6 mg. of nicotine, by subcutaneous injection, are enough to produce such symptoms as sweating, faintness, tachycardia, nausea, and vomiting in non-smokers; much larger doses are tolerated by the habitué (Johnston, 1942). Nicotine's main effect is on the sympathetic nerve endings, first stimulating and later paralysing them. Cigarette smoke, however, contains a large number of other products, such as hydrocyanic acid, ammonia, carbon monoxide, pyridines, aldehydes, and tars. It is possible that the nausea and vomiting which occasionally assail the neophyte may be due to some of these substances. A man who habitually smokes 20 cigarettes a day absorbs enough carbon monoxide to maintain 5% of his haemoglobin in the carboxy form (Dixon, 1921).

Some observations on the mechanics of smoking are of interest. The average smoker consumes one cigarette in 17 puffs, with each of which he draws into his mouth 33 ml. of air; every 66 seconds he inhales the smoke, but by the time it has reached his lungs it has been diluted fifteenfold by the air in his respiratory passages (Fabricant, 1946).

The Physical Effects of Smoking

It is clear that the uses of tobacco and the effects of smoking upon the healthy and upon the diseased body must be a matter of close concern to our profession. The herb has, in fact, aroused medical interest ever since its introduction to Europe. It was for its medicinal virtues that it was cultivated in the sixteenth century, when, for a time, it enjoyed the reputation of a panacea. Application of tobacco leaves would heal a cancerous ulcer, it was claimed, and the apparently drowned were rapidly revived by insufflation of tobacco smoke into the rectum when they were suspended by the heels. It was widely used as a prophylactic against infection, and in 1665 the boys at Eton were given instruction in smoking, that they might ward off the plague; one pupil has recorded that he was never flogged so severely as when he refused his pipe.

Gradually attention shifted from the beneficent to the malignant effects of tobacco. The Victorian attitude accorded well with the view that any custom so enjoyable as smoking must of necessity be harmful; and in 1856 Mr. Samuel Solly was thundering at the students of St. Thomas's Hospital: "Now don't be frightened, my young friends, I am not going to give you a sermon against smoking, that is not my business; but it is my business to point out to you all the various and insidious causes of general paralysis, and smoking is one of them. . . . I know of no single vice which does so much harm as smoking."

Much of the writing on the medical aspects of tobacco-smoking has come from the pens of non-smokers or of those who have renounced the habit and are basking in the sunshine of their own righteousness. For these reasons the appeal is often to the emotions rather than to the intellect. As recently as 1937, an English physician (J. D. Rolleston, 1937) wrote: "The three greatest statesmen of our time, Mussolini, Hitler, and Mr. Gladstone, did not smoke"; his paper closed with a plea to join the National Society of Non-Smokers and to subscribe to its journal, *Clean Air*.

This approach to the problem has made it difficult for us to offer our patients rational advice on the question, and I turn now to the consideration of some of the established facts regarding the effects of this habit. It has been proved that non-smokers live longer than smokers (Pearl, 1938), and that the decrease in survival is greater for heavy than for moderate smokers. Once the age of 70 years has been passed the harmful effects are no longer apparent. In another series (Short, Johnson, and Ley, 1938–9) the effect of smoking was investigated in 2,031 persons proposing for life assurance; 63.7% of these were habitual smokers and 24.4% had never smoked; the two groups were homogeneous in respect of age and sex. No differences in weight, blood pressure, or pulse frequency existed between them, but the smokers were more prone to colds in the head and complained more frequently of cough, palpitation, dyspnoea, and dyspepsia.

Its Effects upon the Cardiovascular System

It will be more profitable, however, for our present purpose to consider the various systems of the body and the effects tobacco is said to have on them. I begin with the cardiovascular system. Tobacco has a well-defined pharmacological action on the heart and blood vessels; the blood pressure shows a transient rise, averaging 15 mm. for the systolic and 10 mm. for the diastolic pressures; the pulse frequency increases by an average of 8 beats a minute; changes in the electrocardiogram, consisting of lowering, or even inversion, of the T waves, are frequent (Graybiel, Starr, and White, 1938; Stewart, Haskell, and Brown, 1945; Levy, Mathers, Mueller, and Nickerson, 1947). These disturbances are ephemeral and disappear when the cigarette is finished. Significant alterations occur also in the peripheral circulation: the skin temperature falls and the volume of the hand, as measured by the plethysmograph, diminishes (Lampson, 1935). These changes are undoubtedly the result of arterial narrowing, but it has been pointed out that a reflex peripheral vasoconstriction takes place whenever a deep breath is drawn and that inhalation alone might be responsible for the decrease in limb volume (Mulinos and Shulman, 1940). However, it has now been established that a progressive reduction in the volume of the limb occurs while cigarettes are being smoked, as well as the transient decrease which accompanies each inhalation (Shepherd, 1951). It must therefore be accepted that cigarette-smoking does lead to constriction of peripheral vessels, although it is possible that these effects are brought about by nicotine stimulating the release of adrenaline from the suprarenal glands (Short and Johnson, 1938–9).

