genetic psycho-somatic theory was attributed to him and pooh-poohed. Wynder described his investigations with Seventh Day Adventists in Los Angeles area where there is a high smog density. Lung cancer was found in only 2 Adventists, both of whom were smokers before joining the sect and becoming abstainers.

Wynder then described the "last hope" of some sections of the Tobacco Industry, i.e. 95% of the population immune to lung cancer. Therefore weed out the 5% susceptibles and prevent them smoking.

3. Pathological - Auerbach et al and "carcinoma in situ". Wynder did not elaborate this - perhaps because the evidence has been queried by a number of pathologists as unsound.

4. Biological - Wynder described his painting experiments, which have now yielded cancers with 3 species - several strains of mice, rabbits (ear painting - thoracic metastases) and rats - Blacklock. Previous British failures, e.g. Passey, to reproduce Wynder were owing to not using high enough dosage. Wynder paints at rate of 10g/year - 360g/year for smokers, i.e. 1 pack a day. Wynder stated that Day had told him he confirmed Wynder.

5. Chemical - Besides the carcinogens already isolated, Wynder and collaborater (Hofmann) had isolated 2 others e.g. 3:4-benzfluoranthene and 10:11-benzfluoranthene. These are quite potent - approximately equal to 1:2:5:6-dibenzanthracene, when tested at 0.5% (100% cancers in 8 months, CAF_1 mice - none in 4 months). Nevertheless, Wynder agreed that the summation of all the activities found individually did not come near that required of whole smoke.

His conclusion: Tobacco smoke is a very weak carcinogen - on the

limits of detection, hence the high doses employed.

After Wynders, his collaborator Hofmann described the fractionation of smoke - following Wright, they find nearly all activity concentrated in $C.Cl_4$ fraction - 1.5% total weight of smoke condensate. An incidental point was that they prefer chromatography on SiO_2-gel rather than Al_2O_3. The fractionation by column and paper chromatography and identification by UV spectra was pretty conventional; some excellent UV traces - if genuine - which indicated strongly the correctness of the structural diagnosis. Also showed a fluorescent photograph of 1mm. long crystal of benzpyrene isolated from smoke - for what that's worth. It was rather a showman's piece.

By radioisotope dilution method, the amount of benzpyrene was calculated to be 1.2 ± 0.1 ppm of smoke condensate. (Assuming 1 cigarette gives 40 mg. condensate, then 500 cigarettes give 20g. and the amount of benzpyrene is then $24 \pm 2 \mu g$/500 cigarettes - rather higher than we find. Hofmann also mentioned that all smoking machines gave benzpyrene <u>except</u> Cigarette Components Ethel Machine - attributed to the high voltage electrostatic precipitator discharge destroying benzpyrene by oxidation. (This needs investigation).

Wynder then summarised remedial measures :-

1. Stop smoking
2. Reduce smoking habits
3. Don't smoke past half way because of repyrolysis. Lindsey's paper cited as evidence of the rapid rise of benzpyrene in smoke with shorter stub lengths. Surveys of stub lengths in U.S. (33 mm.), Canada (29 mm.) and U.K. (19 mm.) cited as evidence why Britain has the highest

incidence despite a greater amount of tobacco per capita being consumed in the U.S.A.

4. Do not inhale deeply. Japanese only mouth-inhale - low incidence of lung cancer in Japan.

5. Choose a brand with low tar and nicotine. In the United States, brands have cut their tar and nicotine output over the last two years by up to 40% "Alone I did it" (E. Wynder). Here Wynder referred to the paper in B.M.J. by Smyth - puncturing the tip of cigarettes. He went on to refer to a "menthelated brand in the U.S." with a slit in the paper (SPUD) - consumers disliked it because of too easy a draw, not enough smoke. He also mentioned three firms in Canada - embossed paper, perforated paper and high porosity paper with rapid burn (Rothman, ? , I.T. Co. (Canada)) and predicted all companies in the United States would follow with paper of greatly increased porosity.