These phenomena are, as I have stressed, manifestations of the pharmacological action of tobacco; it will be obvious that symptoms due to pre-existing cardiovascular disease may be aggravated by them, but there is no proof that tobacco initiates such disease. Nevertheless this contention is often made, and one or two specific instances must be considered. "Smoker's heart," an expression more familiar to our fathers than to us, was applied to a state in which premature contractions occurred in heavy smokers; it seems possible that this causal sequence is to be observed in some patients, but it is decidedly rare. It was regarded more seriously 45 years ago: tobacco might, it was said, "increase vascular tension and lead to tumultuous and forcible cardiac action"; persistence in the habit after these warnings might cause dilatation of the heart with very much more serious symptoms, which might even be fatal (Essex Wynter, 1907).

Attempts have been made to incriminate smoking as a cause of coronary artery disease, but in one series of 750 patients with angina the percentage of smokers was considerably lower than the percentage of non-smokers (White and Sharber, 1934). In another group of 1,000 men above the age of 40 years with evidence of coronary artery disease, 69.8% were smokers, while the figure for a control group without heart disease was 66.3%. Nevertheless, between the ages of 40 and 49 years 1% of non-smokers were found to have evidence of coronary artery disease, while in mild to moderate smokers the incidence was 4.6%, and in heavy smokers 5.9% (English, Willius, and Berkson, 1940). It is hardly necessary to point out that these observations do not imply a causal relationship: everyday experience suggests that the kind of man who has a coronary thrombosis before he is 50 is the kind of man one expects to smoke 25 cigarettes a day.

In some patients tobacco undoubtedly provokes anginal pain. In the majority there are convincing signs of disease of the coronary arteries, and smoking produces its effects by its action in raising the blood pressure and increasing the heart rate (Pickering and Sanderson, 1944–5). Very

occasional instances are recorded of what may with accuracy be called "tobacco angina": in one of these pain was provoked by smoking but not by exertion, there was no rise in blood pressure or heart rate, but transient changes in the ST segments of the electrocardiogram were noted. It was suggested that spasm of the coronary arteries induced by tobacco was responsible (Bryant and Wood, 1947).

The therapeutic deduction seems to be that patients in whom anginal pain follows smoking should be advised to abstain. There is not sufficient reason for forbidding all patients with angina to smoke, although a period of abstinence as a therapeutic trial is justifiable.

In the genesis of peripheral vascular disease tobacco has long been regarded as important. Every medical student reads in his textbooks that thrombo-angiitis obliterans occurs predominantly in chain-smoking Russian Jews. There is now dispute over the very existence of this disease; it is suggested that the name covers a multitude of pathological processes and that it is not to be distinguished from the senile variety of obliterative arterial disease (Boyd, Ratcliffe, Jepson, and James, 1949). It is still, however, the general belief that thrombo-angiitis obliterans is a specific morbid entity and that smoking is more dangerous in it than in senile obliterative arteritis. It has been claimed that occlusive vascular disease is more common in diabetics who smoke than in those who do not; in one series it was noted in 58% of smokers and in only 37% of non-smokers (Weinroth and Herzstein, 1946).

Although skin-sensitivity tests with extracts of cigarette smoke were reported as positive in 83% of patients with thrombo-angiitis obliterans and in only 10% of normals (Harkavy, Hebald, and Silbert, 1932–3), and although allergy to tobacco has been postulated as the basis of this complaint (Sulzberger, 1934), no evidence exists which convincingly incriminates smoking as a cause of this or any other peripheral vascular disease. Injections of nicotine into growing rats do not increase the incidence of arterial change (Thienes and Butt, 1938). The danger is due to the vasoconstrictor effects of tobacco, and there is unanimous agreement that sufferers from peripheral vascular disease should not smoke. It is not clear how much difference this interdiction makes to the elderly man with intermittent claudication; but when there is gangrene or the vitality of the skin is in doubt the ban should be absolute. The additional vasoconstriction may be enough to prevent healing or to precipitate death of tissue. One observer followed up 100 patients with thrombo-angiitis obliterans, who had ceased to smoke, over a period of ten years; in every case the disease was arrested (Silbert, 1945).

Its Effects upon the Respiratory System

In the respiratory system the irritant action of tobacco smoke might reasonably be expected to overshadow any systemic effects. We are all familiar with the patient who replies to our query with, "Just a smoker's cough, doctor," and, although he may have bronchiectasis, carcinoma of the lung, or pulmonary tuberculosis, a "smoker's cough" must be admitted. Tobacco smoke has a considerable local irritant action; a method of measuring this by the effect of six "standard puffs" of cigarette smoke in producing oedema of the rabbit's conjunctiva has been devised (Finnegan, Fordham, Larsen, and Haag, 1947). Researches show that different brands vary greatly in their irritant action, probably owing to substances added in the manufacture. Persistent heavy cigarette-smoking will certainly lead to a chronic pharyngitis and will keep alight chronic bronchitis in those predisposed. Apart from these obvious irritant effects, recent observations, showing that it reduces vital capacity and chest expansion, provide scientific justification for the belief that it is "bad for the wind" (Whitfield, Arnott, and Waterhouse, 1951).

Asthma due to tobacco must be very rare, although the case is recorded of a Turkish lady who was sensitive to cigars and was afflicted by asthma when she walked in the grounds of her estate, which adjoined a tobacco plantation (Urbach and Gottlieb, 1946).

In the past few years interest has been focused on the importance of smoking as a cause of carcinoma of the bronchus. The recorded mortality from this tumour in England and Wales increased fifteenfold between 1922 and 1947; it is now probably the commonest form of malignant disease met by the general physician. This increase has been noted in all countries of the Western World, with the exception of Iceland (Dungal, 1950); records show that bronchial carcinoma provides 27% of all malignant tumours in the post-mortem rooms of London (Bryson and Spencer, 1951) but only 2.9% in those of Reykjavik (Dungal, 1950). Cigarette-smoking has long been suspected as a cause, and some recent statistical investigations have proved this suspicion true. It is of interest, moreover, that the cigarette consumption in Iceland has been negligible until the last few years. In a series of 684 patients with bronchial carcinoma in the United States, only 1.3% were non-smokers and 51.2% had smoked more than 20 cigarettes a day for 20 years; the figures for these classes in the general hospital population without cancer were 14.6% and 19.1% (Wynder and Graham, 1950). Independent observations made in this country have led to the conclusion that after the age of 45 years those who smoke 25 or more cigarettes a day are fifty times more likely to develop carcinoma of the bronchus than non-smokers of the same age. No such correlation with pipe-smoking could be found (Doll and Hill, 1950).

The only known carcinogen in cigarette smoke is arsenic, but there is not enough evidence to inculpate it. It seems clear that some cause other than, or additional to, the increase in cigarette consumption must be sought to explain the increasing frequency of bronchial carcinoma, because the second has risen more rapidly than the first. It is difficult, moreover, to understand why there has been no parallel rise in the incidence of cancer of the upper respiratory tract, although carcinoma of the larynx and pharynx is significantly more frequent in smokers than in non-smokers (Schrek, Baker, Ballard, and Dolgoff, 1950).

The moral we should draw is obscure: perhaps we should caution all young men and women not to smoke more than 20 cigarettes a day. The popular reaction is illustrated by the subscriber to the *Readers' Digest* who was so upset by an article on smoking and cancer that he decided to give up reading magazines.

Its Effect upon the Alimentary Tract

To turn now to the alimentary tract: there is good reason for thinking that cancer of the lip is commoner in pipe and cigar smokers than in the general population, but this predisposition does not extend to cigarette smokers (Levin, Goldstein, and Gerhardt, 1950). Presumably local irritation must be held responsible.

The effect of smoking upon the stomach is of importance, because it has long been traditional to urge the patient with peptic ulcer to abstain. Smoking one cigarette has been shown to diminish hunger contractions and gastric motility as well as to decrease the volume and acidity of gastric secretion; in only one of twenty patients was there an increase in acidity. These effects are probably reflex, because they do not occur after injection of nicotine in dogs (Schnedorf and Ivy, 1939; Ivy, Grossman, and Bachrach, 1950). Wolf and Wolff (1943) were able to watch the behaviour of the stomach in their patient Tom, who had had a large gastric fistula for over forty years. When smoking was pleasurable no change took place in the gastric contractions, vascularity, or acid secretion; when he had no taste for it a cigarette induced slight nausea, contractions ceased, the mucosa became pale, and acid secretion failed; these changes were common to the sensation of nausea however evoked. The increase in appetite, which many who renounce smoking notice, may be due to the removal of the inhibitory influence of tobacco on gastric motility.