Development of filter tipped cigarettes touched on. Consumer coming to enjoy low tar cigarette with no taste, no kink, no cough !!

6. Reduce carcinogens. Wynder has collaborated with Touey and Mushpower (Tennessee Eastman) on temperature measurement. Two factors probably operative - temperature maximum and time it is held. Although cigars and pipes give lower temperature maximum, this is a plateau rather than a sharp peak as with cigarettes. Hence benzpyrene formed. Much work with Al_2O_3 and Al foil. No effect on temperature, and therefore Wynder has turned to catalysis, e.g. $Cu(NO_3)_2$ which reduces amounts of polycyclics but makes cigarette unsmokeable. (Bentley will be interested to know Wynder has tried this). Twenty catalysts tested chemically and twelve evaluated biologically using samples of 50,000 cigarettes/test (thanks to Lorillard).

Papers opened for discussion

LINDSEY - 2 points

(i) Diffusion flames. Normal and reversed diffusion flames compared in order to study mode of formation of polycyclics. Methane is the precurser of the largest amounts of condensate and of 3:4-benzpyrene within this. Five times greater than any other precurser. Simple paraffins give more than do aromatics, e.g. o-xylene, p-xylene, toluene, etc. The route seems to be via the radical $^{\bullet}CH$. This idea misfired a bit and the route cannot yet be traced in the way hoped for.

(ii) Repyrolysis. A rehash of his published letter - but a curve shown with many more points. Benzpyrene in smoke expressed in "arbitrary units".

Butt length mm.	40	35	30	25	20	15	10	5
Benzpyrene units	0.4	0.5	0.6	0.7	?	1.0	1.4	2.3

Checked at 35 and 15 mm. by quantitative determination - results as given in letter.

[DGF asked Lindsey during tea break for smoking conditions. He uses a constant pressure machine - with a suction of approximately 25 cm.W.G. "2 or 3 puffs perminute" - 2 seconds duration. Yes, he had checked the puff volume (but he wouldn't say what it was !). DGF tried to find out more by discussing variability of valve timing altering puff size etc., but Lindsey wouldn't be drawn.]

LYON (Glasgow)

A very bad contribution, largely to jump on the bandwagon. He divided a cigarette into quarters and measured the contributions each quarter made to a number of estimations and confirms the repyrolysis theory. Measurements were:- Caffeine Number (??)/mg. tar. [Caffeine No. - used

by oil chemists. Hydrocarbons extracted with caffeine - caffeine number - ratio of 340/460 μ 727, moisture (Karl Fischer), acidity and reducing power (Intermittent anoxia of tissues - classic paper Goldblatt and Cameron 1952).

CARRUTHERS

He took Wynder severely to task for neglecting effect of air pollution. Wynder is now working on this aspect too. Carruthers also was curious to know why the 1.3% of smoke in the CCl_4 fraction which contains all the activity is not 50-60 times as active as whole smoke, since it is concentrated. Wynder digressed into promoters of unspecified nature - but probably residing in nicotine free basic fraction - active depilatory and hyperplastic activity - but non carcinogenic. C.f. croton oil.

ROE (London Hospital)

Recited his studies with phenol fraction of smoke as co-carcinogen for D.B.A. - already reported to TMSC via Bentley.

PEACOCK.

He digressed amusingly onto how he teaches animals to smoke and how some develop a liking for it. Curiously enough - no bronchitic factor - only one pigeon that has a smoker's cough - no ill effects otherwise.

A break for tea occurred, when rather desultory discussions took place. Opportunity seized by H.D.A., L.C.L. and D.G.F. to leave. On explaining reason to Haddow, he exclaimed "What a pity ! I was just going to call on you !" Wynder also seized opportunity to buttonhole H.D.A. and D.G.F. and said he hoped to see Sir Charles Ellis and perhaps H.D.A./ D.G.F. when he returned to England sometime in August.

DGF/JW/46D