These physiological observations provide no theoretical justification for advising the patient with peptic ulcer to stop smoking, yet many physicians are convinced that tobacco has a deleterious effect on this disease. It is always said that the patient with peptic ulcer is a heavy smoker (Hurst and Stewart, 1929; Bockus, 1944), but in a careful survey it was found that men with chronic duodenal ulcer do not smoke, on an average, more than healthy men of the same age, although twice as many of them inhale (Trowell, 1934). Many experienced clinicians have noted dyspepsia, resembling that of ulcer, to disappear on abstinence from tobacco (Wagner, 1924; Bockus, 1944; Schindler, 1947). On the other hand, a careful follow-up of a group of patients with peptic ulcer (Jamieson, Illingworth, and Scott, 1946) revealed no correlation between alterations in tobacco consumption and variations in the severity of symptoms. Some figures suggest that the response to treatment with antacids is better if smoking is discontinued (Batterman and Ehrenfeld, 1949).

It seems fair to conclude that smoking plays no part in the genesis of peptic ulcer. That notoriously dangerous guide, "clinical impression," has led many to believe that it may aggravate symptoms. The sensible advice is to recommend patients to try a period of abstinence and decide for themselves whether they are better without their cigarettes.

There is some gastroscopic evidence that smoking may lead to changes in the gastric mucosa. In one series the appearances were normal in only 8% of heavy smokers, there was hypotrophic gastritis in 44%, and atrophic gastritis in a like proportion (Annis, 1944).

Cigarette-smoking has been observed to increase the motility of the large bowel in normal subjects (Schnedorf and Ivy, 1939), and this finding provides a physiological justification for Ryle's view (1928) that it is of importance in the causation of spastic colon. A period of abstinence is worth a trial in this disorder.

Its Effect upon the Nervous System

Many curious nervous disorders have been attributed to the use of tobacco. The French journals, in particular, contain numerous case reports: an officer's wife, afflicted with vertigo and signs of pyramidal tract disease, who recovered in two weeks after renouncing the 25 cigarettes she had smoked daily for fifteen years (Barré and Verdier, 1949); a myasthenic and polyneuritic syndrome in chewers of tobacco (Coulonjou, Prévot, Salaun, and Nicolet, 1946); a boy of 13 years who fell victim to the manic-depressive psychosis after smoking 20 cigars a day (Pel, 1911). These instances could be multiplied indefinitely; there are records of fleeting cerebral attacks, of neuralgic pains, of headaches, of fits, all lending support to Calverley's contention of

> How they who use fusees
> All grow by slow degrees,
> Brainless as chimpanzees.
> Meagre as lizards;
> Go mad, and beat their wives;
> Plunge (after shocking lives)
> Razors and carving knives
> Into their gizzards.

There was, however, one condition in which the role of tobacco seemed to be authentic. This was tobacco amblyopia, a disturbance of vision occurring chiefly in men between the ages of 35 and 55 years, starting as a paracentral scotoma for colours at the blind spot and gradually spreading to the point of central vision (Wilson, 1940). It was said to afflict particularly those who smoked strong shag (Moore, 1925). It was more common in the United Kingdom than in France or the United States, where alcohol had long been regarded at least as important as tobacco in its cause (Walsh, 1947). In one American series of 1,100 patients over the age of 50 years with this form of amblyopia, the average consumption of tobacco was less than in 500 healthy persons of the same age (Usher, 1927).

A correlation between malnutrition and the incidence of tobacco amblyopia has long been noted; de Wecker (Schepens, 1946) commented on its frequency during the siege of Paris in 1870, and a tenfold increase was observed under the German occupation of Belgium between 1940 and 1945. Carroll (1944) has reported complete or partial recovery in 25 patients with what he terms "tobacco–alcohol amblyopia" when their diets were supplemented with the vitamin-B complex or vitamin B_1 itself, although they continued to smoke and drink.

In this country alcohol lacks the importance accorded to it elsewhere (Evans, 1939), and tobacco is generally believed to be the essential cause, although malnutrition is allowed a predisposing role. The suggestion has been made that some unknown toxic substance is formed by fermentation in the heavier and darker tobaccos; this substance is rendered harmless by the healthy liver, but, when malnutrition impairs hepatic function, detoxication fails and the retina suffers (Evans, 1939; Schepens, 1946).

The similarity between amblyopia attributed to tobacco and that noted in malnourished prisoners of war (Denny-Brown, 1947) is obvious, but the resemblance is not exact. Proof that "tobacco" amblyopia is purely of nutritional origin is still lacking, and it remains wise to recommend patients with the complaint to abstain from smoking.

Its Effects upon the Genito-urinary System

The effects of tobacco on the genito-urinary system are not of great moment. In the normal man it has an antidiuretic action (Burn, Truelove, and Burn, 1945), due to nicotine provoking liberation of the antidiuretic hormone (Cates and Garrod, 1951). It was at one time believed to decrease libido and a Franciscan monk, Fra Giuseppe da Convertino, recommended it from personal experience as a safeguard for chastity. In more recent years it has been said to lead to abortion and infertility (Mgalobeli, 1931), although another authority asserts that he had found a group of pipe-smoking Frenchwomen, whose habits he had studied, to be of exceptional fertility (Chiasson, 1929).

It has been proved that nicotine is secreted in the milk in proportion to the number of cigarettes smoked; in heavy smokers the quantity may rise to 0.5 mg. per litre. Infants fed on this milk thrived normally, although they must have received 0.1–0.25 mg. of nicotine a day (Perlman and Dannenberg, 1942).

Conclusion

The public library in New York is said to contain more than 4,000 books on tobacco in more than 20 languages (Bishop, 1949). It will be appreciated, therefore, that a short paper can only touch the fringe of the subject. It is, however, a matter which closely concerns us as doctors, for patients are constantly asking our advice about smoking. Most of us are prepared to give it without deep reflection, for the view the doctor takes is dictated rather by the number of cigarettes he smokes himself than by a profound knowledge of the pharmacology of tobacco. It is, however, well to remember that some facts have now been established, and it should no longer be said that those of us who are heavy smokers impose no restrictions, while the non-smokers

> Compound for sins they are inclined to
> By damning those they have no mind to.

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During recent years industry has paid increasing attention to colour coding of danger points in factories to indicate high voltage lines, toxic gases, and obstructions such as low doorways and steps; the British Standards Institution considered the possibility of preparing a uniform "safety" colour code. However, following an inquiry by the Royal Society for the Prevention of Accidents it has now been decided to abandon the idea. Examination showed that a distinction must be made between a *safety* colour code and an *identification* code—the one being broadly to classify and give warning of types of hazard by colour and the other primarily to identify the contents of cylinders and so on. It was found that many colours had traditional meanings which were not reconcilable with their identification value—for instance, green CO_2 containers are not consistent with the concept of red for danger. Also, since anything up to 8% of the population is thought to be to some degree colour-blind, the application of a colour system can in no way be universally effective.

RETROLENTAL FIBROPLASIA

A PROBLEM OF PREMATURITY

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Retrolental fibroplasia may lead to blindness in infancy, and it is the gravity of this possible outcome that makes its study so urgent a problem. The disease has been the subject of a large number of papers in the American literature since Terry's first report (1942), in which he recognized it as a condition occurring in premature babies, leading to the formation of an opaque vascularized membrane behind the lens of both eyes, usually with gross visual defect and searching nystagmus. The subject has as yet received little attention in the medical press of this country, but there is reason to believe that the disease is making its appearance here in the same curiously uneven and unpredictable manner as in the United States and, more recently, in other countries.

A team drawn from the Oxford Eye Hospital, the paediatric department of the United Oxford Hospitals, and the Nuffield Laboratory of Ophthalmology has been concerned in a joint investigation since June, 1950.

Diagnosis of Cases

Early in 1950 we started routine ophthalmic examination of all premature babies of low birth weight born in Oxford, in the hope that some clue to the nature of the disease might be gained from observation of the condition as it developed, and later because of the possibility of treatment.

It is unlikely that retrolental fibroplasia occurs in infants weighing over 5 lb. (2.3 kg.) at birth, so this was our dividing line. All infants weighing 5 lb. (2.3 kg.) and under at birth are examined at the discretion of the paediatricians, larger and healthier children within a few days of birth, and small weakly babies, unable at first to tolerate the handling involved in an ophthalmic examination, after several weeks. After the first examination infants are seen every week while in hospital. They are usually discharged on reaching a weight of 5 lb. (2.3 kg.) and are then followed up at special clinics at the Eye Hospital. Generally a baby will be seen fortnightly until it is between 3 and 4 months old, and then monthly until 6 months of age, when it is discharged from supervision if no signs of the disease have appeared. If any suspicious feature is seen in the eyes, particularly retinal vascular dilatation of marked degree, the infant may be examined at shorter intervals.

The examinations are all made by an ophthalmologist, and the infant is held by a nurse experienced in this work. General anaesthesia is unnecessary, though a comforter is invaluable. The pupils are dilated with